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Video Analysis of Sensory-Motor Features in Infants with Fragile X Syndrome at 9–12 Months of Age

Grace T. Baranek,[1,2] Cassandra D. Danko,[1] Martie L. Skinner,[1] Donald B. Bailey Jr.,[1] Deborah D. Hatton,[1] Jane E. Roberts,[1] and Penny L. Mirrett[1]

This study utilized retrospective video analysis to distinguish sensory-motor patterns in infants with fragile X syndrome (FXS) ($n = 11$) from other infants [i.e., autism ($n = 11$), other developmental delay ($n = 10$), typical ($n = 11$)] at 9–12 months of age. Measures of development, autistic features, and FMRP were assessed at the time of entry into the study. Home videos collected from families were edited and coded with previously validated procedures. Findings revealed a pattern of sensory-motor features (e.g., repetitive leg movements, posturing, less sophistication/repetitive use of objects) associated with FXS, and suggest these infants were most similar to the group of infants with other developmental delays, irrespective of co-existing autistic symptoms later in life. Infant sensory-motor features in the FXS group were more predictive of an early developmental milestone (i.e., age walking) than later, more broad, developmental outcomes, or FMRP. Implications for early identification and differential diagnosis are discussed.

KEY WORDS: Home movies; mental retardation; fragile X syndrome (FXS); autism; sensorimotor development; infancy.

INTRODUCTION

Fragile X syndrome (FXS) is the most common inherited form of mental retardation (MR). FXS affects all races, with an estimated frequency at 1 in 4000 males and 1 in 8000 females (Crawford *et al*., 1999; Turner, Webb, Wake, & Robinson, 1996). A genetic marker (i.e., trinucleotide expansion in the 5′ untranslated region of the FMR1 gene at Xq27.3 resulting in disruptions in protein synthesis essential for normal brain functioning) has been identified and DNA testing is available. Physicians typically do not suspect FXS unless a family history of MR or the hallmark dysmorphology (e.g., large ears, elongated face, macroorchidism in males) is noted (Hagerman, 1997).

Dysmorphic features depend upon physical maturation and thus are not particularly useful as markers in the first several years of life. Heterogeneity in behavioral expression in FXS and expected age-related changes in symptoms presentation create challenges for studying early features. A range of atypical behaviors including gaze aversion, inattentiveness, lack of verbalization, hyperactivity, repetitive movements, low muscle tone, and delayed milestones have been reported at various points in development (Bailey *et al*., 1998; Bailey, Skinner, & Sparkman, 2003), but the precursors to these behaviors have not been extensively studied during the first

[1] Division of Occupational Science, Department of Allied Health Sciences, University of North Carolina at Chapel Hill, CB#7120 UNC-CH, Chapel Hill, NC, 27599-7120, USA.
[2] Correspondence should be addressed to: Grace T. Baranek, Division of Occupational Science, Department of Allied Health Sciences, University of North Carolina at Chapel Hill, CB#7120 UNC-CH, Chapel Hill, NC, 27599-7120, USA; Tel.: +1-919-843-4467; Fax: +1-919-966-9007; e-mail: gbaranek@med.unc.edu.

year of life in children with FXS, nor in comparison to children with other diagnoses.

The study of early sensory-motor features may have theoretical as well as clinical implications for differential diagnosis and early identification (Baranek, 1999). Sensory-motor processes are integral to the awareness of stimuli, integration of stimuli into meaningful perceptions of environmental events, and access to physical and social environments that enable infants to actively explore, and engage in meaningful activities (Dunn, 1997; Greenpan & Weider, 1998). These skills are highly salient during the infancy period and precede development of more sophisticated cognitive and linguistic skills. Varied sensory-motor experiences are critical to building a large repertoire of generalizable actions that can be retrieved and modified as needed throughout life in the course of daily activities. Thus, disruptions in the integrity of the sensory-motor systems during infancy may result in altered perceptions and narrow action repertoires that interfere with development of important skills and limited social participation if sufficient supports and environmental affordances are lacking.

Approximately 25% of children with FXS meet clinical diagnostic criteria for autism (Bailey *et al.*, 1998b; Dykens & Volkmar, 1997; Feinstein & Reiss, 1998; Rogers, Wehner, & Hagerman, 2001). Overlapping behavioral features in older children are known to include deficits in social relatedness, play, communication, repetitive behaviors, abnormal sensory responses, and challenging temperament. Such differentiation may have prognostic significance, since developmental trajectories for a subgroup of children with both FXS and autism are noted to be significantly worse than for those children with only FXS or autism (Bailey, Hatton, Skinner, & Mesibov, 2001; Cohen, 1995). Moreover, theoretical conceptualizations (Bailey *et al.*, in press; Cohen *et al.*, 1991) describe several possible sequences of developmental pathogenesis in FXS as related to autism. For example, one possibility is that FXS leads directly to autism, another is that that FXS results in MR which indirectly may affect presentation of autistic features. Given the over-representation of autistic features in FXS, researchers have increased their attention to the study of background genes in FXS that might predispose a child to autism (Feinstein & Reiss, 1998).

