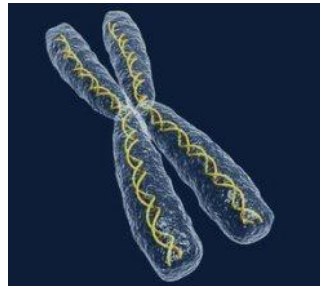


# Fragile X Syndrome In the Academic World



Stramski Children's Developmental Center Outpatient Clinic



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# Miller Children's Hospital Long Beach Memorial Care Health System

## Clinics offered:

- International Adoption Program
- High Risk Infant Follow-up Program
- Craniofacial Program
- Genetic Program
- Sleep Program
- Behavioral and Neurodevelopmental Program
- **Fragile X Program**

# Why?

## “Knowledge and Perceptions About Fragile X Syndrome: Implications for Diagnosis, Implications and Research”

- Brenda Finucane, Barbara Haas-Givler, and Elliot Simon

How would you rate your overall knowledge about fragile X syndrome?

Not at all knowledgeable: 44.2%

Somewhat knowledgeable: 54%

Very knowledgeable: 1.8%

# Fragile X Syndrome

- Leading known cause of **inherited** intellectual disabilities
- 30% individuals with FXS are diagnosed with an **Autism Spectrum Disorder**

In a typical year, how often do you ask parents of new clients about the cause of their child's disability?

Never: 40.1%

Occasionally: 33%

Most of the time: 12.8%

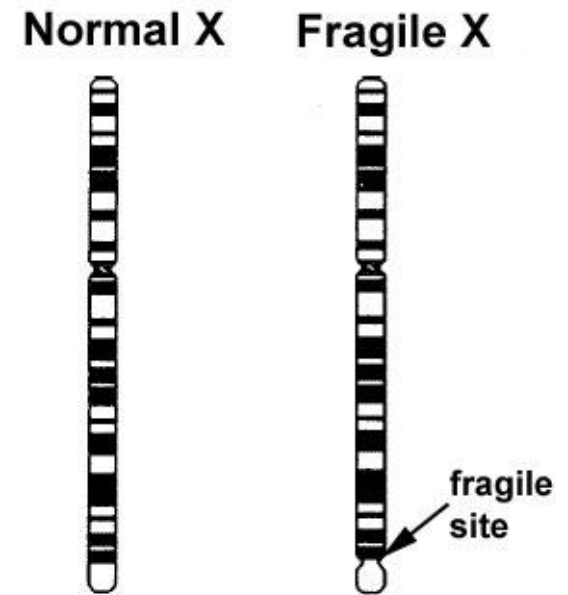
Always: 12.5%

# Prevalence

- 1 of every 2500-4000 individuals
- 1 in 4000 in males
- 1 in every 6000-8000 females
- Premutation:
  - 1 in 130-250 in females
  - 1 in 250-810 in males
- 2-6% of children with Autism have FXS

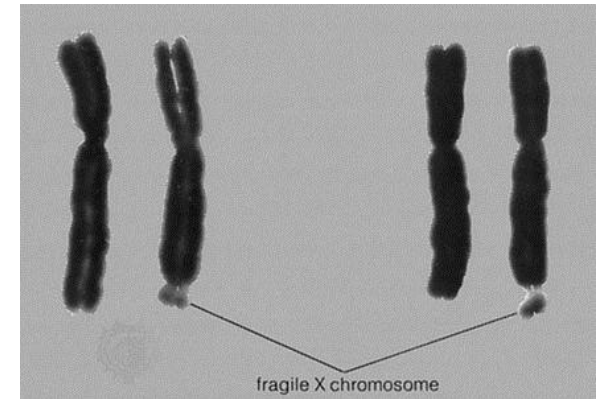
# What Causes FXS

- Abnormality of the fragile X mental retardation 1 (FMR1) gene
- FMR1 responsible for production of fragile X mental retardation protein (FMRP)
- FMRP responsible for brain development
- Individuals with FXS are deficient in FMRP



# What Causes FXS Continued...

- Increased Cytosine-Guanine-Guanine (CGG) repeats accounts for the “fragile” site of the DNA
  - 5-44 repeats = normal
  - 45-54 repeats = grey zone
  - 55-200 = premutation
  - greater than 200 = full mutation (hypermethylation of FRM1 and decreased FMRP production)



