

SOLUTIONS

Fragile X Syndrome

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SOLUTIONS

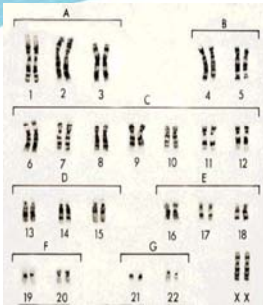
Genotype & Phenotype

- **Phenotype** = The observable manifestations of a person's genotype (which includes physical characteristics such as height & facial features, as well as predisposition to certain health problems: heart disease, strabismus).
- **Genotype** = A person's genetic makeup (the combination of genes of an organism or an individual).
Dykens, Hodapp & Finucane, 2000

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Chromosomes

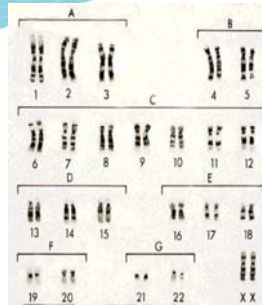


- 46 chromosomes organised in 23 pairs.
- These chromosomes contain condensed coils of DNA code in the form of genes.
- One member of each chromosome pair is inherited from your father & the other from your mother, at conception.

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Chromosomes



- 22 of the 23 pairs of chromosomes are similar in both sexes & are called **autosomes**.
- The chromosomes making up the 23rd pair are called the **sex chromosomes** because they determine a person's gender.

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What exactly is a genetic mutation?

- When one or both copies of a specific gene presents an alteration in the DNA, which alters the designated function of that gene.
- For example,
 - Deletion or microdeletion of part of a chromosome.
 - Repetition of genetic code: CGG


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Chromosomal Abnormalities

FIGURE 2.10 : Caryotype d'un sujet atteint du syndrome de Down*

* Cette illustration des chromosomes d'une fille atteinte de trisomie 21 (photos du bas, figure 2.9) montre les trois chromosomes présents à la 21^e paire.

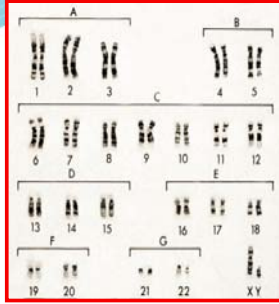


- Most common type= ANEUPLOIDY = an abnormal number of chromosomes (+ or -).
 - Monosomy (rare; ex. Turner syndrome(45X0).
 - Trisomy (ex. Down (21), 13, 18, Klinefelter (XXY))

* Figure élaborée à partir de STREIBENBERGER, M.W. (1985) Genetics, 3^e éd., New York, MacMillan, p. 424, figure 21-20.

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Fragile -X Syndrome SOLUTIONS



- Section q27.3 of the X chromosome
- Prevalence:
 - 1 / 1500-4000 males
 - 1 / 2500-8000 females
 - 1 / 256 females are carriers of the premutation (Rousseau et al., 1995)
 - 1/800 males are carriers
- Present in all ethnic groups

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Fragile -X Syndrome SOLUTIONS

- Most common inherited cause of DD
- Females usually have milder symptoms (compensation by other X chromosome)
- Often initial dx of autism or PDD-NOS
 - 39% of males with fragile X had dx of autism or PDD in childhood
 - 16-17% of adults with fragile X meet DSM criteria for autism
 - 0-16% males with dx of autism test + for fragile X

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Fragile X Syndrome SOLUTIONS

- Fragile X syndrome is associated with an expanded repetition of the trinucleotide CGG which, in « normal » persons, is repeated between 6 and 50 times.
 - 1) normal = 6 - 50 CGG repeats
 - 2) premutation = 50-200 CGG repeats (*FXTAS)
 - 3) full mutation = 200 + CGG repeats (Fragile X)

*increased impact over generations

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*FXTAS: Fragile X-associated Tremor/Ataxia Syndrome SOLUTIONS

- Progressive neurological disorder:
 - tremor & ataxia (& eventually memory problems, moodiness & irritability)
- Onset 50-60yrs (granddads of Fragile X kids)
- ONLY 20-30% of male carriers >50 affected
- Often misdx'ed as atypical Parkinson's, multiple system atrophy, etc
- May provide insight into FMR1 gene deactivation

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Characteristic features: SOLUTIONS

- Long face
- Prominent chin
- Prominent ears
- Larger head circumference
- Joint hypermobility/hyperextension
- Macro-orchidism

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Characteristic features: SOLUTIONS

- Associated medical concerns:

- Strabismus	- Serous otitis
- Flat feet	- Dislocated hips
- Mitral valve prolapse (MVP)	- GERD
- Obs Sleep apnea (OSA)	- ADHD
- Autistic features (poor eye contact, hand-flapping, hand-biting)	- Seizures
	- Mental retardation

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Shyness, social anxiety & hypersensitivity

- Shy, timid personality
- Difficulties w/ peer interactions compared to interactions w/ adults.
- Excessive anxiety in new situations/environments.
- Hypersensitivity: Tendency to 'overreact' to 'minor' frustrations .