Retrospective research can augment prospective methods in understanding the early behavioral manifestations of developmental disorders, especially when physical features are not obvious in infancy or families are unaware of a genetic history of MR. Until recently, retrospective research relied on parents' recall of early developmental patterns. With the advent of video recording, many parents have archived rich sources of data about their child's early development that are subsequently available for research purposes. Retrospective video analysis methodology provides an ecologically valid procedure for objectively viewing early behavioral symptoms in their natural environments (Baranek, 1999; Osterling & Dawson, 1994; Walker, Grimes, Davis, & Smith, 1993). Although such studies have been conducted with children with autism and those with schizophrenia, such analyses have not been attempted with children with FXS.

The purpose of this study was to use retrospective video analysis methods to determine salient sensory-motor features of FXS during the first year of life, and to distinguish specific behavioral patterns in infants with FXS from known patterns in infants with autism and other developmental delays. This study aims to extend findings of a previous study of retrospective infant videos (Baranek, 1999) that was conducted with two developmental risk groups (i.e., autism and developmental delay) and a typical comparison group. The previous study was foundational for establishing a valid methodology, and for confirming hypotheses that infants with autism could be identified on the basis of sensory-motor features at 9–12 months of age. The specific variables utilized in the previous study were based upon existing literature from retrospective parental reports (e.g., Gillberg *et al.*, 1990), and theoretical foundations that sensory responses to environmental stimuli, and sensory-motor play repertoires are disrupted in children with autism (e.g., Wing & Gould, 1979).

Our research questions for the current study were: (1) What specific behavioral features discriminate infants with FXS from three comparison groups at 9–12 months of age? (2) Are sensory-motor patterns associated with FXS more similar to those exhibited by infants with autism or those with general developmental delays? and (3) Are infant features of FXS correlated with fragile X mental retardation protein (FMRP) levels and later developmental outcomes?

METHOD

Participant Recruitment

This study is an extension of previous work comparing children with autism, other developmental

delay and typically developing children at 9–12 months of age (Baranek, 1999). Only children with FXS were recruited in the present study so that their video data could be compared with existing video data for the other three groups. The recruitment method consisted of contacting families that were participating in a larger longitudinal study examining the developmental impact of FXS (Bailey, Hatton, & Skinner, 1998a). Families in the longitudinal study were contacted by telephone and told about the present study via a telephone script. Inclusion criteria for the current video study stipulated that the child was currently above 12 months of age, had a diagnosis of full mutation FXS verified by DNA analysis, and the family had videos they were willing to share. A total of 22 families were interested in participating. All families were asked to sign an informed consent, contribute their home videotapes for analysis, and release extant data from the ongoing longitudinal study.

In the next stage of screening procedures, the subject pool was narrowed to include only those families ($n = 11$) that had provided sufficient video quality and footage from 9 to 12 months of age. We chose 9–12 months for several reasons. First, we had good comparative data at these ages from the previous study of children with autism, and other developmental delays (Baranek, 1999). Furthermore, an examination of this developmental period could provide validation of early parental concerns reported in the literature on average by 9 months of age in infants with FXS. Finally, this prelinguistic period prevents a bias of discriminating children on the basis of verbal language alone, a predictor that is known to be useful in identifying children with FXS and/or autism at older ages.

Participant Characteristics

Forty-three children, belonging to one of four groups [autism ($n = 11$), FXS ($n = 11$), other developmental delay ($n = 10$), or typically developing ($n = 11$)] were participants in this study. Despite the fact that the chronological ages of the children varied at the time of recruitment and assessment, videotaped segments used for analyses represented all groups of subjects within the same age range (i.e., 9–12 months chronological age, adjusted for prematurity). There were 14 girls (FXS = 1, autism = 1, other developmental delay = 7, typically developing = 5) and 29 boys (FXS = 10, autism = 10, other developmental delay = 3, typically developing = 6). Thirty-eight children were Americans of Caucasian origin (FXS = 11, autism = 10, other developmental delay = 8, typically developing = 9). The remaining five participants were distributed as follows: one Hispanic American, two Asian Americans, one African American, and one Native American. There were no statistically significant differences between groups with respect to Caucasian versus minority participants.

All FXS children had been diagnosed with full mutation FXS through DNA testing as part of their participation in a larger longitudinal study (Bailey *et al.*, 1998a). All children in the autism group were diagnosed with autism by a licensed psychologist/psychiatrist, confirmed with DSM-IV criteria, and received scores of 30 or above on the Childhood Autism Rating Scale (CARS) (Schopler, Reichler, & Renner, 1988) administered in a previous study (Baranek, 1999). Available medical records were thoroughly reviewed and resulted in no reports of FXS in this group. All children with other developmental delays had a documented developmental delay or diagnosis associated with MR as reported in school or medical records. Specifically, this group included six children with Down syndrome, two with Williams syndrome, and two with nonspecific developmental delays. Children with significant hearing, vision, or motoric impairments, or symptoms of autism as measured by the CARS were excluded. Available medical records were screened and resulted in no reports of FXS in this group.

