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Cognitive, Environmental, and Linguistic Predictors of Syntax in Fragile X Syndrome and Down Syndrome

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Abstract

Purpose—We examined which cognitive, environmental, and speech/language variables predict expressive syntax in boys with fragile X syndrome (FXS), Down syndrome (DS), and typical development (TD), and whether predictive relationships differed by group.

Method—We obtained Index of Productive Syntax scores for 18 boys with FXS only, 20 boys with both FXS and autism spectrum disorder, 27 boys with DS, and 25 younger TD boys of similar nonverbal mental age (MA). Predictors included group (diagnosis), nonverbal cognition, phonological working memory (PWM), maternal education, speech intelligibility, and expressive vocabulary. We addressed the research questions via hierarchical linear regression.

Results—Diagnostic group, nonverbal cognition, and PWM predicted 56% of the variance in syntactic ability, with approximately three-fourths of the predicted variance explained by group membership alone. The other factors did not contribute any additional significant variance in this final model. There was no evidence that predictor effects differed by group.

Conclusions—Nonverbal cognition and PWM have an effect on expressive syntax beyond that of diagnostic group. These effects are estimated to be the same in FXS, DS, and TD. We discuss explanations for residual variance and the relative role of different predictors.

Keywords

Fragile X Syndrome; Down Syndrome; Syntax; Phonological Working Memory; Modularity; Autism Spectrum Disorders

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Syntax is particularly vulnerable in many developmental disorders (Down syndrome (DS): Abbeduto & Chapman, 2005; SLI: Rice et al., 2004; high-functioning autism: Roberts et al., 2004). Of note, syntactic difficulties have an enormous impact on the daily living of

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individuals with disabilities (Hewitt, Hinkle, & Miccio, 2005). Recent studies have demonstrated weaknesses in expressive syntax in fragile X syndrome (FXS) as well (Estigarribia, Roberts, Price, & Sideris, 2010; Roberts, Hennon, Price, Dear, Anderson, & Vandergrift, 2007; Price, Roberts, Hennon, Berni, Anderson, & Sideris, 2008). Although the average syntactic performance of boys with FXS might be delayed, there is still enormous individual variability in syntactic skills. Understanding which factors underlie this variability is crucial. In fact, one of the main challenges to an etiology-specific approach to intervention is the lack of understanding of individual variation in the development and outcome of language phenotypes both within and across disabilities (Fidler et al., 2007). A predictor model is a first step from descriptive models of impairment to positing explanatory mechanisms of impairment that could potentially be targeted in intervention. The present study has adopted this analytic approach.

Accordingly, we investigate which cognitive, social-environmental, and speech-linguistic factors predict individual variability and syntactic skill in FXS. We consider predictors that have been shown or hypothesized to be related to language level, or to syntactic level in particular: nonverbal cognition, phonological working memory (PWM), maternal education, speech intelligibility, and expressive vocabulary. Additionally, we examine differences in syntax predictors between boys with FXS, DS, and typically developing boys (TD) to clarify whether impaired systems in DS and FXS result from deviant mechanisms underlying syntactic development and whether patterns of association differ according to diagnosis or are common across intellectual disabilities (ID). Differences in predictors would suggest mechanisms of impairment different from typical pathways or even specific to each disorder. Conversely, if the same predictors are significant in all groups, this would support a classic delay scenario, where lower performance on other aspects of cognition/language, or particular combinations of environmental factors, if present in TD boys, would entail similar lower levels of skill.

Syntax in FXS and DS

Young children with FXS produce shorter sentences, fewer grammatical morphemes, and a narrower range of syntactic constructions than mental age or mean length of utterance (MLU) matches (Estigarribia et al., 2010; Levy et al., 2006; Paul et al., 1984; Price et al. 2008; Roberts, Hennon, et al. 2007).

Likewise, considerable evidence points to syntax delays in DS. Both receptive and expressive syntax are at lower levels than expected for nonverbal cognitive ability, vocabulary, or MLU (Abbeduto et al., 2003; Berglund & Eriksson, 2000; Berglund, Eriksson, & Johansson, 2001; Caselli et al., 2008; Chapman et al., 1991, 1998; Eadie et al., 2002; Hesketh & Chapman, 1998; Iverson et al., 2003; Laws & Bishop, 2003; Price et al., 2007, 2008; Rutter & Buckley, 1994). In fact, young individuals with DS demonstrate even more syntactic delay than do those with FXS (Finestack & Abbeduto, 2010; Price et al., 2008).