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Sensory Issues:

- hyper arousal (sound of fluorescent lights, sight of too many decorations on wall)
- hypo arousal (sound of the teacher's voice, rather than the sound of the humming computer, fluorescent lights, and aquarium bubbler)
- sensory motor integration problems (including motor planning issues and fine motor weaknesses)
- tactile defensiveness (hypersensitivity to touch)
- difficulty in many new, confusing, or loud situations (because of a combination of sensory integration problems, anxiety, and attention deficit disorders)

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Tactile Defensiveness

- Affects 60-90% of FXS boys & some FXS girls
- Overreaction to touch & may avoid it
- Increased or decreased reactions to textures:
 - Clothing & tags
 - Need soft fabrics, no elastic cuffs or hems
 - May prefer deep pressure of heavy clothing for increased feedback
- Have difficulty identifying objects or feeling & receiving info by touch

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Tactile Defensiveness

- Firm, sure touches (handshakes & bearhugs) may be tolerated better than light touch (tickling, soft touch of face)
- May prefer to be at end of the line, separate from crowd
- Infants may/may not be comforted by cuddling
- May not enjoy finger painting or other tactile art activities

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Tactile Defensiveness

- Difficulties with hygiene:
 - Bathing, face & hair washing, shaving, nail cutting
- Dental visits may be difficult & anxiety provoking
- Difficulties with eating:
 - Difficulty nursing from breast or bottle
 - Strong food preferences related to textures of food
 - Mouth stuffing of mouth, due to high "cathedral" palate, before realizing they may gag

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Remember:

- A specific problem in the environment that can be modified will often effect a much larger improvement in behavior than medication!
- Maximize environment FIRST to get a reasonable baseline!

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Tactile Defensiveness: strategies for intervention

- Sensory diet: individualized by an OT
- Uses neurodevelopmental therapy working with muscle tone & sensory integration therapy (SI), involving all senses plus proprioception (body position in space) & vestibular (sense of gravity & motion) input
- To find best combination & timing of various sensory inputs & decreases sensory overload

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Tactile Defensiveness: strategies for intervention

- Calming activities:
 - Rocking, swinging child
 - Applying deep pressure
 - Brushing child's skin with therapeutic brush
 - Break time: quieter area, playing computer game or listening to music or a story on headphones

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Tactile Defensiveness: strategies for intervention

- Environmental changes:
 - Increase natural light
 - Limit/avoid exposure to loud situations
 - Gradual desensitization to be able to tolerate more noise
 - Adapted seating to help maintain upright posture with enough feedback:
 - Donut-shaped cushions, foam wedges

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Fine & Gross Motor skills

- Movement therapy to improve balance, muscle tone & proprioception:
 - dance, martial arts, sports, physical play
- Practice to improve use of
 - pens/pencils for writing & drawing
 - utensils, scissors & tools
 - Keyboard (computer use)

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Oral-motor activities

- Activities to
 - increase tolerance to touch around face & mouth
 - improve chewing, swallowing & speaking
- Use of foods & toys:
 - Blow toys, whistles, straws
 - Crunchy or chewy food: fruit snacks, celery, bagels, gum
 - *may decrease chewing on clothing, straps or skin!

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Fragile X Syndrome - attention deficits/hyperactivity

- ↓ distractions: study cubicles, desk at front of classroom or in calm area (facing a wall), periods of quiet time, decreased flow of traffic in room, adequate natural lighting & heat, small group instruction, reduced noise level
- Seating near an exit, allow removal from stressful events
- ↑ use of visual cues (photos, etc) for transitions
- Provide non-verbal cues & feedback
- Simple phrases & concrete communication
- Structure/routine/predictability

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Fragile X Syndrome - general approach

- Do not force eye contact! (gaze aversion)
- Be careful invading personal space & touching the person! (tactile sensitivity)
- Consistency important! (staffing, schedules, environment)
- *Provide a book to carry with them containing info that may be difficult to remember

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FXS - more teaching approaches...