The group of typically developing children had no history of developmental or learning difficulties, as reported by their parents. This information was collected from a self-report medical information form used by the project. In addition, the Vineland Adaptive Behavior Scales, Interview Edition, Survey Form (VABS) (Sparrow, Balla, & Cicchetti, 1984) was administered to the primary caregivers of all children by project staff. All children in this group were functioning in the average range for overall development on this scale.

Participant Assessments

Participants in the autism, other developmental delay, and typical groups were assessed at the time of recruitment in the preliminary video analysis study (Baranek, 1999) for descriptive and matching purposes. Measures included the VABS to assess overall developmental maturity in all four groups, and the CARS to assess level of severity of autistic symptoms in the three clinical groups. Level of MR was also

obtained from existing records for the three clinical groups. Participants in the FXS group were part of an ongoing longitudinal study, thus their most recent developmental assessments were pulled from existing research records (i.e., within 6 months of recruitment) to be used for group comparison data reported in Table I.

The CARS was administered to the clinical groups (autism, other developmental delay, FXS) through an individualized parent interview and supplementary play observation of each child. The typical children were not assessed with the CARS. Scores at or above 30 are indicative of autism on the CARS. Selection criteria ensured that all children in the autism group obtained scores of 30 or above on the CARS, whereas all children in the other developmental delay group had scores below 25. The CARS was used to characterize symptoms of autism in the FXS group also. Three of the subjects with FXS had scores of 30 or higher, consistent with prevalence reports of autism in the literature. The remaining children's scores in the FXS group were fairly well distributed between 19 and 30 (see Table VI for individual scores in the FXS group).

All children were assessed for developmental maturity using the VABS. The parent most familiar with his/her child's daily functioning (usually the mother) was used as the informant. The interviews were conducted at a location and time convenient to each family. Since the children's chronological ages varied at study entry, the VABS composite standard score was used as an index of current developmental maturity to describe and compare the groups (see Table I). A one-way ANOVA (with *post hoc* Tukey HSD) showed that the three clinical groups were well matched on the VABS. As expected, the typically developing group was significantly different from the other three [$F(3,39) = 63.36$, $p < .000$]. The three clinical groups' standard scores were not significantly different from each other on any of the subdomains or overall composite score, with the exception of the autism group showing lower social skills [$F(2, 29) = 7.729$, $p < .002$] as expected.

Since level of MR for the three clinical groups was also of interest for matching purposes, standardized scores (overall IQ) on current cognitive assessments were obtained from psychological reports. All children with FXS were assessed with the Batelle Developmental Inventory (BDI) (Newborg, Stock, Wnek, Guidubaldi, & Svinicki, 1984) as part of the larger longitudinal project from which they were recruited. The specific assessments varied for the children with autism and other developmental delays since these children had been tested at widely different times, and by different clinics; however, assessments were individually appropriate to each child based on their age and diagnosis as determined by the administering psychologist. Consistent with previously published infant video data (Baranek, 1999) overall level of MR was coded as follows for the purposes of matching the three clinical groups at time of recruitment: 0 = Average/Above Average Intelligence (standard scores above 85); 1 = Borderline (70–84); 2 = Mild MR (55–69); 3 = Moderate MR (40–54); 4 = Severe/Profound MR (< 39). There were no statistically significant differences on level of MR across the three clinical groups.

Because our third question pertained to developmental outcomes for the FXS group only, additional measures were obtained from the extant research data and included a biological measure (i.e., FMRP), a measure of parental first concerns (i.e., age developmental problems were first noted), a measure of early developmental milestones (i.e., age walking independently as reported by parent), as well as two developmental outcomes measured during the

Table I. Subject Characteristics at Study Entry

Characteristic	Autism M (SD)	Other DD M (SD)	Typical M (SD)	FXS M (SD)
Chronological age (months)	63 (17)	65 (27)	53 (25)	49 (22)
Mean level of mental retardation	2 (1) Mild	2 (1) Mild	0 None	2 (1) Mild
Vineland Adaptive Behavior Scales				
Composite Standard Score	56 (11)	65 (8)	106 (7)	58 (12)
Communication Standard Score	63 (23)	71 (8)	110 (10)	63 (11)
Daily Living Standard Score	53 (13)	65 (12)	96 (6)	58 (13)
Social Standard Score	60 (8)	80 (13)	105 (7)	66 (13)
Motor Standard Score	73 (14)	62 (9)	108 (11)	60 (14)
Childhood Autism Rating Scale	36 (5)	20 (2)	–	27 (5)

preschool years (i.e., between 47 and 54 months chronological age). The later developmental measures included the age equivalent score on the VABS, as well as the age equivalent score on the BDI. The descriptive results for these assessments are reported in Table VI.