Cognitive profile of FXS and DS

FXS—Approximately 80% of males with FXS have ID, with most in the moderate to severe range (Dykens, Hodapp, Ort, Finucane, Shapiro, & Leckman, 1989). Of interest, nonverbal mental age has been consistently found to predict expressive and receptive language in FXS (Abbeduto & Chapman, 2005; Roberts, Mirrett, & Burchinal, 2001), and language production in children with DS (e.g., Chapman, Seung, Schwartz, & Kay-Raining Bird, 2000). Other important cognitive deficits in FXS include weaknesses in working memory, and inhibitory control and attention (Baker, Hooper, Skinner, Hatton, Schaaf, Ornstein, et al., 2011; Cornish, Turk, & Hagerman, 2008; Freund & Reiss, 1991; Hodapp, Dykens, Ort,

Zelinsky, & Leckman, 1991; Hooper, Hatton, Sideris, Sullivan, Hammer, Schaaf, et al., 2008; Ornstein, Schaaf, Hooper, Hatton, & Mirrett, 2008; Sullivan, Hatton, Hammer, Sideris, Hooper, Ornstein, et al., 2007). All these factors have been suggested to impact language development and processing in FXS (Abbeduto et al., 2005; Cornish et al., 2008; Roberts, Hennon, et al. 2007; Roberts, Price, et al. 2007; Price et al, 2007), but no studies to date have investigated these hypothesized links.

DS—Individuals with DS have ID ranging from mild to severe, with around 80% of individuals in the moderate range, and some with IQ scores in the average range (Pueschel, 1995; Roizen, 2007). Verbal short-term memory impairments are well-documented in DS (Jarrold & Baddeley, 2001; Laws, 2002) and predict concurrent difficulties in syntactic production in individuals with DS ages 5–20 (Chapman et al., 2002). Weaknesses in auditory or phonological working memory have been proposed as an explanation of language deficits in DS (Jarrold, Hewes, & Baddeley, 2000; Laws, 2004; Tager-Flusberg, 2006). Still, further research on the relationship between short-term memory and language in DS and other populations is needed (Chapman et al., 2002; Hick, Botting, & Conti-Ramsden, 2005), especially studies that control for other variables that might have an impact at the syntactic level.

Speech and expressive language in FXS and DS

Speech intelligibility is an area of concern in FXS (Barnes et al., 2009). Expressive vocabulary is also delayed in FXS, but its relationship with concurrent syntactic delays is unclear (Roberts, Hennon, et al., 2007).

Expressive language is an area of particular weakness in DS as well (Martin, Klusek, Estigarribia, & Roberts, 2009), and is more impaired than receptive skills in young individuals (Caselli, Vicari, Longobardi, Lami, Pizzoli, & Stella, 1998; Chapman, Hesketh, & Kistler, 2002; Laws & Bishop, 2003). Young individuals with FXS outperformed those with DS on a global measure of expressive language in one recent study (Finestack & Abbeduto, 2010). Expressive vocabulary is delayed with respect to mental age (Caselli et al., 2008; Chapman et al., 1998; Hick et al., 2005; Roberts, Price et al., 2007). Intelligibility is also lower than for mental age-matched TD children (Barnes et al., 2009; Chapman, 1997; Chapman & Hesketh, 2000; Chapman, Seung, Schwartz, & Kay-Raining Bird, 1998; Roberts et al., 2005) but not different from that seen in FXS according to one study (Barnes et al., 2009). Intelligibility can affect syntax multiply: (a) by hindering children's monitoring of their own speech, potentially limiting feedback and practice in acquisition; and (b) by "masking" underlying syntactic skills—more complex syntactic structures are more likely to be impacted by unintelligibility. In fact, Bray & Woolnough (1988) found children with DS to be less intelligible in more complex syntactic structures than in simple structures. Syntactic simplification, then, might be an adaptive skill to compensate for unintelligibility (Martin et al., 2009).

In sum, boys with DS or FXS have mild to severe levels of ID, deficits in verbal short-term or phonological working memory, reduced intelligibility, and general expressive language deficits, including deficits in vocabulary and syntax. Whether these similar cognitive backgrounds affect syntactic skill equally in both populations is at present unknown.

Social-environmental factors in FXS and DS

The importance of environmental factors in typical language development is well established (e.g., Dollaghan et al., 1999; Gallaway & Richards, 1994; Hoff-Ginsberg, 1991). In FXS, higher quality home environments are associated with higher IQs and fewer autistic features (Dyer-Friedman et al., 2002; Glaser et al., 2003). High maternal responsivity, in

particular, is associated with better expressive language in toddlers with FXS (Warren et al., 2010), and preschoolers with autism (Siller & Sigman, 2002, 2008).

Several studies have highlighted positive relationships between more organized home environments and higher maternal education, and the developmental scores of young children with DS (Piper & Ramsay, 1980; Sharav, Collins, Shlomo, 1985). However, Chapman et al. (2000) found maternal education did not predict expressive syntax in DS beyond cognitive and age variables.

