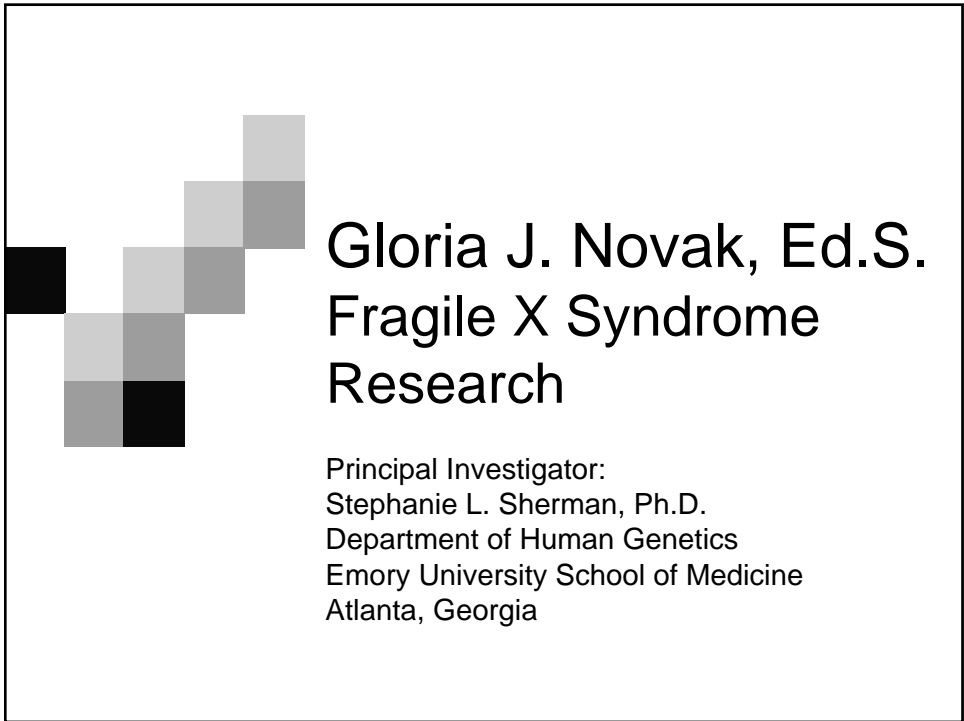


Parent's, Let's Unite for
Kids
(PLUK)



Gloria J. Novak, Ed.S.
Fragile X Syndrome
Research

Principal Investigator:
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Thanks to . . .

- Dennis Moore, Executive Director of Parent's, Let's Unite for Kids (PLUK)
- Roger Holt , Director of Technology, PLUK
- Mary DeBernardis, Director of the Montana Fragile X Association
- Each member of the audience

Montana is
MAGNIFICENT!



Tonight's Topics

- How is Emory University involved with Fragile X Syndrome (FXS)?
- What is Fragile X Syndrome or FXS?
- Who is affected by FXS?
- What causes FXS?

Tonight's Topics

- What cognitive, physical, behavioral, emotional, and social characteristics are associated with FXS?
- How is FXS diagnosed?
- What treatments and interventions are available?

Tonight's Topics

- What resources are available to learn more about FXS?
- How can I contact Emory University researchers if I am interested in supporting research on FXS or participating in a research project on FXS?
- How can I get a copy of this presentation?

How is Emory University involved with FXS?

- In 1991, Dr. Stephen Warren, Chair, Department of Human Genetics, at Emory University, and a team of researchers discovered the gene responsible for FXS.

- One of the longest standing research program on FXS in the world.
- Dr. Warren and Dr. Stephanie Sherman, FXS Principal Investigator, are international authorities on FXS.
- Dr. Warren and Dr. Sherman have been doing research on FXS for over 20 years.

What is FXS?

- Is the most common inherited form of mental retardation
- Causes a wide range of learning difficulties from mild learning disabilities with a normal IQ to severe developmental disabilities and mental retardation
- Is associated with a spectrum of cognitive, physical, behavioral, social, and emotional characteristics.
- Has been identified as the most common known genetic cause of autism



Who is affected by FXS?

- About 1 in 4000 males
- About 1 in 8000 females
- Approximately 100,000 Americans
- 2 million people worldwide



Genetics 101

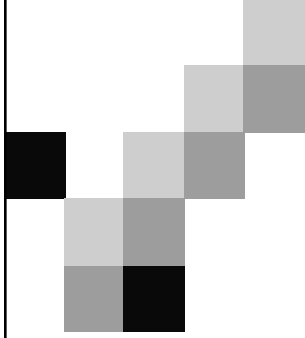
YIKES! Not to worry.
No test at the end!