Videotape Collection, Editing, and Coding Procedures

The collection, review, and editing processes for these tapes were identical to the methods validated by Baranek (1999). Interested families were asked to provide all videotapes of their child that were taken during infancy (i.e., under 2 years of age). Copies of the tapes were made in VHS format and the originals were returned to each family. All participants were assigned an identification number to preserve confidentiality. Each tape was screened for minimum quality standards before being edited. Videos included footage from typical family routines and occupations such as playing, feeding, bathing and some special events such as birthdays or holidays. Although none of the FXS participants were born prematurely, some participants in the other groups that participated in the previous study had been. For these children, the videotapes were corrected for gestational age (<36 weeks) during the content coding phase.

A research assistant naive to the purposes of the study edited the videotapes by randomly selecting footage of situational events (e.g., play time, bath time, eating, party), systematically sampled across the 9–12-month age range. This footage was assembled into two 5-min video segments, for a total of 10 min of tape per subject to be consistent with previously validated procedures (Baranek, 1999). Content of these 5-min segments was compared to check whether or not the groups were matched with respect to the following variables (noted in Italics). No statistically significant differences were found in the video segments between the groups with respect to the *age* of the infants in months [($M=11$, $SD=.97$), $F(3, 84)=1.415$, $p>.05$], *average number of situational events* [($M=4$, $SD=1$), $F(3, 84)=.694$, $p>.05$], *average number of persons evident* [($M=4$, $SD=2$), $F(3, 84)=2.225$, $p>.05$], *level of physical restriction* [($M=1.6$, $SD=.5$), $F(3, 84)=1.993$, $p>.05$], and *level of social interaction/structure* [($M=2.13$, $SD=.41$, $F(3, 84)=.658$, $p>.05$]. Both level of physical restriction and social interaction were judged on a 3-point intensity scale (i.e., low, medium, high) for each situational event, and then scores were calculated to reflect the mean level of restriction or social interaction per second, across situations, for each subject. Participant's video segments were dubbed onto master VHS tapes and superimposed with a 20-s audio interval timing system. Coders could hear simultaneously the natural sounds on the video and the cues for scoring intervals.

The coding instrument and procedures used by Baranek (1999) for the autism, other developmental delay and typical groups were replicated in the current study with the FXS group. Fourteen variables of interest (See Table II) were included in this study and coded as either ratings (3 or 4 point scales depending on the variable), or conditional probabilities (frequency of behavior divided by the number of intervals or opportunities). The variables were chosen based on their previous utility in our earlier empirical

Table II. Description of Variables Used for Coding Each 5 min Video Segment

Variable	Description of Items
Looking at camera	Probability of looking at the camera (or person behind camera) across 20 intervals
Visual orientation	Probability of attention to (non-social) novel visual stimuli based on opportunities
Mouthing objects	Probability of mouthing of non-food objects (utensils during meals excluded) across 20 intervals
Spinning objects	Probability of repetitive spinning of objects across 20 intervals
Visual fixation on objects	Probability of staring at objects at close proximity (>3 s) across 20 intervals
Object play rating	Overall rating of quality (range and function) of object play on a 4 point scale
Tactile response rating	Mean of ratings of aversion/withdrawal from non-social tactile stimuli across opportunities
Number of name prompts	Rate of prompts following initial name call, based on number of opportunities by adult caller
Affective rating	Overall rating of range and intensity of affective expressions on a 4-point scale
Social touch aversion	Probability of withdrawal/aversion to touch from people, based on opportunities for physical contact
Arm stereotypy	Probability of repetitive arm movements across 20 intervals
Head/mouth stereotypy	Probability of repetitive head, mouth or tongue movements across 20 intervals
Leg stereotypy	Probability of repetitive leg movements across 20 intervals
Posturing	Probability of unusual static arm or body postures ("fixed" or held >3 s) across 20 intervals

study using retrospective video analysis (Baranek, 1999), and/or theoretical conceptualizations from the literature that would predict additional differences in the FXS group. For example, we chose to include variables that tapped repetitive motor stereotypies, even though these did not discriminate infants with autism from infants with other developmental delays at 9–12 months of age in our previous study. Repetitive movements are known to modulate arousal (Soussignan, Koch, & Montagner, 1988), and children with FXS are often described as hyper-aroused (Cohen, 1995; Hessl *et al.*, 2002; Roberts, Boccia, Bailey, Hatton, & Skinner, 2001).