Autism in FXS

Autism spectrum disorder (ASD) is present in one-half to three quarters of males with FXS, with boys with FXS and ASD showing lower language levels than boys with FXS alone (Bailey et al., 2001; Clifford et al., 2007; Hall et al., 2008; Kaufmann et al., 2004; Philofsky et al., 2004; Roberts, Martin, Moskowitz, Harris, Foreman, & Nelson, 2007; Rogers et al., 2001). Notably, morphosyntactic impairments have been detected in individuals with idiopathic autism (Landa & Goldberg 2005; Roberts et al., 2004). Recent studies show contradictory evidence as to the existence of syntactic differences when boys with both FXS and ASD are examined as a group separate from boys with only FXS (FXS-O) (Estigarribia et al., in press; Price et al., 2008). We will analyze these two groups separately since it is possible that group differences in syntax predictors exist, even though the outcome levels in the groups may not differ.

Study questions

This study aims to answer the following questions:

1. Which cognitive, environmental, and speech/language factors predict syntactic skill in FXS and DS?
2. Are there differences between the FXS groups (with and without ASD), the DS group, and the TD group in these predictive relationships?

Method

Ninety-eight boys participated in this study as part of a larger longitudinal investigation of speech and language in school-age boys with fragile X syndrome FXS, DS, and TD (Roberts, Price, et al., 2007). This study examines concurrent predictors of expressive syntax at baseline during the first year (i.e., all measures come from the first data collection session). These baseline findings are the first step in investigating possible changes in syntax predictors over time. There were 33 boys with fragile X syndrome only (FXS-O, mean age 10.56, SD 2.41), 28 boys with fragile X and autism spectrum disorder (FXS-ASD, mean age 9.98, SD 3.04), 31 boys with DS (mean age 10.19, SD 2.80), and 46 TD boys (mean age 5.03, SD 1.18). The TD group was recruited to establish differences between FXS and TD at similar mental age stages, and the DS group was recruited to determine which language characteristics were common in both groups with ID as opposed to specific to each syndrome.

Participants came from English-speaking homes, and were at or beyond Brown's (1973) Stage III (MLU 2.5–3.0). All boys with FXS had full mutation. ASD was excluded from the DS and TD groups if children scored above ADOS (*Autism Diagnostic Observation Schedule*; Lord, Rutter, DiLavore, and Risi 2001) cutoffs for "spectrum." Boys were excluded if their average hearing threshold was greater than 25 dB HL in the better ear (screened across 500, 1000, 2000, and 4000 Hz using a Grason Stadler GSI 16 or 17, or MAICO MA 40 audiometer). Participants' ethnic distribution was 81% white (non-

Hispanic), 14% African-American, 4% Hispanic, 1% Asian-American, and 1% Native American. Ethnicity did not vary significantly with group. The data do not include females because FXS is an X-linked disorder with a considerably higher incidence among males, and the degree of ID and developmental consequences for males are substantially greater. The other groups exclude females to preserve gender-matching. Boys with DS were screened for FXS and vice versa using a project-developed parent questionnaire, as were TD boys for FXS or DS.

Group matching

The FXS, DS, and TD groups were not significantly different on nonverbal mental age determined by Leiter-R Age Equivalents (Roid & Miller, 1997). The mean mental age for the FXS-O group was 62.48 months (SD=7.75); for the FXS-ASD group, 62.45 months (SD = 7.38); for the DS group, 65.27 (SD=11.56); and for the TD group, 59.74 months (SD=9.91). Group differences in mean mental age were not significant, $F(3,94) = 1.44$, $p = .23$. Although Mervis and Robinson (2003) recommend that groups be considered well-matched only if the p value is equal to or greater than .50, we do not believe our lower p-value is a problem because: a) mental age is a covariate in the analysis; and b) there is substantial overlap in mental age in all groups, making a regression covarying mental age adequate from the point of view of interpretability.

Autism status

We determined autism status in the boys with FXS with the ADOS, a 45-minute series of structured and semi-structured interactions with an examiner that provide contexts to elicit behaviors characteristic of autism. Trained examiners (clinically-trained professionals holding either a B.S. or a Ph.D.) scored videotapes of the ADOS sessions. We administered three modules of the Autism Diagnostic Observation Schedule based on each child's developmental and language levels. Each child received a categorical score of 'no autism,' 'spectrum,' or 'autism', with the latter two scores combined to form a single group (FXS-ASD). To be classified in the FXS-ASD group, each child had to meet the autism spectrum cutoff score for each subtotal: Communication and Social, and the autism spectrum cutoff for the Communication + Social total. For Module 1, communication cutoff is two or higher, social interaction four or higher, and total seven or higher. For Module 2, the respective cutoffs are three, four, and eight. For Module 3, they are two, four, and seven. A second examiner scored 16% of the interactions, with reliability equaling .89 for the individual items (range .83 to .96) and .93 for diagnosis (range .81 to 1.00).

