Fragile X Syndrome
In the Academic World

Stramski Children’s Developmental Center Outpatient Clinic

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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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References Continued...


References Continued...

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