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Journal of Early Intervention 2001; 24; 207

DOI: 10.1177/10538151010240030601

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Development and Behavior of Male Toddlers With Fragile X Syndrome

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This report presents findings from an ongoing longitudinal study of the developmental and behavioral characteristics of 26 boys with fragile X syndrome between the ages of 12 and 36 months. Multiple measures and analyses were used to describe the characteristics of these boys. Results indicated that there is an increase in the developmental skills of male toddlers with fragile X syndrome over time, although there is a great deal of variability within the sample. Global developmental delays might be evident by 12 months of age in some children, but other children might not display delays until later ages. In general, motor skills appear least delayed, whereas communication skills appear most delayed. Standardized in-depth assessments might be more efficient at detecting delays than ratings of clinical impressions, and professionals might be more sensitive to detecting delays at earlier ages than parents.

Fragile X syndrome (FXS) is the most common inherited cause of mental retardation known and is responsible for about 30% of X-linked retardation (Hagerman, 1997), with an incidence between 1:2,500 and 1:4,000 (Sherman, 1995). FXS results from an expansion of a trinucleotide DNA sequence (CGG) on the long arm of the X chromosome and is diagnosed through DNA analysis. Individuals considered negative for FXS have approximately 6-52 CGG repeats. Premutation carriers have 53-200 repeats and typically appear to be unaffected. Individuals with the full mutation have greater than 200 repeats, typically resulting in a reduction of FMRP, a protein necessary for normal brain function (Small & Warren, 1995; Weiler et al., 1997).

Because FXS is carried on the X chromosome, both males and females can have the premutation or full mutation. Males are usually more affected than females, however, because they have only one X chromosome. The syndrome expands from carrier to full mutation status when transmitted by a female, and the chances of expansion increase with successive generations. Thus, the gene could be

passed down in the premutation phase for several generations without anyone suspecting that the family has an inherited genetic disorder.

Most research describing the development and behavior of males with FXS has been conducted with older children and adults. This research clearly shows that there is a spectrum of involvement in children affected by FXS. Most males with the full mutation have moderate to severe mental retardation, and many display characteristic behavioral problems, such as hand flapping, hand biting, and gaze aversion (Bailey, Mesibov, et al., 1998; Hagerman et al., 1986; Merenstein et al., 1996). In addition, anxiety, social avoidance, sensory processing problems, (Bregmen, Leckman, & Ort, 1988; Einfeld & Hall, 1994) hyperactivity, aggression, challenging temperament traits, attention deficits (Baumgardner, Reiss, Freund, & Abrams, 1995; Boccia & Roberts, 2000; Hatton, Bailey, Hargett-Beck, Skinner, & Clark, 1999; Turk, 1992), and hyperarousal (Boccia & Roberts, 2000; Miller et al., 1999; Roberts, Boccia, Bailey, Hatton, & Skinner, 2001) have been documented.

In recent years, research efforts have expanded to include the early development of males with FXS, with a focus on development after 36 months of age. The majority of these studies indicate that preschool males with FXS are on average moderately delayed (Bailey, Hatton, & Skinner, 1998; Borghgraef, Fryns, Dielkens, Pyck, & Van Den Bergh, 1987; Lachiewicz, Gullian, Spiridigliozzi, & Aylsworth, 1987; Prouty et al., 1988; Simko, Hornstein, Soukup, & Bagamery, 1989), with a rate of learning approximately half that expected for typically developing children (Bailey, Hatton, et al., 1998; Prouty et al., 1988). In contrast, some studies have indicated that cognitive development during the preschool years might be average or borderline (Freund, Peebles, Aylward, & Reiss, 1995; Hagerman et al., 1994). There is general consensus, however, that the severity of delay increases over time (Bailey, Hatton, et al., 1998; Borghgraef et al., 1987; Lachiewicz et al., 1987; Simko et al., 1989).

Within the broad arena of preschool development, several studies have indicated that there are strengths and weaknesses across specific domains. Similar to school-age cohorts, preschool boys with FXS display relative strengths in motor and adaptive behavior skills, whereas communication and cognitive skills are relative weak areas of development (Bailey, Hatton, et al., 1998; Dykens et al., 1996). In addition, quantitative reasoning and short-term memory have been described as particular areas of weakness (Freund et al., 1995).

In addition to investigating the developmental characteristics of preschool males with FXS, other researchers have begun to investigate behavioral characteristics. The research on preschool behavioral functioning can be categorized into three domains: socialization, attention deficit/hyperactivity (ADHD), and autistic behavior. In terms of social interactive behavior, attachment to caregivers does not appear to be problematic (Freund, 1994). There are indications, however, that problems in social interaction during the early childhood years might be specifically related to peer interaction beginning between 3 to 4

years of age (Reiss & Freund, 1992). Specifically, some preschool boys with FXS have been described as socially withdrawn, manifesting behaviors such as being shy; less approachable; upset by parental separation, new people, and environments; and avoiding eye contact (Freund, 1994; Hatton et al., 1999).

With regard to ADHD, maternal ratings of temperament suggest that young boys with FXS display elevated levels of activity, poor attention, limited persistence, and less adaptability than typically developing peers (Hatton et al., 1999; Kau, Reider, Payne, Meyer, & Freund, 2000). Estimates of the percentage of young males with FXS with hyperactivity range from 65% to 93% (Borghgraef et al., 1987; Hagerman, 1996; Simko et al., 1989); twice the rate of hyperactivity in children with developmental delays who do not have FXS (Borghgraef et al., 1987). There is some suggestion that hyperactivity decreases by puberty, whereas attention problems increase in severity among older children (Dykens et al., 1989).

Autism or autistic-like behaviors are often associated with FXS. In studies that have included young children, the presence of autistic features ranges from 16% (Hagerman et al., 1986) to 55% (Simko et al., 1989). In two prospective studies 25% (Bailey, Mesibov et al., 1998) to 29% (Turk & Graham, 1997) of the children exhibited autistic characteristics. In the only study using the Autism Diagnostic Interview-Revised (Lord, Rutter, & LeCouteur, 1994) and the Autism Diagnostic Observation Scale (Lord, Rutter, DiLavore, & Risi, 1999) with individuals with FXS (age range of 21 to 48 months), a prevalence rate of 33% was found (Rogers, Wehner, & Hagerman, 2001). In this study of autism in very young children with FXS, two subgroups of children with FXS were identified: those who were virtually identical to children with generalized developmental delays, and those who were virtually identical to children with idiopathic autism (Rogers et al., 2001).

Specific autistic behaviors reported in preschool children include hand flapping, body rocking (Hagerman, 1996; Reiss & Freund, 1992), word repetitions, and perseverative

Reiss & Freund, 1992). Specific school boys with FXS have been socially withdrawn, mannerisms such as being shy; less approachable by parental separation, new environments; and avoiding eye contact (Bailey, Mesibov, et al., 1994; Hatton et al., 1999).

ADHD, maternal ratings of suggest that young boys with elevated levels of activity, poor persistence, and less adaptability developing peers (Hatton et al., 1994; Reider, Payne, Meyer, & Hatton, 1999). Estimates of the percentage of children with FXS with hyperactivity range from 60% to 93% (Borghgraef et al., 1996; Simko et al., 1989); hyperactivity in children with developmental delays who do not have FXS is 30% (Simko et al., 1987). There is some suggestion that hyperactivity decreases by puberty and attention problems increase in older children (Dykens et al., 1999).

