Fragile X Syndrome and Speech & Language

by Joanne Roberts, Elizabeth A. Hennon, and Kathleen Anderson

Henry is an energetic 6-year-old boy with fragile X syndrome (FXS). Physically he does not appear different from other children his age, though with a long face and fairly large ears. Henry enjoys giving hugs and singing, but when he meets new people he becomes very quiet and avoids eye contact. Transitions are stressful for Henry, so his teachers provide him with a set schedule for each day and give him ample time to prepare for new activities.

Most of Henry’s utterances are two to three words in length, with more advanced comprehension than expression. Although in single words Henry’s speech is intelligible, he talks rapidly and is quite difficult to understand in conversational speech. He has difficulty responding to questions and quickly changes the topic to something of greater interest.

Rachel is an 8-year-old girl with FXS. She engages adults and her friends in conversation, but when she meets new people she becomes very quiet and avoids eye contact. Transitions are stressful for Rachel, so her teachers provide her with a set schedule for each day and give her ample time to prepare for new activities.

Rachel is an 8-year-old girl with FXS. She enjoys talking about her favorite subjects, using simple sentences of up to eight words. Rachel will engage adults and her friends in conversation, although it takes her a few seconds to initiate a topic and then she tends to stay on her own topic. Her third-grade teacher says she is cooperative in school, but anxious about her performance, often seeking reassurance about her work. Although Rachel is reading, she has difficulty describing the main ideas of what she reads and finds math, especially solving word problems, very difficult.

Genetics of Fragile X Syndrome

FXS is the most common inherited cause of mental retardation, affecting both males and females. Although a distinctive profile of specific physical, cognitive, psychosocial, and communication features characterize those with FXS, there is considerable variability, with some individuals more affected than others.

FXS is an X-linked condition that is estimated to affect one in every 4,000 individuals. In the 1940s, Julia Bell and James Martin identified “Martin-Bell syndrome,” a form of mental retardation that could run in families. Under the microscope, researchers noticed that the ends of the X-chromosomes of children with FXS looked as if they were pinched. Females have two X-chromosomes, while males have only one. Males always inherit their X-chromosome from their mothers; fathers pass on a Y-chromosome instead. Therefore, sons can only inherit FXS from their mothers. In contrast, females inherit one X-chromosome from each parent. Either parent can pass on an affected X-chromosome to their daughter.

During the 1980s, the fragile X mutation was identified using cytogentic testing, in which genetic mutations are assessed at the cellular level, and the syndrome was renamed fragile X syndrome. In 1991, the Fragile X Mental Retardation-1 (FMR-1) gene, the specific gene affected in FXS, was identified and a DNA test was established. The FMR-1 gene instructs the cells to produce the FMR-1 protein (FMRP), which is believed to be essential for normal brain functioning.

The FMR-1 gene includes a DNA sequence of cytosine, guanine, guanine (CGG). Most normal individuals have a mean of 29–30 CGG repeats, which is stable across generations. In FXS, there is an expanded number of CGG. If this code is repeated 50–200 times, the individual is a “premutation carrier” of FXS. Although these individuals are usually not affected, their children can inherit the full mutation. More than 200 copies of the repeat occur in the full mutation, with the number of repeats ranging from several hundred to thousands.

In individuals with full mutations, the FMR-1 gene becomes methylated (shuts down) and, as a consequence, production of FMRP is inhibited. The resulting deficiency of the FMRP appears to be responsible for the syndrome. Approximately 12%–15% of those who carry a full mutation have a mosaic pattern, in which an individual has a blend of cells with fully mutated (>200 repeats) X-chromosomes and cells with premutation and/or unaffected X-chromosomes. Infrequently, individuals have a full mutation that is not fully methylated.

Physical and Developmental Characteristics

Individuals with FXS vary in symptomatology, with males more severely affected than females. In boys, specific physical characteristics are typically present by age 8, such as an elongated face, large head, and prominent ears. The physical characteristics of girls are generally normal, although some girls share some of the features with boys, such as a long face and prominent ears. Most affected males exhibit significant intellectual impairment. The range of functioning in males varies from profound retardation to average intelligence, with the majority showing deficits in the moderate-to-severe range. These cognitive deficits appear to become greater in later childhood.