A graduate student, unaware of the hypotheses of the study or the children's specific diagnoses, served as a naïve coder and was trained to reliability (>80%) on all coding categories from existing tapes by the first author. The coder had a general understanding that the research broadly related to FXS and autism. Once training was accomplished, the graduate student coded only the tapes of the children with FXS since all other tapes had been previously coded using identical procedures (Baranek, 1999). Since FXS dysmorphology is not evident in early infancy, the children's physical features were unlikely to bias the coder. Likewise, the two undergraduate coders in the previous study were unable to accurately judge diagnosis from physical features alone; rates of correct group assignment for the autism and other DD groups were below chance occurrence.

Twenty percent of the FXS videos were double coded for reliability. Intraclass correlations (ICCs) were computed for all variables for FXS group and resulted in the following coefficients: Looking at Camera (.88); Visual Orientation (.90); Object Play Rating (.13); Mouthing Objects (.98); Visual Object Fixation (.91); Spinning Objects (.96); Name Prompts (1.0); Affective Rating (.62); Social Touch Aversion (.98); Tactile Response Rating (.71); Posturing (.98); Head Stereotypy (.96); Arm Stereotypy (.96); and Leg Stereotypy (.98). All ICC coefficients were in the acceptable ranges with the exception of Object Play Rating due to limited variability within the FXS group. Thus, a second viewing of training tapes was instituted and following a calibration of scores, all FXS participant's videos were double coded by a second independent rater for Object Play Ratings. Remaining disagreements were resolved through consensus resolution; consensus scores were used in the final analyses for this variable.

Data Analysis

Preliminary data analysis included examining the frequency distributions of the 14 variables for normality and dichotomizing the variables into meaningful categories when distributions were not normal. Subsequent analyses included one way ANOVA and chi square tests to determine which behaviors/ratings should be included in a predictive model, and a multinomial logistic analysis in which behaviors/ratings from the videotapes were used to predict the probability of being in the FXS group versus being in any of the other three groups (autism, other developmental delay, or typical). The relatively small sample precluded further separation of the FXS group into those with ($n=3$) and without autism for analysis purposes.

RESULTS

The first set of results pertain to our first two questions—(1) what specific infant features discriminate FXS from the three comparison groups, and (2) are these patterns more similar to autism or general developmental delay?

All 11 children with FXS were retained in these analyses, including the one girl since she showed no indication of being an outlier with respect to the behavioral data at 9–12 months of age, and because all three comparison groups also included girls. Each of the 14 coded variables was examined. Four of the 14 were found to have reasonably normal distributions. These included the three overall ratings (Affect, Object Play, and Tactile Response), and one of the interval-coded behaviors (Looking at Camera). The other 10 interval-coded behaviors were skewed, were bimodal, or contained significant outliers. Each of these variables was therefore dichotomized using the median and standard deviation for the typically developing group as a referent (see Table III). If the score was greater than or equal to 1 standard deviation above the median, the dichotomous variable was set to equal 1 indicating a significant amount of this behavior was observed. Otherwise the dichotomy was set to equal 0. Given the distributions of these variables the median appeared to be a better estimate of the midpoint than did the mean. The means and standard deviations for each of the normally distributed variables and the percentages for each of the dichotomized variables are also presented in Table III.

Table III. Means (Standard Deviations) or Frequencies (Percentages) of Observed Behaviors by Group

Behaviors	Autism	Other DD	Typical	FXS
Affective rating mean	2.23 (.56)	1.65 (.71)	2.18 (.64)	1.77 (.79)
Object play rating mean	2.41 (.80)	1.55 (.83)	2.41 (.49)	1.55 (.76)
Tactile response rating mean	1.87 (.43)	2.25 (.61)	2.05 (.51)	2.25 (.44)
Looking at camera mean	.57 (.19)	.38 (.22)	.60 (.23)	.48 (.18)
Arm stereotypy frequency (Median = .13, s.d. = .08)	3 (27.3%)	2 (20%)	2 (18.2%)	3(27.3%)
Head/mouth stereotypy frequency (Median = .05, s.d. = .05)	4 (36.4%)	6 (60%)	4 (36.4%)	7 (63.6%)
Leg stereotypy frequency (Median = .00, s.d. = .05)	4 (36.4%)	6 (60%)	2 (18.2%)	9 (81.8%)
Mouthing objects frequency (Median = .05, s.d. = .07)	6 (54.5%)	3 (30%)	3 (27.3%)	4 (36.4%)
Name prompts frequency (Median = .19, s.d. = .17)	8 (72.7%)	5 (50%)	1 (9.1%)	5 (45.5%)
Posturing frequency (Median = .03, s.d. = .04)	4 (36.4%)	10 (100%)	3 (27.3%)	5 (45.5%)
Spinning objects frequency (Median = .00, s.d. = .00)	1 (9.1%)	1 (10%)	0 (0%)	4 (36.4%)
Social touch aversion frequency (Median = .00, s.d. = .02)	5 (45.5%)	4 (40%)	2 (18.2%)	4 (36.4%)
Visual object fixation frequency (Median = .00, s.d. = .01)	4 (36.4%)	4 (40%)	2 (18.2%)	6 (54.5%)
Visual orientation frequency (Median = .84, s.d. = .06)	2 (18.2%)	3 (30%)	3 (27.3%)	3 (27.3%)

Note: Medians and standard deviations (s.d.) for dichotomized variables are based on distributions of the typical group.