Data collection

Depending on family preference, we tested children in their homes, at school, or at the Frank Porter Graham (FPG) Child Development Institute at UNC-Chapel Hill. Sessions were audiotaped with a portable Digital Auditory Tape TASCAM (DA-P1) recorder and a Shure WBH headset microphone system. Videotaping was done using a Sony Digital8 videocamera (DCR-TVR 27).

Conversational sampling procedures

Trained research assistants transcribed 100 usable spontaneous child utterances from videotapes of ADOS sessions using CLAN software and CHAT conventions (MacWhinney, 2000). This is not substantially different from the common practice of eliciting language samples using age-appropriate toys or prompts, except that the semi-structured character of the ADOS interview (a) facilitates language elicitation from children with ID, and (b) adds a measure of consistency in the sampling context for all participants. The ADOS has recently been recommended especially for collecting natural language samples (Tager-Flusberg,

Rogers, Cooper, Landa, Lord, Paul, et al., 2009). Partially or fully unintelligible utterances, exact self-repetitions, parts of routines (e.g., reciting the alphabet, songs), exact imitations of examiner utterances, and yes/no responses to questions were excluded from analysis. Utterances with more than two independent clauses conjoined by *and* were split at the second conjunction, following SALT guidelines (*Systematic Analysis of Language Transcripts*; Miller & Chapman, 1996) to avoid higher MLUs due to clausal chaining. A second researcher with transcription training verified and corrected all original transcripts from audiotapes.

Transcription reliability—A third researcher independently verified via audiotape a randomly selected 19% (i.e., four boys with FXS-O, five boys with FXS-ASD, five boys with DS, and five TD boys) of the original transcripts for reliability. Morpheme-to-morpheme agreement (including agreement on unintelligible segments) between the second and third researchers was 91% overall, 85% for the FXS-O group, 85% the FXS-ASD group, 90% for the DS group, and 95% for the TD group.

Syntax outcome variable

We measured expressive syntax via the Index of Productive Syntax (IPSyn: Scarborough, 1990). The IPSyn measures the range of different syntactic and morphological constructions in language samples from children in the preschool age range. It has proven useful in investigating syntactic skill in typical children, as well as in children with disabilities, including FXS, DS, and autism (Condouris, Meyer, & Tager-Flusberg, 2003; Hewitt, Hammer, Yont, & Tomblin, 2005; Oetting, Cantrell, & Horohov, 1999; Price et al., 2008; Roberts, Hennon et al., 2007; Scarborough, Rescorla, Tager-Flusberg, Fowler, Sudhalter, 1991; Sudhalter, Scarborough, & Cohen, 1991). Two trained research assistants, blind to diagnosis, coded all transcripts with very high reliability (Shrout & Fleiss' (1979) intraclass correlation coefficient (fixed set) = .99, Cohen's kappa = .65). The first author subsequently verified all transcripts to resolve discrepancies.

Predictor variables

Nonverbal cognition—We computed age equivalent scores from the *Leiter International Performance Scale-Revised* (Leiter-R; Roid and Miller 1997) to measure nonverbal cognition. We administered four subtests: Figure Ground (identifying figures or designs within a complex stimulus), Form Completion (recognizing an object from its fragmented parts), Sequential Order (selection of the next item in a logical sequence of items), and Repeated Patterns (supplying the missing portion of a repeated pattern). We used age equivalents, following previous research (Chapman et al., 2002). However, being cognizant of the limitations of age equivalent scores (Maloney and Larrivee 2007), we ran the exact same analyses using raw scores, with results completely unchanged.

Phonological working memory—PWM was measured with the raw scores from the Nonword Repetition Task of the Comprehensive Test of Phonological Processing (CTOPP: Wagner, Torgesen, & Rashotte, 1999). Raw scores were used because standard scores were at floor for many of the participants with intellectual disability (ID).

Maternal education—Total years of education completed by participants' primary caregivers (all mothers in our sample) at the time of enrollment were used as a proxy for the effect of environmental and family factors on verbal and nonverbal skills, since studies have shown that higher levels of maternal education correlate with more advanced speech and language development in TD children and children with developmental disabilities (Campbell et al. 2003, Dollaghan et al. 1999).

Speech intelligibility—The proportion of completely intelligible utterances was computed using CLAN by dividing the total number of completely intelligible utterances by the total number of utterances in the transcript (i.e., fully intelligible plus partially or fully unintelligible utterances).

Expressive vocabulary—Expressive vocabulary was measured with age equivalent scores from the Expressive Vocabulary Test (EVT: Williams, 1997). In this test, the individual is asked to label a picture or give a synonym for the word provided by the examiner that also labels the picture.