Autistic-like behaviors are often reported in children with FXS. In studies that have included children with FXS, the presence of autistic-like behaviors ranges from 16% (Hagerman et al., 1996; Simko et al., 1989). In two studies, 25% (Bailey, Mesibov et al., 1994) and 30% (Turk & Graham, 1997) of children with FXS exhibited autistic characteristics. Using the Autism Diagnostic Interview-Revised (Lord, Rutter, & LeCouteur, 1994) and the Autism Diagnostic Interview-Revised (Lord, Rutter, DiLavore, & Bishop, 1994) in individuals with FXS (age range 3 to 36 months), a prevalence rate of 25% (Rogers, Wehner, & Hagerman, 1996) was found in this study of autism in very young children with FXS, two subgroups of children with FXS were identified: those who were similar to children with general mental delays, and those who were similar to children with idiopathic autism (Rogers et al., 2001).

Autistic behaviors reported in preschool children include hand flapping, body rocking, and perseverative behaviors (Rogers et al., 1996; Reiss & Freund, 1990; Hatton et al., 1999).

speech (Prouty et al., 1988). Although several studies have suggested a decrease in autistic-like behaviors with increasing age (Borghgraef et al., 1987; Rogers et al., 2001; Hagerman et al., 1986; Reiss & Freund, 1990, 1992), this finding has not been reported in some samples (Bailey, Mesibov, et al., 1998). Some researchers have described a relationship between severity of delay and presence of autistic features (Bailey, Mesibov, et al., 1998; Borghgraef et al., 1987; Rogers et al., 2001; Turk & Graham, 1997), whereas others have reported no relationship (Reiss & Freund, 1990, 1992).

In recent years, research has increasingly focused on younger children with FXS, in an effort to understand the presenting signs and early developmental and behavioral characteristics of this population. Yet, no research to date has described the development of toddlers with FXS. Information about early characteristics must be drawn from existing studies of preschool males that are limited by small sample sizes and few participants younger than 36 months of age. This research is challenging to conduct because most children with FXS are not identified with the disorder until 3 years of age or older (Bailey, Skinner, Hatton, & Roberts, 2000).

Despite the challenges of studying very young children with FXS, descriptions of toddlers with FXS are critical for two reasons. First, because the physical features of FXS are not evident at birth, referrals for genetic testing are largely based on the detection of behavioral and developmental delays. Behavioral and developmental features in children with FXS are often variable and subtle during the first years of life, however, making detection of delays very difficult (Bailey, Roberts, Mirett, & Hatton, 2001). Therefore, the availability of detailed descriptive data during the early toddler years might promote earlier identification of behavioral or developmental delays, leading to more timely provision of early intervention services and family support. For example, detailed descriptive data including physical (i.e., prominent ears, elongated face), behavioral (i.e., avoidance of eye contact, generalized anxiety), and historical (i.e.,

familial history of learning problems) data could be gathered to develop a screening checklist to discriminate between infants and toddlers with FXS from those with idiopathic developmental delays such as language delay and behavior problems. Second, description of the early characteristics of toddlers with FXS is critical to individualizing early intervention efforts, including medical, behavioral, and educational interventions geared toward facilitating the child's optimal development.

This article presents findings on the developmental and behavioral features of male toddlers with FXS between the ages of 12 and 36 months. Multiple measures and approaches were used to describe the characteristics of these children and to answer six questions:

1. At what ages do parents report the emergence of key developmental milestones for males with FXS?
2. To what extent is the development of males with FXS delayed during the toddler years?
3. Are measures of development taken at later ages (i.e., 60 months) related to measures of development taken at earlier ages (i.e., 24 months)?
4. Do the developmental skills of toddlers with FXS increase over time?
5. At what ages do mothers and knowledgeable professionals perceive functional impairments in male toddlers with FXS?
6. Is autistic behavior evident in male toddlers with FXS?

METHOD

Participants

The participants were 26 males diagnosed with full mutation fragile X syndrome through DNA analysis. Twenty-four of the participants lived in states in the southeastern United States (Georgia, North Carolina, South Carolina, Virginia) and 2 lived in the states in the southwestern United States (Texas, California). All were enrolled in a prospective longitudinal study of early development (Bailey, Hatton, et al., 1998). These data represent a subset of the youngest children drawn from the larger data set, which is the Carolina Fragile X Project data set. Only children with at

least two assessments between the ages of 12–36 months were included in the analyses. The average age of enrollment in the longitudinal research study was 24 months, with a range from 12 to 36 months. Twenty-three (88%) boys were European American, 2 (8%) were African American, and 1 (4%) was Asian American. Twenty-five children were receiving early intervention at the time of their first assessment in this study, and 1 child entered early intervention 2 months after his first assessment in this study. The average age of enrollment into early intervention was 16 months, with a range from 2 to 25 months. Once enrolled in early intervention, all 26 children continued to receive services throughout their participation in this study. These services consisted of a range of occupational, physical, and speech-language therapies in addition to services to support families and to optimize the child's development that were primarily provided at home.

Parental participants were 26 mothers with the same ethnic background as their children. The mean age of the mothers who participated in this study was 29.5 years ($SD = 7.1$) with a range from 20–51 years. Seventeen (65%) of the mothers had at least some college education whereas 9 had a high school degree (35%). Fourteen (46%) of the mothers reported that their family received some form of public assistance.

Instrumentation

General indicators of development and behavior were used to document the clinical characteristics of this sample. Parental report of developmental milestones and the Battelle Developmental Inventory (Newborg, Stock, Wnek, Guidubaldi, & Svinicki, 1984) were used to document development. The ABILITIES Index (Simeonsson & Bailey, 1991) was used to describe functional abilities, and the Childhood Autism Rating Scale (Shopler, Reichler, & Renner, 1988) was used to rate autistic behaviors.

Development. Attainment of *developmental milestones* was obtained through a parent interview conducted at the entry assessment. Specifically, parents were asked at what age

their child sat, crawled, and walked independently as well as at what age their child spoke their first word. If a child had not attained each of these developmental milestones at the time of the entry assessment, we interviewed parents at 6-month intervals to obtain these data. In addition to parent interviews, we reviewed developmental evaluation records provided to us by parents or secured from early intervention agencies. There was one instance in which the developmental records differed from the parental interview, and we asked the parents to verify which age was accurate.