# Fragile X Mutations & Assoc. Disorders

- Fragile X Syndrome (FXS)
- Fragile X associated primary ovarian insufficiency (FXPOI)
  - Menopause prior to 40 years of age
- Fragile X associated tremor/ataxia syndrome (FXTAS)
  - Affects (mainly) males over 50 years of age



# Physical Characteristics Associated with FXS

- Loose Connective tissue
  - Pronated ankles
  - Hyperextensive joints
  - Pes Planus
- Heart murmurs
- Hypotonia
- Large Cupped Ears
- Single palmar crease
- Visual impairments
- Narrow high arched palate
- Scoliosis
- Motor tics
- Larger head circumference and pronounced forehead

# Physical Characteristics Associated with FXS continued...

- Taller, however 20-25% are significantly shorter than general population
- Soft velvety skin
- Club foot
- Hallucal crease (a single crease between the first and second toes)
- Pectus Excavatum
- Macroorchidism
- Attractive appearance
- Prader Willi Subtype

# Early Developmental History

- Speech Delays
- Gross and Fine Motor Delays
  - Loose connective tissue can impact this.
- Social/Emotional delays
- Delayed adaptive behavior

# Behavioral Characteristics

- **ANXIETY**/Perseverations
- ADHD symptoms
  - Hyperactivity/Impulsivity improves in adulthood but inattention can remain.
- Autism and Autistic-like features
- Depression
- Speech and Language characteristics:
  - Echolalia
  - Scripting

# Behavioral Characteristics Continued...

- Hand flapping
- Hand biting
- Stiffening, “Power Salute”
- Tantrums
- Gaze aversion
- Difficulty relating to others
- Hypervigilance



# Family History

- Early onset menopause before the age of 40
- Difficulty getting pregnant
- Fibromyalgia
- Systemic Lupus
- Arthritis
- Migraines
- Anxiety
- Schizophrenia
- Depression/mood disorders
- Parkinson's/tremors
- Developmental Delays/Intellectual Impairments
- Autism



# Family Dynamics

## ➤ Carriers/Mothers

### ➤ Social Emotional

- Anxiety
- Depression
- Guilt
- “Pleasers”
- Denial

### ➤ Intellectual Abilities

- Accessing service
- Understanding of child's abilities



## ➤ Unaffected Fathers

### ➤ Coping Styles

- Task oriented
- Shut down

## ➤ Extended Family

- Blame
- Denial
- Siblings

# Treatment Recommendations

- Early detection
- Special Education
- Psychological Evaluations
- Speech and Language Therapy
- Occupational Therapy
- Behavioral Therapies
- Social Skills
- Counseling





# Treatment Options Continued

- Parenting Courses
- Ophthalmologist
- Orthopedic
- Dental
- ENT for recurrent Otitis and Sinusitis
- Cardiac
- Endocrine
- Genetics
- **Medication:** Treat the symptom!

# Medications

- Atypical antipsychotics
  - Risperidone
  - Abilify
- Psychostimulants
  - Methylphenidates (demonstrate better efficacy in FXS population)
  - Mixed Amphetamine Salts
- Alpha 2 Agonists
  - Clonidine
  - Guanfacine



# Medications Continued...

- SSRI
  - Zoloft
  - Prozac
- Off label medications
  - Minocycline (speech)
- Drugs in development (Roche, Seaside, Novartis)

# *Evidence for the mGluR Theory of Fragile X*

In FMR1 knock-out mice, mGlu5 pharmacological inhibition:

## **Corrected**

- Excessive protein synthesis in the hippocampus
- Elevated mGlu-LTD in the hippocampus
- AMPA receptor internalization
- Learning and memory deficits
- Hypersensitivity to sensory stimuli
- Elevated locomotor activity and other behavioral phenotypes
- Increased susceptibility to audiogenic seizures
- Dendritic spine phenotype in the visual cortex
- Abnormal intracellular signaling in the cerebral cortex

## **Partially corrected**

- Macroorchidism upon chronic treatment



Before Moving on....

Any Questions?