Hierarchical regression

Our goal was to investigate the successive contributions to explaining variance in expressive syntax of diagnosis, cognitive factors, social-environmental factors, and speech-language factors, in that order. This can be accomplished with sequential regression, where an order of entry of predictor variables is specified a priori, or with statistical regression, which selects the predictors that explain more variance first, and continues doing this for the remaining predictors at each step (Tabachnik & Fidell, 2007). We employed sequential regression to avoid capitalizing on the particular characteristics of our sample (i.e., "overfitting" the data). The order of entry was decided a priori, taking into consideration the relative timing of the effects. Clearly, the "genetic" effect, represented by diagnosis (DS/FXS, or no ID), is temporally prior to all the rest. We assumed, furthermore, that cognitive effects (nonverbal cognition, PWM) are prior to social-environmental and to speech-language effects, and that social-environmental effects are prior to speech-language effects. Of course, this ordering is arguable.

Out of the original pool of 138 subjects, 40 had to be excluded because they had missing nonword repetition (PWM) scores (4 boys with FXS-O, 8 with FXS-ASD, 9 with DS, and 19 TD). An additional 8 (2 from each group) were excluded because their nonword repetition task was scored by a trainee who did not meet reliability criteria. These 48 subjects were included in a post hoc analysis using multiple imputation that we report for completeness at the end of the results section. There remained 18 boys in the FXS-O group, 20 in the FXS-ASD group, 27 in the DS group, and 25 in the TD group, for the regression reported here.

Results

Descriptive statistics for predictor and outcome variables

Figure 1 shows the distribution of scores for the 5 continuous predictors and the outcome variable. There is a slight concern about the lack of overlap in the intelligibility scores, which should be kept in mind when interpreting the model. The groups do not differ significantly in nonverbal mental age, $F(3,86) = 1.30$, $p = .28$, or expressive vocabulary, $F(3,86) = .46$, $p = .71$ (Both of these are age equivalents.) There are group differences in PWM, $F(3,86) = 3.69$, $p = .01$, maternal education, $F(3,86) = 7.91$, $p = .0001$, intelligibility, $F(3,86) = 17.03$, $p < .0001$, and syntax (unadjusted scores), $F(3,86) = 18.26$, $p < .0001$.

Table 1 shows the results of the hierarchical linear regression model. The table uses sequential sums of squares. The first step was a regression of IPSyn scores on diagnostic group. One outlier in the FXS group was identified via examination of residuals and normality plots, and removed. Although removal of this data point did not change the model estimates or significance tests for individual variables appreciably, it had a small influence on the total explained variance. As we expected it, the effect of group was significant,

$F(3,85) = 20.08$, $p < .0001$. This predictor alone accounted for 41.5% of the variance in IPSyn scores.

We examined interactions of all predictors with group in all steps following the first. They were never significant and were not retained in the models. Step 2 showed significant main effects of nonverbal mental age, $F(1,83) = 14.51$, $p = .0003$, and PWM, $F(1,83) = 13.91$, $p = .0004$. The contribution to explained IPSyn variance of these two variables combined was 14.9% beyond the variance explained by group. This change in R^2 was significant, $F_{change}(2,83) = 14.21$, $p < .0001$. This model accounted for 56.4% IPSyn variance.

Step 3 found no significant main effect of maternal education, after group, nonverbal mental age, and PWM are taken into account, $F(1,82) = .26$, $p = .61$. Step 4, finally, showed a main effect of intelligibility, $F(1,80) = 4.11$, $p = .046$, but not of expressive vocabulary, $F(1,80) = 1.60$, $p = .21$. These two variables combined explained an additional 2.9% IPSyn variance. This change, however, was just short of significance, $F_{change}(2,80) = 2.85$, $p = .06$. This last model accounted for a total of 59.4% variance in syntax scores.

Therefore, for prediction, we retained model 2, the last model for which adding variables increased the amount of explained variance significantly. The estimated effects for covariates and model-predicted means (outlier included, full dataset) are shown in table 2. After Tukey's Honestly Significant Difference adjustment for multiple comparisons, the boys in the TD group scored significantly higher than those in the three groups with ID ($diff_{\text{TD-DS}} = 15.39$, $t = 5.89$, $p < .0001$, Cohen's $d = 1.68$; $diff_{\text{TD-FXS.O}} = 17.06$, $t = 6.04$, $p < .0001$, Cohen's $d = 1.87$; $diff_{\text{TD-FXS.ASD}} = 17.19$, $t = 5.94$, $p < .0001$, Cohen's $d = 1.88$), with very large effect sizes. There were no significant differences between the three groups with ID. This model predicted 56.4% of the variance in IPSyn scores.

As explained in the method section, 48 participants had to be excluded due to missing or unreliable nonword repetition scores. Missing data are always a concern, biasing regression coefficients and impacting generalizability. Therefore, we created a dataset with imputed PWM scores (using the scores for the eight excluded children and predictive mean matching for the remaining 40 children). This allowed us to use data from the full sample of 138 subjects. A regression analysis on the imputed dataset showed the same pattern of significance and similar effect sizes for the different factors.