The *Battelle Developmental Inventory* (BDI; Newborg et al., 1984) was used to assess developmental status in five domains (Personal-Social, Adaptive, Motor, Communication, and Cognitive). The BDI was chosen because it spans the age range from birth–96 months, allowing for a common measure for all children. It has solid norms based on a nationally representative sample of children and contains adaptations for children with hearing, vision, and motor impairments. Trained assessors using a combination of interview, observation, and direct testing measures can efficiently administer it. Various reliability and validity estimates based on scores obtained from samples of typically developing children and children with disabilities have been established for the BDI (Sexton, McLean, Boyd, Thompson, & McCormick, 1988; Snyder, Lawson, Thompson, Stricklin, & Sexton, 1993), as has its use in documenting developmental trajectories of children with disabilities (Bailey, Hatton, et al., 1998; Hatton, Bailey, Burchinal, & Ferrell, 1997). Although both developmental age scores and developmental quotients can be obtained from the BDI, our previous work has shown that developmental quotients are less stable when the child is 30 months and younger (Hatton et al., 2000). Therefore, we did not use developmental quotients in any of our analyses. We did, however, consider developmental quotients when we calculated the number of children whose developmental quotient fell below 70, which has been viewed as an indicator of delayed development. The developmental age scores of the BDI were summarized descrip-

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BDI were summarized descrip-

tively and a series of correlations was com-
pleted to determine if BDI scores gathered at
very young ages were predictive of BDI
scores gathered at older ages.

In addition to the descriptive and correla-
tional analyses, hierarchical linear modeling
(Bryk & Raudenbush, 1987; Burchinal & Ap-
pelbaum, 1991) was used to examine BDI To-
tal Scores across time. This approach, some-
times referred to as mixed model analysis of
variance, accounts for the dependence of ob-
servations across time through the estimation
of random effects. These models have been
found to be robust under conditions when
high reliability of scores is obtained, regard-
less of the degree of individual differences
over time (Burchinal, Bailey, & Snyder,
1994).

Functional abilities. The *ABILITIES Index*
(Simeonsson & Bailey, 1991) was used to de-
scribe nine areas of functioning: audition, be-
havior, intellectual functioning, limbs, inten-
tional communication, tonicity, integrity of
physical status, eyes/vision, and structural sta-
tus. Each domain is rated on a scale ranging
from 1 (*normal functioning*) to 6 (*extreme lim-
itation of functioning*). For example, intellec-
tual functioning could be rated from *normal*
for age (1) to *profound disability* (6). The
scale was developed to provide a useful pro-
file of functional status that could be com-
pleted by a knowledgeable observer (profes-
sional or parent) based on a range of interac-
tions with the individual. Research has dem-
onstrated its usefulness as a measure in
identifying subgroups of children with dis-
abilities (Simeonsson, Bailey, Smith, & Buys-
se, 1995), and parents and professionals reach
a high level of consensus in rating the items
(Bailey, Buysse, Simeonsson, Smith, &
Keyes, 1995; Bailey, Hatton, Mesibov,
Ament, & Skinner, 2000; Bailey, Simeonsson,
Buysse, & Smith, 1993). These data were
summarized descriptively (see Table 4).

Autistic behavior. The *Childhood Autism*
Rating Scale (CARS; Shopler et al., 1988)
was used as a measure of autistic behavior.
The CARS was developed to identify children
with autism and to distinguish them from chil-
dren with mental retardation or other devel-

opmental disorders. This scale consists of 15
items (relating to people, imitation, emotional
response, body use, object use, adaptation to
change, visual response, listening response,
taste, smell, and touch response, fear or ner-
vousness, verbal communication, nonverbal
communication, activity level, intellectual re-
sponse, and general impressions). Each item
is rated on a scale ranging from 1 (*within nor-
mal limits for age*) to 4 (*severely abnormal*
for age), with half-point scores possible. Rat-
ings are made by the assessor and are based
on observations of the child in a variety of
contexts (e.g., classroom, assessment). The to-
tal score is derived by adding each of the 15
item scores. The total score will fall in one of
three categories that are interpreted as follows:
nonautistic (score of 15–29.5), mildly or mod-
erately autistic (score of 30–36.5), and se-
verely autistic (score of 37–60). The reliabil-
ity and validity of CARS scores for identify-
ing children with autism has been documented
in numerous studies (Eaves & Milner, 1993;
Garfin, McCallon, & Cox, 1988; Sturney,
Matson, & Sevin, 1992) including compara-
tive studies of children with FXS (Bailey,
Mesibov, et al., 1998; Levitas et al., 1983).
Please refer to Bailey et al. (1998) for training
and reliability procedures. These data were
summarized descriptively.

Procedure

Participants were recruited through genetics
clinics, developmental evaluation centers, and
early intervention programs. Upon entry into
the study, parents were interviewed regarding
their family characteristics and their child's
development, and each child was assessed
within 3 weeks of his next birthday or half-
birthday. Developmental assessments using
the BDI were subsequently readministered ev-
ery 6 to 12 months for children who entered
the study at 24 months and older. For children
who entered the study younger than 24
months of age, assessments were readminis-
tered every 3 to 6 months. The number of data
points varies for participants across age cate-
gories because children entered the study at
varying ages, have been in the study for vary-
ing lengths of time, and have variable number

Table 1.
Milestone Acquisition in Months: Subsets of Boys With FXS Compared to a Norm-Referenced Sample

Milestone	Norm Reference** (<i>n</i> = 2,096)		Toddler Data Subset (<i>n</i> = 26)			Older-Aged Data Set (<i>n</i> = 43)		
	<i>M</i>	Range	<i>M</i>	Range	<i>SD</i>	<i>M</i>	Range	<i>SD</i>
Sitting	6	(5-7)	8	(5-12)	2.24	8	(5-14)	1.45
Crawling	8	(6-12)	11	(6-13)	2.03	12	(11-25)	1.49
Walking	12	(9-15)	16	(9-23)	3.25	18	(11-36)	2.53
First Word	11	(10-18)	28	(9-88)	16.58	25	(8-44)	13.25

**Frankenburg et al. (1992).

of assessments. For example, one child was seen at 12, 15, 18, 24, and 36 months of age, whereas some children were seen at 30 and 36 months. The data reported represent a total of 67 assessment occasions. All children were assessed at least twice, and the average number of assessments per child was 2.6, with a range from 2 to 5.

In addition to varying numbers of participants according to age categories, sources of data varied according to the assessment regime. The BDI and the professional rating of the ABILITIES Index were completed at each assessment interval. The parent rating of the ABILITIES Index was completed at the entry assessment then annually at the child's birthday. We have only included ABILITIES Index ratings for children who were simultaneously rated by a professional and parent. The CARS was administered once, during a single year of the study. For those participants who were not enrolled in the longitudinal study at the time of the CARS assessment, it was administered at the first assessment interval when the child was at least 12 months of age. Because we were interested in the characteristics of very young children with FXS, we have only included CARS scores for the 17 children who were 36 months of age or younger at the time of the rating.

RESULTS

Developmental Status

Milestones. Parent-reported attainment of key developmental milestones for the entire Carolina Fragile X Project data set of 69 boys was

separated into two subsets: the 26 younger boys who comprise the sample for this paper and the 43 older boys who did not have two assessments between the ages of 12-36 months of age (see Table 1). Data on the 26 younger boys with FXS who comprise the toddler subset were not statistically significantly different from the 43 boys who were not included in the toddler subset for sitting ($t(64) = -.55, p = .58, d = .14$), crawling ($t(28) = -1.82, p = .08, d = .62$), and age of first word spoken ($t(33) = .54, p = .60, d = .16$). There was a statistically significant difference, however, between the two groups on age of walking ($t(65) = -2.77, p = .03, d = .52$); the participants in the smaller data set acquiring this milestone 2 months earlier than the participants in the larger data set. Although there was a statistical difference between the groups on age of walking, the clinical significance of this difference is questionable; therefore, the toddler sample resembles the larger data set on the majority of milestone data. The two data subsets were separated and summarized descriptively. Table 1 shows means and ranges for each developmental milestone for a normative sample ($n = 2,096$; Frankenburg, et al., 1992), the present study sample ($n = 26$), and the larger older-aged sample ($n = 43$). Figure 1 displays the age at which a cumulative percentage of boys for the combined sample ($n = 69$) met key developmental milestones.