In an attempt to reduce the number of variables to be included as predictors in a model to predict group membership (i.e., FXS, autism, other developmental delay, or typical) we examined the bivariate association between Group and each of the 14 variables. A generous alpha of .10 was set to detect significant effects given the within group sample sizes and the preliminary nature of this step. We did not want to eliminate any behaviors that might prove important in the next step. ANOVAs were used when examining the relationship between the four normally distributed variables and Group.

Significant group differences were found for two of the four continuously measured variables. Object Play Ratings were significantly higher for typical infants than the FXS infants [$F(3, 39) = 4.15$, $p = .01$] and Looking at Camera was significantly lower in the other developmental delay group than the typical group [$F(3, 39) = 2.49$, $p = .08$]. Chi square tests were used to determine if there were significant relationships between the dichotomized variables and Group. Of the 10 dichotomized variables, significant relationships with Group were detected in four: Leg Stereotypies [$X^2(3, N = 43) = 10.11$, $p = .02$], Number of Name Prompts [$X^2(3, N = 9.27$, $p = .03$], Posturing [$X^2(3, N = 43) = 13.17$, $p = .004$], and Spinning Objects [$X^2(3, N = 43) = 6.73$, $p = .08$]. Affective Rating, Tactile Rating, Repetitive Arm Stereotypies, Mouthing Objects, Social Touch Aversion, Visual Object Fixation and Visual Orientation were not included in the subsequent model.

In the final step to determine which of the observed behaviors would contribute to identifying the children with the correct diagnosis we estimated a multinomial logistic regression model in which Group was the categorical dependent variable and the six variables whose ratings (i.e., Object Play) or probabilities (i.e., Looking at Camera; Leg Stereotypies, Number of Name Prompts, Posturing, Spinning Objects) had been identified in the preliminary analyses were entered as predictors. This analytic strategy was selected because the dependent variable is categorical and contains more than two levels, and the predictors are a mix of continuously measured and dichotomous variables. A discriminant function analysis would have been appropriate if all of the predictor variables had been continuously measured and normally distributed. In a multinomial logistic analysis one group must be used as a comparison, and the probability of being in the comparison group versus each of the other groups is modeled as a weighted average of the predictor variables. The weights are estimated as regression parameters using a maximum likelihood procedure. The significance of the contribution of each variable in the final model is determined by comparing −2 log likelihood of the final model to −2 log likelihood of the model with the variable removed. This difference is evaluated with a chi square distribution yielding a single significance test for each predictor. Results of this analysis are presented in Table IV.

Five of the six predictor variables were significant in the final model. Examination of the group by group comparisons indicated that Object Play Rating and Leg Stereotypies were the most powerful predictors of being in the FXS rather than the autism group, Posturing was the most powerful predictor of being in the FXS rather than the other developmental

Table IV. Likelihood Ratio Tests of Predictors in Multinomial Logistic Regression Predicting Diagnostic Classification

Effect	−2 Log Likelihood of Reduced Model	Chi-Square	df	Significance
Intercept	53.65	–	–	–
Object play Rating	67.53	13.88	3	.003
Looks at camera	63.01	9.36	3	.025
Posturing	73.60	19.95	3	.000
Leg stereotypy	58.89	5.24	3	.155
Spinning objects	62.49	8.84	3	.031
Number of name prompts	64.09	10.44	3	.015

delay group, and Object Play Rating, Leg Stereotypies, and Spinning Objects were the most powerful predictors of being in the FXS group rather than the typical group.

Additionally, the procedure produces a classification table in which classifications based on the predictive model are compared to the actual classification into diagnostic groups. These classifications are presented in Table V. Overall, 76.7% of the children were correctly classified. The typically developing group was more likely to be classified correctly (90%) with only one child being incorrectly classified as autistic. The autism group and the other developmental delay group had similar patterns of incorrect classification with one child being misclassified into each of the other categories. The FXS group had a different pattern. Eight of the eleven children with FXS were correctly identified (72.7%). However, the three children who were misclassified were all incorrectly identified as being in the other developmental delay group.

Our third question regarding whether or not early behaviors of infants with FXS were correlated with FMRP and later developmental outcomes was addressed in the last step of our analyses. The amount of FMRP circulating in blood cells can be estimated in conjunction with DNA analysis and is typically reported as the percent of a sample of 200 lymphocytes. Level of FMRP is believed to be positively correlated with higher levels of functioning (Willemsen *et al.*, 1999). In our sample of ten boys with FXS, the FMRP levels (i.e., percent of lymphocytes expressing protein in samples of 200 lymphocytes) ranged from 1.5 to 20.5 ($M = 7$; $SD = 6.28$) at time of recruitment. The one girl in the sample had an FMRP level of 53.5, thus she was excluded as an outlier from further analyses.