Discussion

This paper provides a model of predictors of expressive syntax in boys with FXS, DS and TD. Although some predictor models have been proposed for DS (Chapman et al., 2002), this is the first such model for FXS. We asked which cognitive, environmental, and speech/language factors predict syntactic skill in FXS. We found that the relative importance of predictors did not differ by group, that is, we found no evidence of deviant pathways of development. Accordingly, in what follows we will discuss a general delay model that applies across all groups. Having FXS or DS affects syntax independently from nonverbal cognition, PWM, and intelligibility level, which are estimated to be the same in TD boys as in the boys with ID. Although we may have been underpowered to detect interactions with group, let us note that we imputed 40 missing PWM scores and the interactions remained non-significant.

We found that diagnostic group, nonverbal cognition, and PWM predicted 56% of the variance in syntactic ability in our sample, with each predictor significant while controlling for all others. Approximately three-fourths of the variance explained was predicted by differences in diagnostic group. This is to be expected, given the documented syntactic impairments in FXS and DS, compared to TD boys of similar nonverbal cognition.

However, even after the group effect was accounted for, our cognitive measures explained an additional 15% variance. Nonverbal mental age and PWM had an explanatory effect beyond that of FXS, DS, or typical development. They both contributed unique variance to syntactic scores.

The relationship between working memory and language development is well established in typical populations. Working memory, in particular, has been linked to first and second language syntax learning in typical populations (Ellis & Sinclair, 1996; Williams & Lovatt, 2005), and to the adult processing of long-distance dependencies (e.g., Lewis, Vasishth, & Van Dyke, 2006). Given the fast-paced demands of conversation, higher levels of auditory working memory presumably allow more efficient on-line language processing. In turn, this would facilitate the kind of categorization and co-occurrence analyses needed for syntactic learning. Note that, although the PWM measure we used, nonword repetition, has a phonological/articulatory component and is influenced by lexicon size, an additional post-hoc analysis found 8.4% variance accounted for by PWM when entered last in the model. We are then confident that the effect of PWM is at least partially independent from other speech/language factors. Moreover, the effect of PWM was assessed covarying intelligibility: thus, it was also independent from it.

Beyond diagnostic and cognitive factors, no other factors contributed any significant variance. Although adding intelligibility to our model did not result in a significant increase in explained variance, this factor reaches significance after controlling for all others (Table 1, model 4). This suggests that lower intelligibility may underlie lower syntactic scores due to an artifact of assessment. For example, less complex utterances might be easier to understand, and therefore only simpler structures would be transcribed fully and coded. However, we would like to suggest deeper, causal reasons for this connection. Children with lower intelligibility see their communicative ability compromised (e.g., Chapman et al. 1998), may simplify their syntax to increase their intelligibility (Martin et al., 2009), and may have fewer opportunities for positive and negative feedback from adults, or perhaps adults might use language of lower complexity with them (e.g., Conti-Ramsden, 1990). Either scenario leads to impoverished language input, practice, and possible subsequent language delays. Furthermore, if the ability of unintelligible speakers to monitor their own language productions is reduced, a probable result is an impoverished capacity for learning by matching one's productions to intended targets (Clark, 1993). These hypothetical connections deserve to be specifically examined in future studies.

We were surprised that our environmental proxy, maternal education, and expressive vocabulary did not have an effect after diagnostic and cognitive variables were included. There is substantial research documenting effects of the environment on children's language (Dollaghan et al., 1999; Fewell & Deutscher, 2003). Because the total correlation of maternal education with IPSyn scores is not significant in any group (r_{TD} = .04; r_{DS} = .17; $r_{FXS\text{-}O}$ = .06; $r_{FXS\text{-}ASD}$ = .06), it is unlikely that its effect is merely masked by concurrent predictors. Rather, maternal education just seems a poor proxy for environmental effects, at least in the age ranges studied here. Moreover, SES effects have been demonstrated for younger, typical populations, not older, clinical populations. Finally, maternal education is only one of many factors that define children's environments (Chapman et al., 2000). Some other dimensions not considered here are family socioeconomic status, amount of language exposure, maternal responsivity.

The lack of significance of expressive vocabulary was also unexpected, since Roberts et al. (2007) had found that between-group differences in syntactic scores disappeared when number of different words in conversation (a type-frequency measure of vocabulary) was controlled for. In this study, the total correlation of EVT with IPSyn was significant in all

groups except DS (r_{TD} = .47; r_{DS} = .22; r_{FXS-O} = .50; $r_{FXS-ASD}$ = .53), but so were the correlations of EVT with MA and PWM except for DS (for MA: r_{TD} = .54; r_{DS} = .55; r_{FXS-O} = .50; $r_{FXS-ASD}$ = .76; for PWM: r_{TD} = .56; r_{DS} = .01; r_{FXS-O} = .73; $r_{FXS-ASD}$ = .40). This seems to suggest that the shared variance between EVT and IPSyn is shared also with our cognitive variables. Cognitive level would then (partially) explain both expressive vocabulary and expressive syntax.