# School Role

- Psych
- Teachers
  - SPED
  - GEN ED
- OT
- PT
- APE
- Speech
- Social Skills
- Social Emotional
- Behavior



# Before determining Placement, we determine ability

- Understand the information yielded from assessment
  - Achievement Scores are typically higher than Developmentally Delayed control subjects.
  - Yet Overall Cognitive Scores are typically more scattered and lower than control subjects (DD)

Cornish et al 2005

# Evaluation of abilities continued

- Simultaneous learning rather than sequential.
  - **Look at the “big picture”**
- Results of Direct Assessment
  - WJ-III
  - K-ABC
  - SB-V



# Cognitive Profile - Strengths

- Long Term Memory *esp. when associated with high interest*
- Verbal-Visual Associations for Learning
- Social awareness – facial perception

# Areas of Need

- Cognitive Shifting, Sustained and Selective Attention
- Short term memory
- Phonemic Awareness/Auditory Processing
- Speech- linguistic processing
  - Syntactic & Pragmatics: Delayed or Deviant?
- Visual Spatial cognition
- **Anxiety**

# Supportive Research

- “Specific areas of cognitive deficit for males include visuospatial abilities, visual–motor coordination and short-term memory ([Kemper et al., 1988](#); [Crowe and Hay, 1990](#); [Freund et al., 1993](#)).
- Behaviorally, males with fragile X syndrome often exhibit hyperactivity, autistic features, difficulties with peer interaction, abnormal social communication, gaze avoidance and motor stereotypies” Eliez et al 2001

# Fragile X in the Academic Environment

## ➤ Triple A

### ➤ Alliance

- Work with the family

### ➤ Attitude

- The tone of the classroom, teacher, the paraprofessionals

### ➤ Approach

- Initiation of relationships, interactions

# Understanding the Child in the Classroom

- “Most important variable to determine positive outcomes of student continues to be the **quality of teacher and structure of the environment**” Symons 2001
- Predictability and Structure
- High interest material assists with sustained attention
- Facilitated Support is *facilitated* and not hand over hand as anxiety is hallmark

# Learning Strategies

- Structure
  - Structure gives a final product to promote awareness
  - Active participation in Schedules
  - Side conversation about schedule with others to prepare
  - Token board/picture schedule

# A Bit more about Structure

- Reduces Anxiety
  - Example: the clinic drug trial days.
- New skills to be embedded in familiar activity/task

# Learning Strategies - *Part Deux*

- High Interest Sustains attention because it is familiar (words, sounds, visuals etc.)
- More Visual Less Verbiage
- Repetition



# Learning Strategies - *Part Trois*

- Allow child to place into context rather than create context (Closure technique)
  - Utilize their need for completion to teach
  - Visual Memory (Backward Chaining)
  - Modeling/Pre-teaching
  - Whole word reading less phonemic reading

# Learning Strategies *Part Quatre*

- Close proximity to instruction though not central focus (again, anxiety)
- Use of Technology for expression
- Behavior Plans:
  - Attention and Learning Behaviors
- Relaxed eye gaze from instructors (consider the approach)

# Learning Considerations

- Consider inclusion in the general education environment with minimal aide support.
- Logo Reading System – Braden
- Math instruction completion based
  - Simultaneous (dot math, patterns, matching)
- Writing instruction also completion based

# Transition

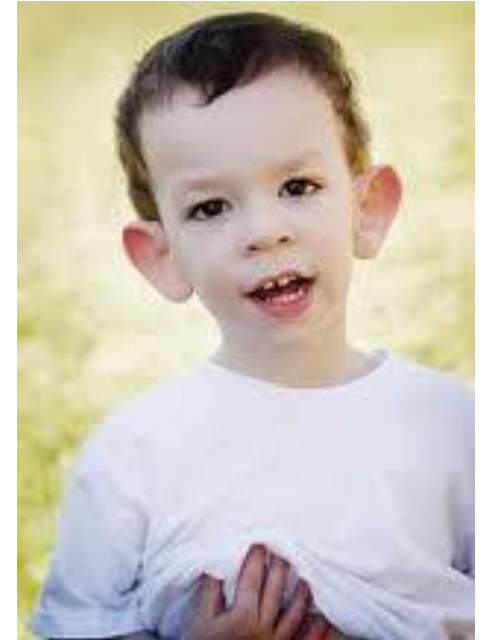
- Adults with Fragile X can live and work successfully independent
  - Video
  
- Struggles: Anxiety

# Sensory Integration Characteristics

- Touch
- Sound
- Sight
- Movement/  
balance



# Case Study





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