Genetics 101

- Everyone has about 30,000 genes


Facts on the FMR1 Gene

- Is one of many genes in the human body
- Is the gene responsible for FXS
- Plays a critical role in brain development



What causes FXS?

A complex change (mutation) in the FMR1 gene that keeps it from functioning properly



FMR1 Mutation

- Expansion, or repeat, of called CGG.
- Repeat sequence regulates the production of FMRP, a protein essential for normal brain function
- Loss of FMRP, or protein, causes the clinical features of FXS

FMR1 Gene

- Is found in four different forms defined by the number of CGG repeats in the gene
 - Normal
 - Intermediate
 - Premutation
 - Full Mutation (FXS)

Different Forms of FMR1 Gene

- Normal: ≤ 40 CGG Repeats
- Intermediate: 41 – 60 CGG Repeats
- Premutation: 61 – 199 CGG Repeats
- Full Mutation ≥ 200 CGG Repeats

CGG Repeats

- **IMPORTANT:**

- With any number of repeats over 200, the number of repeats does NOT predict the level of impairment or future achievement of a child.
- A child with 8000 repeats is not necessarily more impaired than a child with 300 repeats on genetic testing results.

Intermediate Form of FMR1 Gene

- 41 – 60 CGG repeats
- ~ 4% of males
- ~ 8% of females
- Considered “gray zone”
- When passed to offspring, can become unstable and start to expand or contract

■ Premutation Form of the FMR1 Gene

- 61 – 199 CGG repeats
- 1/1000 males
- 1/350 females
- Called “carriers” or “premutation carriers”
- Do not have symptoms of FXS

■ However . . .

- Premutation carriers
 - Have an unstable form of the FMR1 gene, which can cause the CGG repeat sequence to expand as it is passed from generation to generation
 - Are at risk for having a child or grandchild with FXS as the premutation may change to a full mutation when passed from parent to child
 - Do not have FXS, so may not know they are a carrier

Furthermore . . .

- Female premutation carriers

- About 21% are known to be at risk for premature ovarian failure (POF), which is menopause before the age of 40

And . . .

- Male premutation carriers

- FXTAS: Fragile X Associated Tremor/Ataxia Syndrome

FXTAS

- Mainly affects males
- Most often seen in men over age 50
- Associated with premutation form of FMR1 gene
- Appears among individuals who generally have normal intelligence and functioning throughout life

FXTAS

- Progressive neurological disorder
- Executive functioning deficits, such as difficulty solving new problems
- Difficulties with balance, walking, movement, tremors
- Trouble with thinking skills, such as memory
- Emotional/social concerns such as anxiety, moodiness, irritability

Again . . .

■ Forms of FMR1 gene:

- Normal
- Intermediate
- Premutation
- Full Mutation (FXS)

Full Mutation of FMR1 Gene


- ≥ 200 CGG repeats
- Means a diagnosis of FXS
- Can be passed on to a child from a parent who has no signs of FXS

Premutation Mother . . .

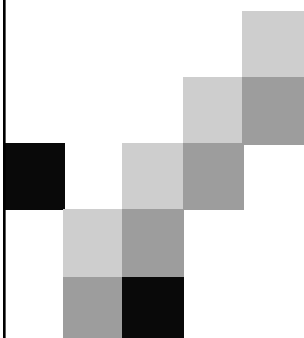
- Has a 50% chance of passing on the gene to each of her children, boys and girls
- Expansion to the full mutation occurs **ONLY** when the mother passes on the gene, not the father

Premutation Father . . .

- Will always pass the premutation gene to all of his daughters, which means all of his daughters will be premutation carriers of the FXS
- Cannot pass the premutation gene to sons
- The only way for a boy to get the fully mutated gene is from his mother



What characteristics
are associated with
FXS?



Special Abilities of
Children with FXS

Like all children, children with
FXS are special!

Relative Strengths

- Attractive appearance
- Lovable personality
- Well developed sense of humor
- Keen memory
- Skilled at imitating
- Interested in music

Relative Limitations

- Mathematics
- Expressive language
- Abstract reasoning
- Auditory processing
- Problem solving
- Responding to change