We were also interested in assessing between-group differences after adjustment for significant predictors, in an attempt to pin down possible specific syntactic impairments in the populations with ID. Adjusted means showed no difference in IPSyn scores between the three groups with ID, which all scored significantly lower than the TD controls. This is surprising since Price et al. (2008) had found lower IPSyn scores for boys with DS than those for boys with FXS. It is possible, then, that differences in syntax skill are explained away when PWM or intelligibility are covaried (they were not in Price's study). This would imply that any apparent syndrome-specificity in FXS or DS is not due to syntax but rather to the effect of other cognitive and speech factors which may be differentially affected, supporting again a delay interpretation.

There was a remaining 44% unexplained variance in syntactic skills in the retained model. While we do not intend to claim our final model as theoretically complete, we would still like to interpret this residual variance as indicating possibly syntactic specific differences between children with intellectually disability and typical children, plus some random variation. The issue of whether there is a syntactic impairment independent of cognitive impairments, environmental factors, and interactions with other linguistic variables, is of great theoretical import. It speaks to the issue of modularity, that is, whether syntax (or subdomains thereof) develop and function truly independently from general cognitive and environmental influences. Only by developing more comprehensive and more accurate predictor models will we be able to decide whether the remaining variability is a reflection of the difficulty of measuring syntax in conversation, or related to specific syntactic challenges.

Lastly, the importance of validation of a model with independent samples cannot be overemphasized. We based our hierarchical regression on the following assumptions: that diagnosis could affect all other factors; that cognitive factors could affect social-environmental and speech-language variables; that social-environmental factors could affect speech-language variables; and that these effects were unidirectional. Clearly, the assumption of unidirectional causality is too simplistic, and other scenarios should be considered in future studies. If larger samples were available, researchers could carry out structural equation modeling to test causal hypotheses. However, the gold standard for causation is experimental control of independent variables. One could manipulate phonological working memory availability in an artificial grammar learning study with a TD group and a FXS group to test causation, but it is currently difficult to envisage a methodology that would work in the clinical population.

Strengths and future directions

This study proposes the first predictor model of syntax skills in FXS, and supplements the results of Chapman et al. (2000, 2002) in DS. We collected data from a rather large sample of boys with FXS and DS to examine diagnostic, cognitive, social-environmental, and speech-linguistic variables, all of which were theoretically well founded. This study focuses on males with FXS (as do most) because of the relatively higher severity of impairment, and also because syntactic deficits in FXS have been shown only for boys. We are cognizant of this limitation and are currently collecting language, cognitive, and environmental data from girls affected with FXS for future analyses.

Future work should explore other possible predictors of syntax, for example receptive syntax (or language), since Chapman et al (2000, 2002) demonstrated syntax comprehension was the best (indeed, only) predictor of concurrent syntax production in individuals with DS, aged 5–20. In that study, auditory short-term memory predicted syntax production at study start, as long as comprehension was not in the model. Perhaps comprehension mediates the effect of short-term memory in FXS as well. Other important predictors for FXS are perseveration, hyperarousal, attention, and family SES. Perseveration (excessive repetition of topics, words, or phrases) is common in individuals with FXS (Kau et al., 2002; Levy et al., 2006; Roberts, Martin, et al., 2007, Sudhalter et al., 1990). Hyperarousal is common in FXS and might slow the decay of sentence representations in memory, leading to perseveration (Belser & Sudhalter, 1995). Presumably, an inability to shift from a particular behavior can affect syntactic parsing in conversation and, therefore, syntax learning (Mazuka et al., 2009). Like intelligibility, perseveration can lower test performance by masking skills (Helm-Estabrooks & Albert, 2004). Furthermore, there are known sequential processing, attention, and inhibition deficits in FXS that have potential effects on language development. As for SES, Hoff (2003) showed effects of SES and maternal language on vocabulary development. Lower SES is related to lower syntax complexity for TD children (Huttenlocher et al., 2002). Finally, we included no biomarker or genetic information for FXS (e.g. FMRP/cortisol levels, CGG repeats). Even though excluded variables potentially bias regression estimates, it is impossible to know the impact of these omitted variables (Berry, 1993, Gelman & Hill, 2007).

Finally, to the extent that obtainable sample sizes allow, future models should move towards understanding causation paths in a more complex fashion, perhaps through the examination of possible mediation and moderation scenarios between variables identified in predictor studies.