Battelle Developmental Inventory. The means and standard deviations for the BDI total developmental age (DA) score and domain

compared to a Norm-Referenced

Older-Aged Data Set (<i>n</i> = 43)		
<i>M</i>	Range	<i>SD</i>
8	(5-14)	1.45
12	(11-25)	1.49
18	(11-36)	2.53
25	(8-44)	13.25

two subsets: the 26 younger boys comprise the sample for this paper (see Table 1). Data on the 26 boys who did not have two milestones between the ages of 12-36 months were not statistically significant from the 43 boys who were assessed in the toddler subset for sitting ($p = .58, d = .14$), crawling ($p = .08, d = .62$), and age ($t(33) = .54, p = .60, d = .03$), and age ($t(33) = .54, p = .60, d = .03$) was a statistically significant difference between the two groups ($t(65) = -2.77, p = .03$). Participants in the smaller data set met milestone 2 months earlier than participants in the larger data set. Although there is a statistical difference between the two groups on age of walking, the clinical significance of this difference is questionable. The toddler sample resembles the older sample on the majority of milestone attainment. Data subsets were separated and analyzed descriptively. Table 1 shows the mean ages for each developmental milestone for the normative sample ($n = 2,096$; Battelle et al., 1992), the present study ($n = 69$), and the larger older-aged sample ($n = 43$). Figure 1 displays the age at which the cumulative percentage of boys for the entire sample ($n = 69$) met key developmental milestones.

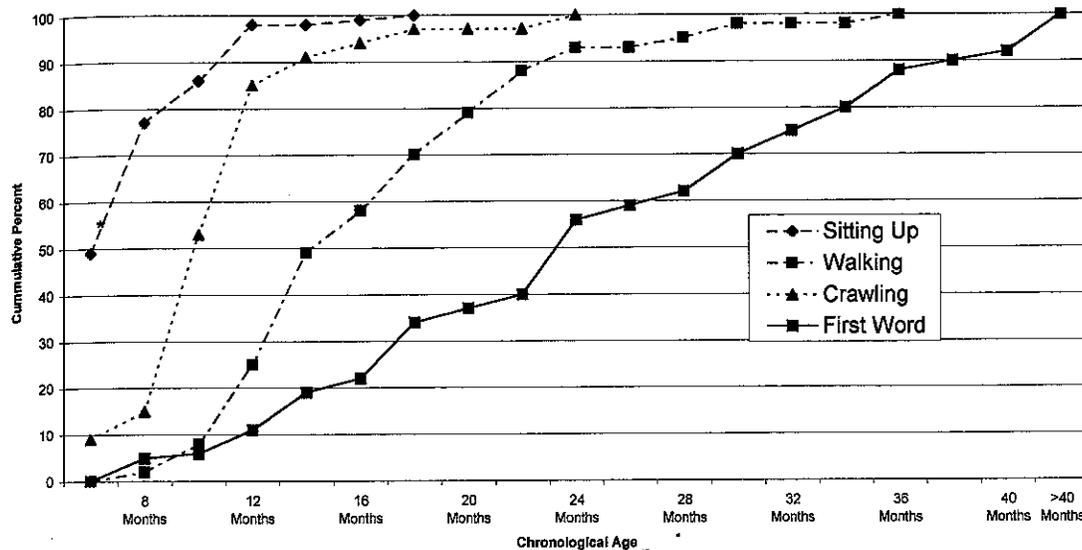


Figure 1. Attainment of developmental milestones for the entire sample ($n = 69$).

DA scores are reported in Table 2. The total scores for the toddler group are graphically illustrated in Figure 2 and for individual children in Figure 3. Considerable variability was evident among the children. Most boys displayed delays across the majority of assess-

ment periods, including the first assessment at 12 months. In fact, all 4 children assessed at the 12-month age interval achieved developmental quotients lower than 65, suggesting that all were at least moderately delayed at this time.

Table 2. BDI Development Quotient (%) and Developmental Age Scores (Mean [SD]) Across Chronological Age Categories

BDI Scores	Chronological Age in Months				
	12 Months (<i>n</i> = 4)	18 Months (<i>n</i> = 7)	24 Months (<i>n</i> = 12)	30 Months (<i>n</i> = 20)	36 Months (<i>n</i> = 23)
DQ \geq 70 (%)	0	60	25	20	39
Total Score DA	9.00 (.82)	13.86 (1.86)	16.67 (3.45)	18.15 (3.92)	20.65 (3.55)
Adaptive DA	8.75 (.50)	12.86 (2.27)	14.83 (3.10)	16.75 (4.52)	19.52 (5.14)
Cognitive DA	10.50 (1.73)	14.86 (1.21)	16.25 (4.03)	18.05 (3.73)	20.61 (3.62)
Communication DA	7.5 (1.29)	12.43 (2.51)	14.83 (4.04)	15.50 (4.11)	17.87 (4.30)
Motor DA	9.5 (1.29)	13.40 (.79)	16.83 (4.06)	19.10 (4.18)	22.52 (4.30)
Personal-Social DA	8.00 (2.45)	12.71 (2.06)	15.25 (3.91)	16.70 (4.92)	19.00 (4.35)

Note. BDI = Battelle Developmental Inventory, DQ = Developmental Quotient, DA = Developmental Age.

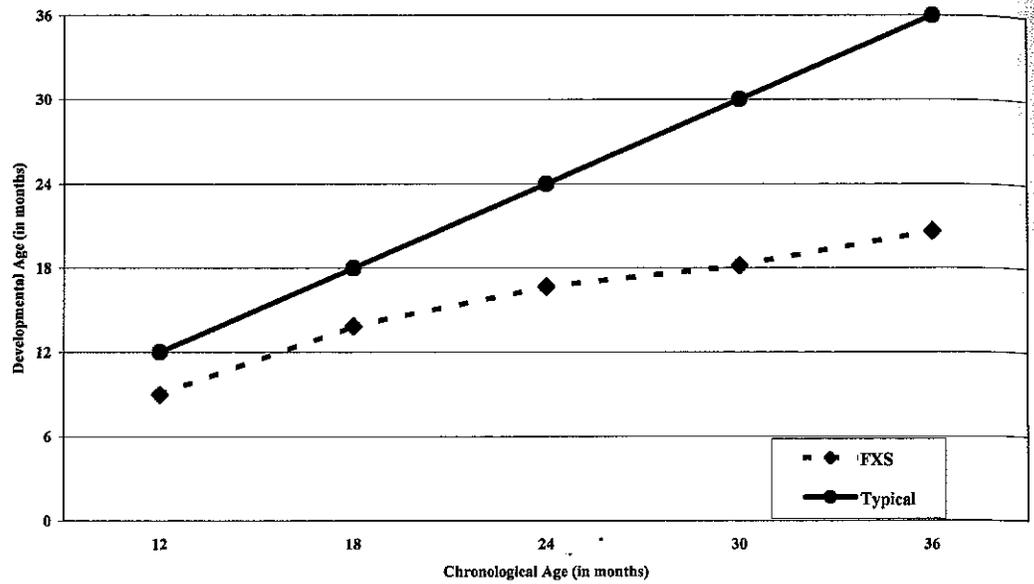


Figure 2.
Total developmental age scores on the BDI for the group at each assessment interval ($n = 26$).