Cognitive Characteristics

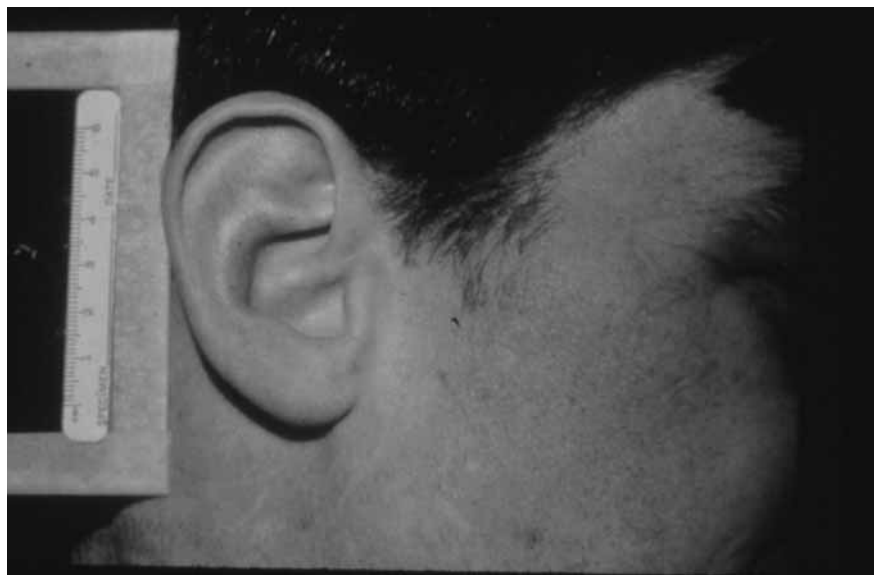
- Mental retardation
- Developmental delay
- Learning disabilities
- Limited attention span
- Speech and language difficulties

Children with FXS

- Normal intelligence
- Learning disabled
- Severely cognitively, or mentally, impaired

Physical Characteristics

- Large, prominent, and/or cupped ears
- Long face
- Square or long jaw
- Flat feet
- Hyperextensible finger joints
- Seizures





Behavioral Characteristics

- Aggression
- Hyperactivity
- Frustration
- Impulsiveness

Behavioral Characteristics

- Hand flapping and/or biting
- Tantrums and/or outbursts
- Ritualistic and/or repetitive actions
- Hypersensitivity to environment
- Tactile defensiveness
- Difficulty tolerating change

Emotional/Social Characteristics

- Social anxiety
- Poor eye contact
- Shyness
- Difficulty relating to others
- Depression
- Anxiety



Speech and Language

- Delayed speech and language development
- Difficulty expressing self with speech
- Rapid and/or repetitive speech
- Talkativeness
- Difficult to understand



Boys with FXS

Girls with FXS

Boys with FXS

- Usually have more features of FXS than girls with FXS
- Facial characteristics associated with FXS tend to be more noticeable in boys than girls
- Intellectual functioning is in the moderate to severe range, which is lower than girls

Boys with FXS

- Approximately 80% of boys affected with FXS exhibit three common physical features, often called the “triad” by doctors
 - Large testicles
 - Prominent or long ears
 - Long narrow face

Girls with FXS

- 20 – 30% test in the borderline range
- 40 – 50% test in the normal range
- Recognized for creative writing ability
- Enjoy written language and English classes
- Many have no distinguishable physical features associated with FXS

How is FXS diagnosed?

- Genetic testing is accurate at any age
- Prenatal through adulthood
- By a blood test, FXS DNA Analysis

Prenatal Diagnosis of FXS

- If FXS exists in a family, genetic counseling is important for members who plan to have children
- Individuals considering prenatal diagnosis should meet with genetic counselor before becoming pregnant to discuss techniques, limitation, benefits, and options

Prenatal Diagnosis of FXS

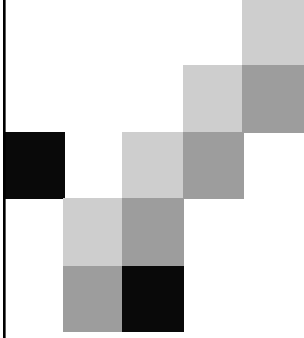
- Prenatal diagnosis is generally available to any person shown to be a premutation carrier of FXS
 - Chorionic villus sampling (CVS) at 10 weeks of pregnancy
 - Amniocentesis at 16 – 20 weeks of pregnancy

Early Detection of FXS

- After the birth of a child
- Difficult to detect in babies and young children
- Many physical symptoms are not noticeable until a child is older
- Most doctors and parents usually have no idea anything is wrong with their child at birth

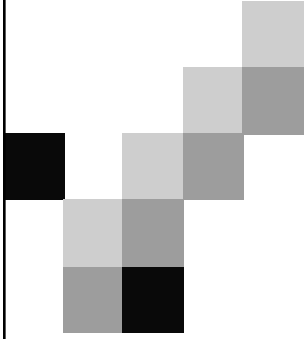
POSSIBLE Early Signs of FXS

- Tactile defensiveness
- Extreme sensory reactions, such as to light, sound, and touch
- Delays in fine or gross motor skills
- Delays in speech and language skills
- Difficulty in toilet training



Parenting is a
challenge and a
reward !