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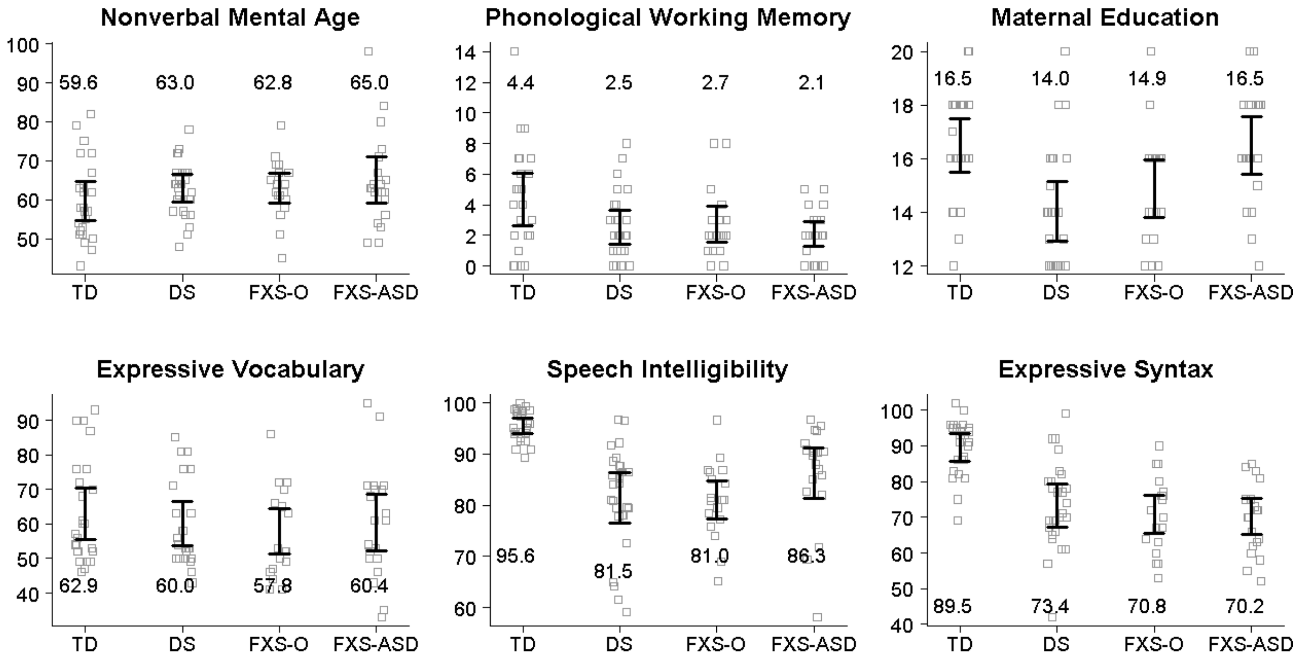

TD: Typically developing
DS: Down syndrome
FXS-O: Fragile X syndrome without autism spectrum disorder
FXS-ASD: Fragile X syndrome with autism spectrum disorder

Figure 1.
Descriptive plots for all variables in the full model (with mean values provided and standard deviations indicated by bars)

Table 1

Coefficients and significance tests for the hierarchical linear regression (sequential sums of squares).

Model	IVs	df1	df2	F	p	R^2	R^2 change	F change	Sig F change
1	Group	3	85	20.08	<.0001	.415	--	--	--
2	Group	3	83	26.32	<.0001	.564	.149	14.21	<.0001
	Mental Age	1	83	14.51	.0003				
	PWM	1	83	13.91	.0004				
3	Group	3	82	26.09	<.0001	.565	.001	.26	.61
	Mental Age	1	82	14.38	.0003				
	PWM	1	82	13.78	.0004				
	Mat Ed	1	82	0.26	.61				
4	Group	3	80	27.27	<.0001	.594	.029	2.85	.06
	Mental Age	1	80	15.03	.0002				
	PWM	1	80	14.41	.0003				
	Mat Ed	1	80	0.28	.60				
	Intelligibility	1	80	4.11	.046				
	Exp Vocab	1	80	1.60	.21				

Table 2

Regression coefficients and model-predicted means from retained model (model 2).Means with different superscripts are pairwise significantly different after adjustment for multiple comparisons.

	Estimate	SE	*t*	*p*
Intercept	88.20	1.89	46.76	< .0001
DS	−15.39	2.61	−5.89	< .0001
FXS-O	−17.06	2.83	−6.04	< .0001
FXS-ASD	−17.19	2.89	−5.94	< .0001
Nonverbal Mental Age	0.25	0.11	2.31	.02
Nonword Repetition	1.49	0.40	3.73	.0003
Model Residual Standard Error	8.73			

	Adjusted Means
TD (n = 25)	88.20[a]
DS (n = 22)	72.81[b]
FXS-O (n = 18)	71.14[b]
FXS-ASD (n = 20)	71.02[b]

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