We examined the relationships between the early behaviors observed in the videos at 9–12 months of age and later developmental outcomes for the boys with FXS. FMRP levels were available for nine boys. Our early developmental milestone (i.e., age walking independently as reported by parents) was available for 10. Developmental age equivalents were available (between the chronological ages of 47 and 54 months of age) on the BDI for nine boys, and Vineland on seven. These individual developmental profiles and FMRP levels are presented in Table VI. ANOVAs were conducted to determine if each of the dichotomized behavior categories were predictive on each of the four outcomes. High levels of Leg Stereotypies were predictive of later onset of independent walking [$F(1,9) = 5.56$, $p = .043$], and showed a trend toward prediction of lower FMRP [$F(1,7) = 5.25$, $p = .056$]. High levels of Name Prompts indicated a trend toward predicting later onset of independent walking [$F(1,9) = 4.27$, $p = .069$]. Spinning Objects and Posturing were not statistically significant as predictors of developmental outcomes in this sample.

Table V. Observed and Predicted Classification of Children into Diagnostic Groups

Predicted:	Autism	DD	Typical	FXS	% Correct
Observed					
Autism	8	1	1	1	72.7%
DD	1	7	1	1	70.0%
Typical	1	0	10	0	90.9%
FXS	0	3	0	8	72.7%
Overall %	23.3%	25.6%	27.9%	23.3%	76.7%

Table VI. Biological and Developmental Outcomes for Individual Children with FXS

Child	FMRP	First concern (months)	Video group prediction	CARS score	Age walking (months)	BDI* age equiv.	Vineland* age equiv.
1	8	10	DD	23	12	25	26
2	2.5	9	FXS	22.5	18.5	28	29
3	20.5	–	FXS	28	11	25	23
4	2	–	FXS	29.5	18	19	15
5	1.5	5	FXS	27	18	22	20
6	–	–	FXS	30	17	–	–
7	8.5	–	DD	25.5	14	41	–
8	12.5	<1	FXS	21.5	16	26	–
9	2.5	<1	FXS	34.5	24	20	18
10	5	Birth	FXS	32.5	14	22	15
11**	53.5	–	DD	19	14	–	–
Mean	7	4.2	–	27.4	16.25	25.33	20.86
(SD)	(6.28)	(4.48)		(4.34)	(3.77)	(6.56)	(5.40)

* Results from the Battelle Developmental Inventory and the Vineland Adaptive Behavior Scales are reported as age equivalents in months; children were tested between the chronological ages of 47–54 months on these two outcome measures.
** Girl excluded from developmental analyses and calculation of group means.

Non-parametric (Spearman's ρ) correlations were computed to estimate the magnitude of relationships between the two continuously measures behaviors and the four outcomes for the boys with FXS. Of the eight correlations presented in Table VII, three were significant and one was marginal. Amount of Looking at Camera was associated with delayed onset of independent walking, lower FMRP levels, and possibly lower BDI age equivalent scores. Lower Object Play Ratings also correlated with later age walking.

DISCUSSION

This study is the first to utilize retrospective video analysis to validate the contribution of sensory-motor variables in characterizing the phenotype of children with FXS, and to compare these features to early symptoms of autism at 9–12 months of age.

Table VII. Non-Parametric Correlations (and Probabilities) between Developmental Outcomes and Two Early Behaviors

Outcomes	Looking at camera	Object play rating
Vineland Adaptive Behavior Scales *(N=7)*	−.47 (.29)	−.07 (.89)
BDI *(N=9)*	−.64 (.06)	−.04 (.93)
Age walking independently *(N=10)*	.65 (.03)	−.68 (.02)
FMRP *(N=9)*	−.80 (.01)	.31 (.41)

This research extends previous developmental comparisons between FXS, other developmental delay, and autism groups to a much younger sample than has been previously conducted (e.g., Rogers *et al.*, 2001).

Retrospective video analysis methods were sensitive to developmental concerns in all eleven children with FXS at 9–12 months of age, and identified a pattern of features specifically associated with the FXS phenotype in 8 of 11 (72.7% accuracy). These findings further legitimize parental reports endorsing the presence of developmental differences by 9 months of age on average (Bailey *et al.*, 2003). Despite the fact that most children with FXS are not identified by professionals as having developmental concerns until closer to 2 years of age, these findings have important implications for earlier developmental screening.