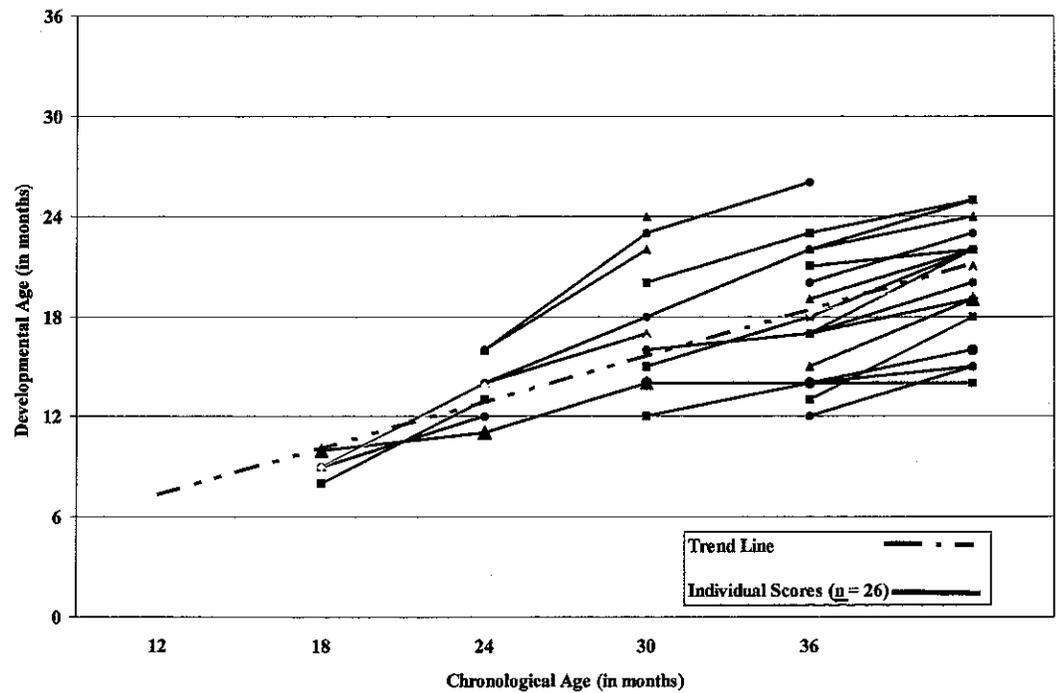
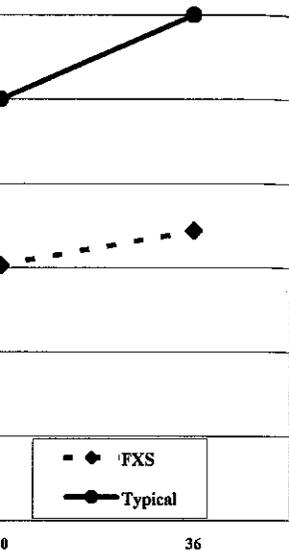
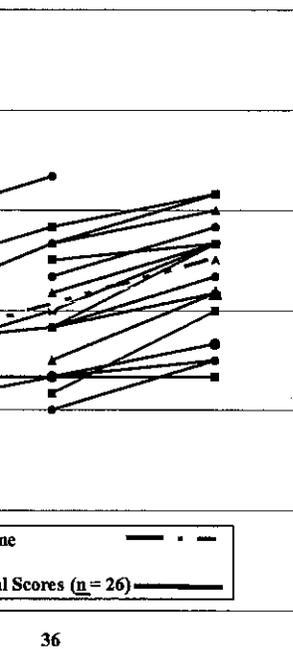


Figure 3.
Total developmental age scores on the BDI for each child at each assessment interval ($n = 26$).



assessment interval ($n = 26$).



assessment interval ($n = 26$).

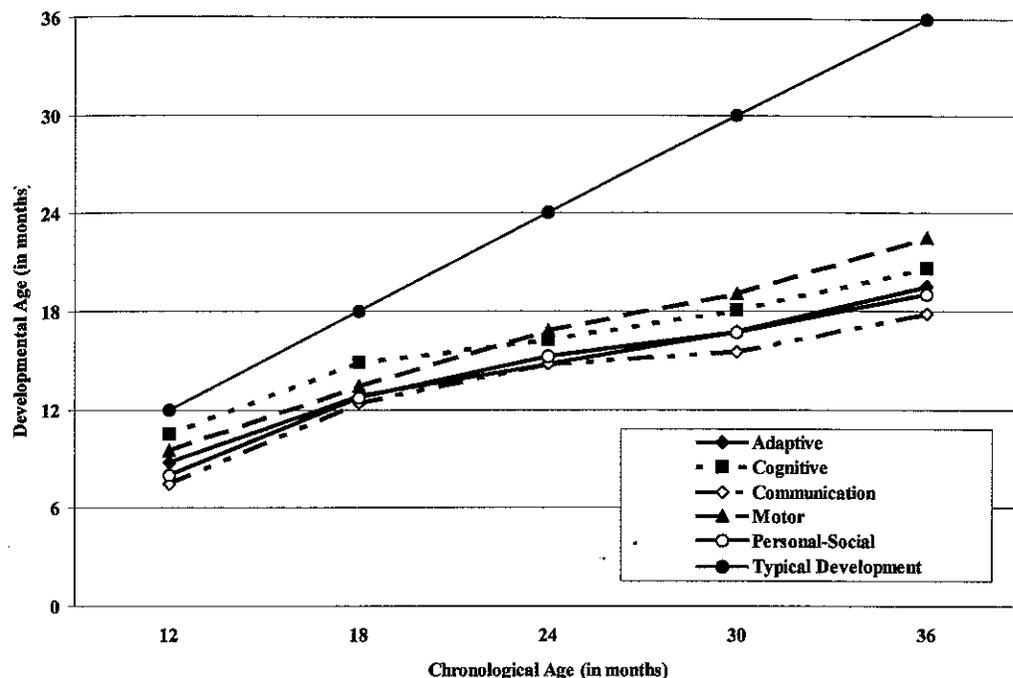


Figure 4.

Domain developmental age scores on the BDI for the group at each assessment interval ($n = 26$).

There was a statistically significant main effect for chronological age on the BDI total DA scores, $F(1, 25) = 33.37, p = .0001$, suggesting that the developmental skills of the young boys with FXS increased with age (see Figures 2 and 3). Although we were only able to test for a linear effect because of our small sample size, the visual analysis suggested that the rate of growth might decrease across time, again with variability within the group (see Table 2). For example, at 12 months of age the average total DA was 9.00 months, a delay of 3 months whereas at 36 months of age the average total DA was 20.65, a delay of 15 months.