Parenting a child with FXS is
a challenge and a reward!



Parenting a Child
With FXS

Likely will bring greater
challenges . . .
and great rewards, too.



Parents and Caregivers

- Seek, invite, and accept
- Vast amount of education and support available
 - From physicians, geneticists, psychologists, family therapists, ministers, family members, friends, schools, churches, synagogues, parents with children with the same disability, and community services for parents of children with disabilities.



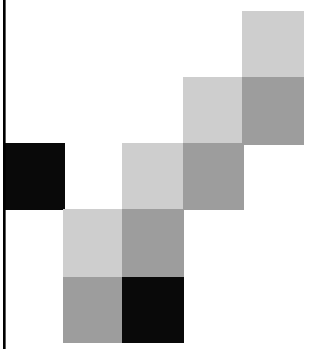
After the Diagnosis

Treatment and Interventions



Treatment and Interventions

- No cure for FXS
- Many therapies and interventions that can benefit families affected with FXS



Remember, no two children are alike.

No two children with FXS are alike.



Interventions

- Medications
- Behavior Management
- Family and Couples Counseling
- Therapy Support
- Special Education Support
- Genetic Counseling



Medications

- Help control seizures
- Manage behavioral challenges
- Address emotional and mood concerns, such as anxiety and depression

Behavior Management

- Can be coupled with medications, counseling, and other therapies

- Address challenges such as
 - Aggression
 - Temper tantrums
 - Outbursts

Family and Couples Counseling

- Addresses concerns with the entire family system, including siblings, in living and loving a child with special abilities

- Helps couples focus on the importance of their relationship

- Provides information on parenting a child with special abilities

Genetic Counseling

- To provide information on genetic testing, including prenatal diagnosis
- To help a family understand what a diagnosis of FXS means for the future of the family
- To offer limited psychosocial counseling and appropriate referrals as needed

Therapy Support

- Occupational Therapy
- Physical Therapy
- Sensory Integration Therapy
- Speech and Language Therapy



Occupational Therapy

- Improves fine motor skills
- Decreases tactile defensiveness
- Develops skills in activities of daily living, such as dressing and eating



Sensory Integration Therapy

- Decreases sensitivity to environmental stimuli



Physical Therapy

- Improves gross motor skills
- Improves balance



Speech and Language Therapy

- Improves communication

Special Education Support

- Eligible for special education services
- Services offered vary by state
- Eligibility requirements vary by state
- Each state has its own approach to providing supportive services

Resources

- Dennis Moore, Executive Director
Parent's, Let's Unite for Kids (PLUK)
516 North 32nd Street
Billings, MT 59101-6003
1 800 222 7585 or 406 255 0540
plukinfo@pluk.org

- The National Fragile X Foundation
PO Box 190488
San Francisco, CA 94119
1 800 688 8765
www.FragileX.org

Resources

- Children with Fragile X Syndrome: A Parent's Guide, Edited by Jayne Dixon
Weber
- Fragile X Syndrome: Diagnosis, Treatment, and Research, Third Edition, Randi Jenssen Hagerman, M.D., and Paul J. Hagerman, M.D., Ph.D.



Resources

- Fragile X Syndrome: A Handbook for Families and Professionals, The National Fragile X Foundation, 2002
- Go to www.fraxa.org and click on Family Listserv to join
- My Extra Special Brother by Carly Heyman



Special Thanks

- Aimee E. A. Anido, MS, CGC
Board Certified Genetic Counselor
FXS Research Team
Department of Human Genetics
Emory University School of Medicine



And . . .

- Emily Graves Allen, Ph.D
Postdoctoral Fellow
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- Michele J. Rusin, Ph.D., Consultant
- Lisa Shubeck, Research Project Coordinator
- Darlene Sowemimo, Research Project Coordinator
- Stuart W. Tinker, B.S.E., Database Analyst & Software Developer
- Maneesha Yadav-Shah, Senior Research Specialist, Lab Director

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In closing . . .

- “Just keep moving forward to help your child achieve as much as he or she can. Don’t ever expect less just because of a number on a piece of paper.”
 - Quote from a parent of a child with FXS

References

- Children with Fragile X Syndrome: A Parent’s Guide, Edited by Jayne Dixon Webber
- Fragile X Syndrome: A Handbook for Families and Professionals, The National Fragile X Foundation
- Fragile X Syndrome: Diagnosis, Treatment, and Research, Third Edition, by Randi Jenssen Hagerman, M.D., and Paul J. Hagerman, M.D., Ph.D.
- Thompson & Thompson, Genetics in Medicine