In addition to intellectual impairments, both males and females can evidence difficulties in adaptive and social skills, as well as behaviors characteristic of children with autistic disorder, such as poor eye contact, social avoidance, stereotypic/repetitive behaviors, and hyperactivity.
About one-third of females with FXS exhibit mental retardation of a mild-to-moderate degree. The remaining females have average intelligence but generally have learning disabilities and psychosocial disabilities. Among females with FXS, deficits in attention, executive functioning, visual-spatial skills, and math achievement are common, as are shyness and social anxiety. Approximately 7%-25% of individuals with FXS also have autistic disorder.

The substantial behavioral variability seen in FXS is currently attributed to differences in FMRP expression. In males, FMRP expression can vary based on degree of methylation. In females, the X-chromosome inactivation ratio influences FMRP production. Although females have two X-chromosomes, only one is active in each cell. The ratio of affected cells to unaffected cells is directly linked to the amount of FMRP expressed. FMRP is partially responsible for the reduction of neuronal connections that normally occurs during early development. Lower levels of FMRP are believed to be related to less neuronal pruning, and therefore to atypical brain development. Neuroimaging studies have shown that males and females with FXS often have a smaller cerebellar vermis and larger caudate, thalamus, and hippocampus.

Speech, Language, and Hearing in Fragile X Syndrome

Most males show moderate-to-severe delays in communication skills, while the communication skills of females are considerably less affected. Distinct profiles of speech and language have been described as characteristic of males with FXS, based almost exclusively on data from adolescents and adults. Little information on the communication development of females with FXS has been published, although the literature generally does not suggest deficits in communication, except for the pragmatic aspects of language. Occasionally, selective mutism occurs in males and females with FXS.

**Speech**

The speech of males with FXS has been described as "peculiar" or "distinct." Phonological difficulties are common, including consonant substitutions, omissions, and distortions, which is characteristic of developmentally younger children. Conversational speech is often unintelligible, although single-word utterances often are intelligible. Other speech characteristics reported among males with FXS include rapid and fluctuating rate and dysfluent and perseverative speech. Oral motor difficulties are reported with difficulty repeating multisyllabic sequences, low muscle tone, motor planning problems, and tactile defensiveness.

**Language**

Males with FXS have been reported to have delays in grammatical and vocabulary development, although some researchers suggest that there may be a specific deficit in syntax and/or semantic aspects of language development.

Grammatical skills and vocabulary levels of males with FXS appear to be consistent with their nonverbal cognition level. Higher scores in comprehension than production of syntax and vocabulary have been reported in a few studies. Males with FXS have been reported to have atypical pragmatic language, including frequent perseveration of words, sentences, and topics; self-repetitions; poor topic maintenance in conversation; difficulty answering direct questions; and gaze aversion. The cause for these pragmatic impairments has most often been attributed to hyperarousal, although word retrieval difficulties, syntactic difficulties, and executive function deficits also have been cited as possible causes.

Difficulties in pragmatic discourse also have been reported for females with FXS, including disorganized tangential language, poor topic maintenance, delay in initiating conversation, and difficulties with abstract language, such as reasoning and making inferences. These deficits for females have been attributed to executive functioning deficits, hyperarousal, and memory constraints.

**Hearing**

There have been some suggestions in the literature that hearing could be affected in individuals with FXS. Given that individuals with FXS often have atypical outer-ear morphology (i.e., loss of antihelical folds and the upper pinnae cupped out), it is possible that auditory function also is affected. There have been a few reports of an increased incidence of otitis media or ear infections in boys with FXS, possibly due to the loose connective tissue and loose muscle tone affecting the drainage of the Eustachian tube. A few studies have reported prolonged latencies in auditory brainstem responses in males with FXS, suggesting central rather than peripheral auditory involvement. However, others have suggested that the atypical ABR findings could have been explained by sedation at the time of the hearing testing or a history of otitis media; further peripheral hearing loss was not examined at the time of the assessment. It is well documented that males and females with FXS have attention and learning difficulties, yet based on the current literature, it is unclear if hearing is atypical or if difficulties in auditory processes are playing a role in these learning difficulties.