In Figure 4, the BDI domain DA scores over time are graphically presented. Consistent with findings reported for the larger sample through 72 months (Bailey, Mesibov et al., 1998), visual inspection of the data reveals that communication was a relative weakness for this sample of children, whereas motor development was a relative strength. It should be noted, however, that this interpretation is

based on visual analysis, as statistical examination was not possible because of the limited sample size. In addition, previous work has shown that BDI domain DA scores might not be independent; thus performance scores in the domains should be interpreted with caution (Snyder et al., 1993).

A series of correlations were completed to determine if BDI developmental age Total Scores gathered at very young ages (i.e., 24 months) were predictive of development at older ages (i.e., 60 months). As displayed in Table 3, results indicated a strong relationship between the age equivalent Total Scores on the BDI at 60 months of age to the age equivalent Total Score on the BDI at 54, 48, 42, 36, 30, and 24 months of age.

Functional Impairment

Parents' and professionals' mean ABILITIES Index ratings across chronological age categories are presented in Table 4. There were differences in detection and ratings of severity between parents and professionals, with pro-

Table 3.
Correlations Between Total Scores of the BDI Across Chronological Age Categories

Age Categories	24 Months	30 Months	36 Months	42 Months	48 Months	54 Months
30 Months	.95 (<i>n</i> = 8)	—	—	—	—	—
36 Months	.92 (<i>n</i> = 12)	.94 (<i>n</i> = 19)	—	—	—	—
42 Months	.97 (<i>n</i> = 5)	.84 (<i>n</i> = 14)	.93 (<i>n</i> = 14)	—	—	—
48 Months	.95 (<i>n</i> = 8)	.79 (<i>n</i> = 17)	.87 (<i>n</i> = 20)	.92 (<i>n</i> = 14)	—	—
54 Months	.83 (<i>n</i> = 4)	.86 (<i>n</i> = 10)	.80 (<i>n</i> = 10)	.69 (<i>n</i> = 10)	.88 (<i>n</i> = 10)	—
60 Months	.92 (<i>n</i> = 5)	.94 (<i>n</i> = 13)	.91 (<i>n</i> = 13)	.84 (<i>n</i> = 13)	.91 (<i>n</i> = 13)	.95 (<i>n</i> = 10)

professionals detecting delays at younger ages and rating delays as more severe. For example, at 12 months of age all four parents rated their child's social skills as normal compared to same-aged peers, whereas one professional was suspicious of a delay, two professionals rated the child's social skills as mildly delayed, and one professional rated the child's social skills as moderately delayed. In the area of thinking and reasoning, three parents suspected delays and one parent noted mild delays at 12 months of age, whereas all four professionals rated the thinking and reasoning skills of these same children as mildly delayed.

Although the time of detection and severity of ratings differed between raters, the pattern of delays was fairly consistent. Delays were consistently suspected in social skills, inappropriate behavior, receptive language, and hypotonia across the 12- to 30-month-age categories. In addition, delays in expressive communication and intellectual functioning were also suspected at young ages (12 months), yet rated more severely as mildly delayed at later ages (36 months).

Autistic Behavior

The mean total CARS score for 17 boys rated at an average age of 26 months (range 12–37 months) was 25, a score that falls within the nonautistic range. There was measurable var-

iability, however, with a standard deviation of 3.6 and a range from 19 to 31 for total CARS scores. Fourteen (82%) of the participants had total scores that fell in the nonautistic range, whereas 3 (18%) had total scores that fell in the mildly to moderately autistic range, and none had ratings that placed them in the severely autistic range.

DISCUSSION

This article describes findings from an ongoing, longitudinal study of the early developmental and behavioral characteristics of young boys (between 12 and 36 months of age) with FXS.

Limitations

Broad measures of development and behavior were used for this study, rather than discrete indices of development within a single domain, and the number of data points for participants varied across age categories. In addition, we did not use a comparison group, and the sample size was small, limiting the generalizability of these findings. Furthermore, we included few environmental variables in this study, limiting interpretation of the data from a transactional viewpoint. Despite these limitations, this study is the first to describe the development and behavior of children with FXS at these very young ages.

Age Categories

48 Months	54 Months
—	—
—	—
—	—
.88 (n = 10)	—
.91 (n = 13)	.95 (n = 10)

with a standard deviation of 19 to 31 for total CARS (2%) of the participants had all in the nonautistic range, had total scores that fell in the moderately autistic range, and that placed them in the severe.

These findings from an ongoing study of the early developmental characteristics of young children (and 36 months of age) with

development and behavior study, rather than discrete development within a single domain of data points for parents across age categories. In addition, use a comparison group, sample size was small, limiting the generalizability of these findings. Further, a few environmental variables, limiting interpretation of the nonactional viewpoint. Therefore, this study is the first to examine development and behavior of children at these very young ages.

Table 4. Summary of Professionals' and Parents' ABILITIES Mean (SD) Index Ratings Across Chronological Age Categories

ABILITIES*	Chronological Age Categories											
	12 Months		18 Months		24 Months		30 Months		36 Months		36 Months	
	Prof.	Parent	Prof.	Parent	Prof.	Parent	Prof.	Parent	Prof.	Parent	Prof.	Parent
Audition	n = 4 1.00 (0)	n = 4 1.00 (0)	n = 5 1.00 (0)	n = 5 1.20 (.41)	n = 7 1.00 (0)	n = 7 1.00 (0)	n = 11 1.09 (.30)	n = 11 1.27 (.65)	n = 18 1.32 (.46)	n = 18 1.19 (.54)	n = 18 1.32 (.46)	n = 18 1.19 (.54)
Social skills	2.50 (5.80)	1.00 (0)	2.20 (.89)	2.00 (1.26)	2.71 (1.16)	2.29 (1.11)	2.91 (.83)	2.45 (.93)	3.16 (.67)	2.28 (1.24)	3.16 (.67)	2.28 (1.24)
Inappropriate behavior	2.75 (1.5)	1.50 (.58)	1.60 (.84)	1.40 (.41)	2.71 (1.16)	2.29 (1.50)	3.00 (.77)	2.27 (1.10)	2.79 (1.21)	2.89 (1.08)	2.79 (1.21)	2.89 (1.08)
Thinking/Reasoning	3.00 (0)	2.25 (.50)	2.20 (.82)	1.60 (.98)	3.29 (.97)	2.86 (1.57)	3.18 (.75)	3.00 (1.0)	3.42 (.59)	2.89 (.76)	3.42 (.59)	2.89 (.76)
Limbs	1.00 (0)	1.00 (0)	1.00 (0)	1.25 (.50)	1.00 (0)	1.50 (.79)	1.09 (.30)	1.45 (1.04)	1.07 (.21)	1.06 (.37)	1.07 (.21)	1.06 (.37)
Expressive communication	3.25 (.50)	2.50 (.58)	3.00 (.98)	2.00 (1.19)	3.43 (.97)	3.14 (.90)	3.91 (.54)	3.82 (.75)	3.63 (.56)	3.39 (1.07)	3.63 (.56)	3.39 (1.07)
Receptive communication	3.00 (0)	2.00 (1.15)	2.60 (.86)	1.60 (.90)	3.43 (.97)	3.14* (1.35)	3.18 (.60)	1.91 (1.04)	3.42 (.67)	2.44 (1.19)	3.42 (.67)	2.44 (1.19)
Hypertonicity	1.00 (0)	1.15 (.41)	1.00 (0)	1.20 (.49)	1.30 (.65)	1.29 (.76)	1.00 (0)	1.36 (.81)	1.16 (.35)	1.17 (.32)	1.16 (.35)	1.17 (.32)
Hypotonicity	3.00 (0)	2.50 (.58)	2.40 (.84)	1.40 (.32)	2.86 (1.0)	2.29 (1.38)	2.18 (.98)	1.82 (.98)	2.58 (.84)	1.78 (.68)	2.58 (.84)	1.78 (.68)
Health	1.00 (0)	1.00 (0)	1.60 (.84)	1.60 (.41)	1.00 (0)	1.29 (.76)	1.55 (.93)	1.45 (.82)	1.26 (.75)	1.17 (.43)	1.26 (.75)	1.17 (.43)
Vision	1.00 (0)	1.25 (.50)	1.60 (.29)	1.00 (0)	1.00 (0)	1.14 (.47)	1.09 (.30)	1.09 (.30)	1.05 (.21)	1.11 (.28)	1.05 (.21)	1.11 (.28)