- Using pictograms, photos, objects of special interest or hands-on approach
- Using clocks, license plates & cooking to help with number concepts
- Indirect explanation: teach task to neighbour
- Apply person's strengths: long-term memory, imitation skills, sense of humour
- Teach complete tasks: present whole process (not step-by-step) & use cover up method to follow sequence (Ø lose his place)

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FXS – ADL stuff

- Sleep:
 - PJs & bedding
 - Dark room/shades
 - Soothing sounds, music
 - Bedtime routine
- Eating:
 - Try various nipples/positions
 - OT interventions for improved oral motor functioning

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FXS – ADL stuff

- Dressing:
 - Remove tags, soft fabrics
 - Buttons, snaps easier or T-shirts
 - Shoes w/ velcro, curly laces
- Hygiene:
 - Desensitization to water on skin, calming strategies
 - Pictures of sequence of activities
 - Firm pressure with facecloth vs light strokes
- Dental
 - Egg timer
 - Desensitization: books, visits w/ mom, sibling

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FXS - strategies vs. aggression

- **Functional analysis: A-B-C data collection**
- Aggression may be preceded by giggling, non-compliance or avoidance
- Most common cause: anxiety!
- May be d/t sensory processing problems or hypersensitivity: sensory stimulation 'adds up' during the day & sensory activities may be more challenging later in the day (↑ demands are more difficult)
- *higher incidence in adolescents: hormones!

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FXS - strategies vs. aggression

- Indications of anxiety:
 - Worry/anxiety over changes in routine or upcoming stressful events (fire drills, assemblies): 'hyper vigilance'
 - Will stiffen up when angry or upset, becoming rigid & tense
 - May simply tighten up hands
 - Crying, whining tantrums may all be d/t overwhelming settings!

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FXS - strategies vs. aggression

- “Catch them being good!” with reinforcement of + behavior
- Specific interventional approaches: ABA, Lovaas, token economy, ‘time-outs’ (removal of attention)
- Psychotherapy & individual counselling (self-esteem, depression, anxiety, coping skills, frustration, anger management, social skills)
- Family Therapy

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Fragile X Syndrome - strategies vs. aggression

- Relaxation training, sensory stimulation/ sensory integration (OT), music
- Deep pressure massage
- Use of imagery
- Group Therapy & Social Skills training (role playing, especially with behavioral consequences)

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*Fragile X Syndrome - issues around sexuality

- Social Sexual skills
- Sex Ed. throughout & beyond puberty
- Sexual abuse prevention information
- Psychotherapy & counselling (self-esteem, depression, anxiety/frustration) (especially helpful for transition from parents’ home to independent living)

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FXS - strategies vs. aggression

Consider differentials:

1. Panic episodes: ‘fight or flight’: flushing, turning pale, rapid breathing, sudden sweating
2. Mood disorders: Depression or Bipolar disorder (disturbed or absent sleep, excess or loss of appetite, changes in activity level, mood changes, increased irritability)
3. Seizure disorder (aggression appears aimless, or unassociated with any ongoing event, occurring with unusual movements, brief loss of consciousness, confusion or need to sleep afterwards)

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Treatment

- Referrals to : speech Tx, OT, behavioural Tx
- Medications for medical problems: epilepsy, MVP & HTN
- Medications for psychiatric problems: anxiety (anti-anxiety: SSRIs) & ADHD
- Future prospects: gene therapy

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Websites

- Geneclinics : <http://geneclinics.org/> (see: Gene Reviews)
- Your Genes, Your Health: <http://www.ygyh.org/>
- Online Mendelian Inheritance in Man: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>
- Genetics Education Center, University of Kansas Medical Center: <http://www.kumc.edu/gec/support/>
- The Family Village: <http://www.familyvillage.wisc.edu>

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Websites 

Genetics Website

(In English, French, Spanish, German, Italian & Portuguese!):

- Orphanet: <http://www.orpha.net/consor/cgi-bin/index.php>

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Websites 

Health Watch tables for several genetic syndromes & other tools from the Canadian Consensus Guidelines developed at Surrey Place in Ontario, Canada:

www.surreyplace.on.ca/Clinical-Programs/Medical-Services/Pages/PrimaryCare.aspx

- The Fragile X Research Foundation of Canada
Website: <http://www.fragile-x.ca>
- FRAXA Research Foundation (USA)
Website: www.fraxa.org
- The National Fragile X Foundation (USA)
Website: <http://www.nfxf.org/html/what.htm> or <http://www.fragilex.org/html/home.shtml>

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