Parents of children with FXS often experience barriers in the medical community, and frustration dealing with a variety of professionals who may or may not take their early concerns seriously (Bailey, Roberts, Mirrett, & Hatton, 2002). Lag time in accurate diagnosis affects timely entry into early intervention and prevents families from obtaining necessary support services. Given that early intervention is known to have positive outcomes for children with developmental disorders, especially when it is geared to the specific needs of children and their families (e.g., Dawson & Osterling, 1997; Guralnick, 1998), facilitating the earliest possible intervention for these children is important. This study provides a

description of early phenotypic characteristics of FXS that could facilitate earlier diagnosis and provide access to individualized behavioral, educational, and medical interventions.

Many presenting symptoms in the infants with FXS (e.g., delayed object play skills; repetitive movements) are consistent with a picture of generalized maturational delay. Unusual posturing may reflect more specific deficits in motor control and these difficulties may interact with concomitant cognitive deficits to further impact exploratory play abilities (Case-Smith, 1995). Despite the hypotonia and delayed walking skills that are phenotypically characteristic of FXS, these children appeared more physically active than comparisons with respect to level of repetitive leg movements at 9–12 months of age. These findings suggest implications for further study of hyperarousal mechanisms (Roberts *et al.*, 2001).

Although early behaviors varied across individuals, the FXS infants as a group were most similar to the infants with other (non-autistic) developmental delays, irrespective of a co-diagnosis of autism. None of the children with FXS were misclassified as autistic at 9–12 months of age in our analyses despite the fact that three met cut-offs, and another four children manifested several symptoms of autism on the CARS by 4 years of age. The two features that best discriminated FXS from autism were level of object play skills and amount of repetitive leg stereotypies.

Although more comprehensive diagnostic assessments of autism status (i.e., Autism Diagnostic Interview-Revised) are needed, these preliminary findings appear consistent with an indirect sequence of pathogenesis from FXS to autistic features (Cohen *et al.*, 1991). Prospective longitudinal research with more sensitive measures of social relatedness (e.g., vocal imitation, coordinated gaze/joint attention) would help to confirm whether autistic features are developmental sequela in children with FXS, rather than early phenotypic characteristics. However, studies have yet to confirm that such deficits can be identified in all children with autism prior to one year of age; thus, our ability to differentially discriminate these features among infants with related disorders will be an even greater challenge. Physiological measures (i.e., vagal tone) taken early in life could provide support for putative mechanisms that may impact on ability for children with FXS to sustain social engagement later in life.

We were also interested in exploring whether or not symptoms of FXS viewed in naturalistic home videos at 9–12 months were associated with a biological marker (i.e., FMRP) and later developmental outcomes. The findings suggest that such inferences are elusive, but that early sensory-motor features were related more to early motor milestones (i.e., age walking), rather than later and broader developmental outcomes. In particular, four of the six infant behaviors (repetitive leg stereotypies, frequency of name call prompts, amount of looking at the camera, and level of object play) were predictive of onset of independent walking which occurred on average in this group at 16 months of age, whereas only one infant symptom (amount of looking at camera) correlated negatively with broader developmental outcomes (i.e., BDI) at 4 years of age, and only two correlated with FMRP. Future studies may wish to evaluate specific sensory-motor components (e.g., anticipatory control, sensory feedback, etc.) that contribute to reduced environmental exploration in general, and subsequently affect acquisition of specific skills during the second year of life. Likewise, the link between biological and behavioral variables requires much larger samples to show small effects that may be present in this population (Bailey, Hatton, Tassone, Skinner, & Taylor, 2001). The finding that early sensory-motor features in infants with FXS were not significantly related to outcomes in preschool in our sample also points to the relative lack of stability of symptoms over time as children acquire more complex developmental skills or become involved in a variety of therapeutic interventions targeted at their unique impairments.

In conclusion, this study represents the first to directly compare children with FXS, other DD, and autism with respect to sensory-motor features during the first year of life, and offers insights for future research on differential diagnosis. Maturational delays in object play, as well as stereotyped manipulations (e.g., spinning objects), and unusual motor patterns (e.g., posturing, repetitive leg movements) were discriminating features of FXS at 9–12 months. Specific autistic features (e.g., prompted/delayed response to name) may be less evident in FXS at this age. Video analysis of these early sensory-motor patterns in the context of natural family occupations and routines offers a viable research method for systematically observing developmental differences in infants with FXS and related developmental disorders. Although developmental problems become more evident to health care professionals and early interventionists over time as the gap between *expected* or "typical" performance and *actual*

performance of a child with a disability widens throughout the preschool years, appropriate developmental surveillance and screening during infancy, particularly around parental concerns, are critical.

The small sample size of the study and caveats inherent in retrospective methods pose constraints for generalizing these findings. Larger samples would allow for replication, as well as separate analyses for subgroups of FXS children with and without autism that have important prognostic implications (Bailey, Hatton, Mesibov, Ament, & Skinner, 2000). Prospective studies sampling across multiple time points and developmental domains are needed to more definitively determine stability of these early features and their predictive validity.

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