North Carolina Studies

Most of the studies examining the communication skills of males and females with FXS have included adolescents and adults; few have included children. At the Frank Porter Graham Child Development Institute at the University of North Carolina at Chapel Hill, we have initiated several studies of the communication skills of young males and females with FXS.

---

**Common Signs of Fragile X Syndrome**

- A family history of autism, mental retardation, fragile X syndrome, or learning problems
- Physical signs
  - long or protruding ears
  - long or wide forehead
  - high, arched palate
- Cognition
  - males: moderate mental retardation, range from profound retardation to average intelligence
  - females: normal intelligence, with learning disabilities to mild-to-moderate mental retardation
  - males and females: visual spatial, attention, executive function, and math difficulties
- Speech
  - perseverative and repetitive speech
- reduced speech intelligibility (particularly in males)
- rapid and uneven rate
- phonological delays
- Oral motor
  - low muscle tone
  - motor planning and sequencing difficulties
  - tactile defensiveness
- Language
  - difficulty maintaining a topic
  - interested in social interactions
  - word retrieval difficulties
  - delays in vocabulary and syntax
- Adaptive behavior
  - social anxiety and gaze aversion
  - hyperarousal and hypersensitivity to stimuli
  - stereotypic behavior such as hand flapping
  - short attention span and hyperactivity

---

**Help Him Do This Freely Again**

Products for —

- Counseling
- Dysphagia Rehab
- Staff Training
- Dietary and Nutrition

References on CDs —

- Dysphagia: The Experienced Clinician Series by Irene Campbell-Taggar, Ph.D.
- Medications and Dysphagia
- Oral & Dental Abnormalities
- Dysphagia A — Z

Visit our website or call 1-800-253-5111
www.interactivetherapy.com

---
males with FXS who are 12 years of age or younger.

Funded by the National Institute of Child Health and Human Development (NICHD) and the March of Dimes in 2001 under the direction of Joanne Roberts, the studies are examining the language phenotype of young males with FXS in comparison to males with Down syndrome and typically developing males, and whether young males with FXS have atypical hearing and auditory processing. The studies also are investigating the factors affecting poor speech intelligibility in the conversational speech of young males with FXS. Ongoing studies at the Frank Porter Graham Child Development Institute directed by Donald Bailey and funded by NICHD and the U.S. Department of Education are examining the neuropsychological development from infancy of males and females with FXS, family adaptation to FXS, and procedures to screen infants and newborns for FXS.

Assessment and Intervention Implications

Language impairments may be the first sign of difficulty; almost all young males with FXS and some females with FXS have communication problems. Unlike some other forms of mental retardation, such as Down syndrome, physical characteristics are generally not present in early childhood. Thus, individuals with FXS typically cannot be differentiated from infants with other developmental disorders. Early markers of FXS in older children include the physical, cognitive, communication, and adaptive behavioral characteristics shown in the sidebar on page 7. It is important to determine the developmental level of each individual with FXS with regard to language acquisition and the person's particular strengths and challenges. Given the typical characteristics of FXS, communication assessment should focus on all domains of language (i.e., phonology, syntax, semantics, and pragmatics), as well as related domains, such as oral motor skills and hearing. Particular areas that need further examination, such as speech intelligibility, should involve more in-depth testing, including, for example, assessment of individual sounds, phonological simplification processes, and measures of prosody, such as rate of speech. Communication skills should be examined using both standardized tests and more contextual methods for assessment. Since speech and pragmatic difficulties of males and females with FXS may be particularly evident in conversational speech, communication assessments of individuals with FXS should sample communication in conversational speech.