*ABILITIES Index ratings: 1 = Normal Functioning, 2 = Suspected Disability, 3 = Mild Disability, 4 = Moderate Disability, 5 = Severe Disability, 6 = Profound Disability.

Therefore, the results constitute an important first step in increasing our understanding of the early characteristics of boys affected by FXS that might lead towards earlier identification and intervention with these children.

Developmental Status

Milestones. Our data suggest that the age at which young boys with FXS acquire early milestones might become increasingly discrepant from typically developing children over time (see Table 1 and Figure 1). For example, the mean age of sitting for the boys with FXS is delayed by 2 months, the mean age of crawling for the boys with FXS is delayed by 3 months, the mean age of walking for the boys with FXS is delayed by 4 months, and the mean age for first word spoken for the boys with FXS is delayed by 17 months. Although we recognize that this pattern of increasingly delayed milestone acquisition is based on a limited sample and a visual analysis, this pattern is similar to the larger data set and to previous reports (Prouty et al., 1988; Reiss & Freund, 1992).

Whereas the mean age of milestone acquisition appears below age expectations for boys with FXS for all milestone tasks, there was great variability within our sample and a number of boys with FXS met motor milestones within age expectations. For example, 43% of the boys in our sample sat within the expected age range, 74% crawled within the expected age range, 50% walked within the expected age range, and 31% spoke their first word within the expected age range. This finding highlights the challenges of early identification; delays might not be present during the early years of life and broad measures such as acquisition of milestones might not be sufficiently sensitive to detect delays that are present.

Battelle Developmental Inventory. According to the scores on the BDI, the early development of boys with FXS is delayed in all major developmental domains, and these delays might be evident as early as 12 months of age. Developmental age scores steadily increase over time suggesting that these children gain skills during this age period, and BDI

Total Scores from assessments of very young children (i.e., 24 months) were related to assessments taken of these same children when they were older (i.e., 60 months).

According to the descriptive data, the developmental skills of young boys with FXS appear delayed in all five domains of the BDI: motor, adaptive, cognitive, communication, and personal-social skills. Although all domains of development appear to be delayed, visual analysis of the data indicates that communication scores consistently appear to be the lowest. In contrast, there is inconsistency in which domain appears to be the highest. At the 12-month and 18-month age intervals cognitive scores are highest whereas at 24-, 30-, and 36-month age intervals motor scores are the highest. This change in relative domain strengths might be due to the effect of delayed communication on later cognitive tasks (24-, 30-, and 36-month intervals) and to the reliance on motor skills in earlier cognitive tasks (12- and 18-month intervals). For example, items such as feeling objects, reaching for a removed object, and pulling a string to obtain a toy are items in the cognitive domain that would be presented to children under 24 months of age, whereas items such as responding to "one" and "one more," repeating a two-digit sequence, and identifying objects by their use are items in the cognitive domain that would be presented to children over 24 months of age.

In our sample of 67 BDI assessments, 27% ($n = 18$) of the Total Scores fell within the average to borderline range. Inspection of the individual scores revealed that 11 out of the 18 scores in this range were from boys who were older than 24 months of age, suggesting that the higher developmental quotients in this study cannot be exclusively attributed to young age. The proportion of average to borderline developmental scores in this study is lower than the 44% reported by Freund et al., 1995, yet higher than the range of 0–20% reported by others (Bailey, Hatton et al., 1998; Borghgraef et al., 1987; Lachiewicz et al., 1987; Simko et al., 1989). The different proportions of high-functioning children in these studies could be because of the different ages

assessments of very young (18 months) were related to assessments of these same children when they were older (i.e., 60 months).

Based on the descriptive data, the delays of young boys with FXS across all five domains of the BDI: cognitive, communication, and motor skills. Although all domains appear to be delayed, the data indicates that communication consistently appear to be the most delayed. In contrast, there is inconsistency in the motor domain which appears to be the highest. At 18-month age intervals cognitive scores are highest whereas at 24-, 30-, and 36-month intervals motor scores are highest. The change in relative domain scores is due to the effect of delayed performance on later cognitive tasks (24-, 30-, and 36-month intervals) and to the reliability of skills in earlier cognitive tasks (18-month intervals). For example, naming objects, reaching for a string, and pulling a string to obtain a reward in the cognitive domain that is delayed in children under 24 months of age whereas items such as repeating words and "one more," repeating words, and identifying objects are delayed in the cognitive domain presented to children over 24 months of age.

Of 67 BDI assessments, 27% of Total Scores fell within the normal range. Inspection of the data revealed that 11 out of the 27 in the normal range were from boys who were under 24 months of age, suggesting developmental quotients in this range are exclusively attributed to a proportion of average to below-average scores in this study is consistent with the 20% reported by Freund et al., 1998, and the range of 0–20% reported by Bailey, Hatton et al., 1998; Lachiewicz et al., 1987; Lachiewicz et al., 1989). The different proportions of non-functioning children in these studies are because of the different ages

of participants and different instruments used to measure development.

It should be noted that 15 out of the 26 participants in this study were identified because of a family history of FXS. Therefore, these 15 participants might be more mildly delayed than the majority of children who were identified because of documented delays of sufficient magnitude to warrant genetic testing. In this regard, our sample might be biased towards inclusion of children considered to be higher functioning than the majority of children with FXS. Small and unequal numbers of participants in these groups ($n = 15$, $n = 11$, respectively) limited a statistical comparison of the data, but a visual inspection of the data did not suggest differences in level of functioning.

The BDI findings of this study are consistent with results from a larger ($n = 46$) and older (24- to 72-months of age) cohort of children using the same instrument (Bailey, Hatton, et al., 1998). Although the participants from this study were drawn from the same sample as that of Bailey, Hatton, et al., the previous study had fewer participants at the 24- and 30-month age categories and no participants younger than 24 months of age. Although the sample size is smaller and analyses are largely descriptive in the current study, the patterns of performance over time on the BDI appear consistent across these two studies.