Intervention

Early intervention is important for children with FXS, given the reported decline in adolescence of cognitive skills for many children with FXS. To decrease anxiety and arousal, behavior and attention needs should be considered, and the use of familiar routines and providing structure when transitioning between activities is important in intervention. Consulting with a child's occupational therapist and/or physical therapist also will be very helpful. For children who are nonverbal or highly unintelligible, some means of augmentative and alternative

For School-Based SLPs

INTRODUCING

AFRICAN AMERICAN ENGLISH: STRUCTURE AND CLINICAL IMPLICATIONS

The English language comprises many linguistic varieties, or dialects, which differ in phonology, grammar, semantics, and pragmatics. One such variety is African American English (AAE). This new interactive CD-ROM is designed to help you understand the dynamics of African American dialect. You will learn about the structure, features, and rules of AAE in order to work more effectively with children who speak vernacular dialects.

African American English: Structure and Clinical Implications is designed primarily for SLPs but will be useful for any educator who works with AAE speakers.

You will be able to—
• recognize the major phonological, grammatical, and pragmatic characteristics of AAE
• describe the procedure for identifying regional varieties of AAE
• recognize issues surrounding the use of standardized assessment tools for speakers of AAE and describe appropriate alternative approaches to assessment

Instructional level: Intermediate
CD-ROM and manual.
Earn 0.4 ASHA CEUs (2003-4/2006)
Item #0112483
$159 ASHA members
199 nonmembers
Order today.
Call ASHA Product Sales at
1-888-498-6699
Monday-Friday, 9 a.m.-5 p.m.
Or, visit us on the Web at www.asha.org
communication, such as a picture board, and introduction of signs should be incorporated into intervention.

Communication intervention should be personalized by considering each individual's developmental level, strengths, and needs. Although there is a common phenotype described in FXS, there is a broad spectrum of involvement of communication skills among both males and females with FXS. The next step in language acquisition should be defined to determine how to capitalize on the individual's unique strengths and advantages. The cause of an individual's speech and language difficulties and the particular domains affected will have important implications for intervention, although the specific contributing factors may be difficult to define. For example, if poor speech intelligibility is due to difficulties with segmental aspects of speech, then intervention should focus on particular sounds or suppression of specific phonological processes. However, if difficulties relate to suprasegmental aspects of speech, such as rate of speech, then a focus on prosody, such as slowing the rate of speech, would be useful. For children whose communication difficulties are particularly evident in conversation, using scripts and routines in more structured environments and transitioning to more naturalistic environments with peers, teachers, and family members whenever possible would be useful.

Final Thoughts

FXS is an X-linked condition and is the most common inherited cause of mental retardation. A distinct profile of the communication skills in males and females with FXS has been described, although there is considerable variability among individuals. These descriptions of the communication phenotype are based primarily on studies of adolescents and adults with FXS. Research is needed that describes the communication skills of children with FXS, examines the differences in communication skills from individuals with other forms of mental retardation, and assesses the sources of variability—such as FMRP and the family environment—that may explain differences in communication functioning among individuals with FXS. Communication assessment and intervention should be personalized by considering each individual's developmental level, strengths, and needs while considering the characteristics common among individuals with FXS.

Visit www.asha.org/about/publications/leader-online/archives/2003/031021e.htm for more resources.

Joanne Roberts is a senior scientist at the Frank Porter Graham Child Development Institute and a professor of pediatrics and speech and hearing sciences at the University of North Carolina at Chapel Hill. She directs two NICHD-funded grants studying the speech, language, and hearing characteristics of young males with fragile X syndrome. Contact her by e-mail at joanne_roberts@unc.edu.

Elizabeth A. Hennon is a post-doctoral fellow at the Neurodevelopmental Disorders Research Center and the Frank Porter Graham Child Development Institute. She works with Roberts on studies of the communication development of children with fragile X syndrome, Down syndrome, and typically developing children. Contact her by e-mail at hennon@email.unc.edu.

Kathleen Anderson is a research associate at the Frank Porter Graham Child Development Institute. She is project coordinator for the Carolina Communication Project, which is studying the speech and language development of young males with fragile X syndrome. Contact her by e-mail at kathleen_anderson@unc.edu.