Functional Abilities

The ABILITIES Index ratings are consistent with the results of the BDI and attainment of developmental milestones in that developmental delays of boys with FXS might be suspected or observed as early as the first year of life and that delays are most likely documented by 30 months of age. It should be noted, however, that project research associates detected delays at an earlier age and rated the functional abilities of these boys as more severely delayed than did their parents. Although there were differences in the age of detection and rating of severity, the patterns of ratings between parents and project research associates were similar. Specifically, ABILITIES Index ratings of inappropriate be-

havior, thinking/reasoning, expressive communication, receptive communication, and hypotonicity progressed from no detection or a suspicion of delay at 12 months of age to a judgment of mild to severe delays at 30 months of age. At every age interval, expressive communication was the domain rated as most significantly delayed while audition, vision, hypertonicity, overall health, and use of limbs were not rated as delayed.

Autistic Behavior

Ratings of autistic behaviors suggest that challenging behaviors might be observed during the 1st year of life. According to the CARS ratings, there was significant variability in the presence of autistic behaviors with 18% ($n = 3$) of the scores falling in the mildly to moderately autistic range. This finding is limited because of the small sample size, but the rate of 18% is generally consistent with the rate of 25% from the larger sample (Bailey, Mesibov, et al., 1998) but lower than the rates of 29% and 33% Turk and Graham (1997) and Rogers et al. (2001) reported respectively. Although there is some overlap of participants between this and the Bailey, Mesibov et al. study, the previous study included children 25 months and older, whereas 8 out of 17 participants in this study were younger than 25 months of age.

Of the 3 individuals whose scores fell in the autistic range, 2 boys were 24 months of age and 1 boy was 30 months of age. This suggests that autistic behaviors can be observed as early as 24 months of age (Bailey, Mesibov, et al., 1998; Rogers et al., 2001). Because of the limited sample size, we were unable to analyze statistically the relationship of chronological age and severity of delay in relation to autistic behavior in this sample. Nevertheless, the average age for the 3 boys whose scores fell in the autistic range was 26 months and the average age for the 14 boys whose scores did not fall in the autistic range was 26.1 months. In addition, out of the 23 boys with BDI scores at 36 months of age, the two lowest Total Scores were from boys rated as autistic.

CONCLUSIONS

The primary findings of this study are that delays might be documented in multiple areas of development as early as the first 2 years of life, and developmental skills increase between the ages of 12 and 36 months. It should be noted, however, that there was great variability within the sample and across the measures. The findings that boys with FXS demonstrate global developmental delays and problem behaviors (i.e., autistic-like behaviors, delayed personal-social skills) that might be evident in the first 2 years of life is consistent with findings from previous reports of older children. These findings represent an extension of the literature, as this is the first study to describe the development of these boys during the infant and toddler years. Although it is not surprising that infants and toddlers appear to display developmental delays given previous reports of delays during the preschool years (Bailey, Mesibov, et al., 1998; Borghraef et al., 1987; Lachiewicz et al., 1987; Simko et al., 1989), this phenomenon has not been well-studied. Indeed, some reports suggest that infants and toddlers might look average or borderline in development (Freund et al., 1995).

The findings of this study highlight the importance and challenges of early identification and intervention with very young boys with FXS. In terms of early identification, it appears that developmental delays are mild to moderate during the first 2 years of life and that standardized developmental assessments might be more sensitive to detect delays than reliance on broad screening measures or attainment of developmental milestones. In addition, professionals knowledgeable about FXS might be more sensitive to detecting delays than parents. Nevertheless, all four parents of children with FXS at *least* suspected delays in communication and intellectual domains when their children were 12 months old, which suggests that pediatricians should be sensitive and responsive to parental concerns and refer for early intervention or follow-up diagnostic services based on parental concerns. This is important given that the

pathway to a diagnosis of FXS is typically through medical services, namely a referral from a pediatrician (Bailey, Skinner et al., 2000). Because many pediatricians are more likely to refer children older than 3 years of age and children with severe developmental delays for early intervention (Epps & Kroeker, 1995), and they often rely on parental report of milestones and developmental screening indices rather than developmental or behavioral tests to detect or confirm developmental delays (Dobos, Dworkin, & Bernstein, 1994; Li & Logan, 1996), we need to develop more sensitive measures and early indicators of FXS during the first years of life. In the absence of efficient and effective early indicators of FXS, the diagnosis of FXS might be delayed; children might be deprived of early intervention services, and families might not be informed regarding future family planning decisions.

This study also has implications for early intervention service delivery. First, early interventionists can play a role in families' quest for a diagnosis. The average age at which a child with FXS is identified with a developmental delay is 23 months, and the average age at which a child is diagnosed with FXS is 35 months (Bailey et al., 2000). Therefore, many children with FXS might not be receiving early intervention services during their infant and toddler years because a diagnosis of FXS has not been made or their delays are too subtle to be detected. In addition, many children with FXS are involved in early intervention before the diagnosis of FXS is made, and this puts early intervention professionals in a unique role of providing support to children and their families who are pursuing a definitive diagnosis. The type of family support from early interventionists might take many forms such as providing the family with information about FXS or sharing information regarding a child's unique developmental and behavioral characteristics with professionals who are pursuing a diagnosis. In our work, we have found that a knowledgeable early interventionist can be the key to obtaining a diagnosis of FXS (Bailey et al., 2000). Therefore, it is critical that early interventionists be

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o has implications for early ice delivery. First, early in n play a role in families' gnosis. The average age at ith FXS is identified with a lay is 23 months, and the av ch a child is diagnosed with s (Bailey et al., 2000). There ren with FXS might not be intervention services during oddler years because a diag s not been made or their de e to be detected. In addition, ith FXS are involved in early ore the diagnosis of FXS is uts early intervention profes- ue role of providing support heir families who are pursu- gnosis. The type of family y interventionists might take s providing the family with t FXS or sharing information s unique developmental and cteristics with professionals a diagnosis. In our work, we a knowledgeable early inter- e the key to obtaining a di- (Bailey et al., 2000). There- that early interventionists be

familiar with the characteristics of FXS to support families in their quest for a diagnosis.

Second, if an infant or toddler has been diagnosed with FXS and therefore meets criteria for early intervention services under the established condition category, early interventionists might urge families to consider implementation of services as soon as the diagnosis of FXS is made rather than to wait for delays to become more severe in the future. This is particularly critical in the area of communication because communication skills appear most severely delayed in the first 2 years of life, and they are critical to other areas of development such as personal-social skills and cognition. Third, it appears that young children with FXS might have unique needs related to behavior management, ADHD, and autistic characteristics that have not been reported in other studies of young children with developmental delays (Hatton et al., 2000). Therefore, early interventionists who are familiar with these unique needs might be better able to provide services to these young children and their families. Of course, there is great variability in the developmental and behavioral status of children with FXS, and the uniqueness of each child and family should be considered in designing appropriate intervention plans for any child.

Finally, more research is needed to document the development of individuals affected by FXS during their first 2 years of life. In particular, studies of discreet cognitive processes and specific problem behaviors should be conducted. In addition, guidelines and procedures for deciding whether to refer a child for genetic testing for FXS need to be tested and refined. Last, early intervention agencies and school systems need to be aware of the developmental trajectories and specialized needs of boys with FXS and their families.

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