Health and Development in XYY Syndrome

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Slides contribution from Nicole Tartaglia, MD

Outline

- Medical Problems in XYY
- Development and Neurodevelopmental Disorders in XYY

XYY Syndrome

- 1 in 1000 live-born boys
- 85% or more males with XYY are never diagnosed
  - No dysmorphic facial features, normal IQ range
  - Biased early studies of males in prisons or had psychiatric diagnoses
  - Lack of large scale studies
  - Ascertainment bias
    - Clinic based sample
    - No newborn screening
Sources...

- Medical Literature
  - Prospective cohort studies 1970’s & 80’s
  - Genetics Textbooks
  - Journal Articles
- Parents & Patients

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**XYY** (Bardsley, 2013)

- Age range (n=90)
  - 6 months-36.5 years
  - Mean = 9.6 years
- Diagnosis
  - 35 Prenatal
  - 55 Postnatal
  - 5 hypotonia
  - 7 language delay
  - 17 behavior
  - 26 Other (dysmorphic, parent’s request)

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**Medical Care in XYY**

- Growth
- Bones and Joints
- Acne
- Tics and Tremors
- Motor Tone and Coordination
- Puberty, Testosterone, Fertility
- Other
Growth in XYY

- Tall stature
- Mean height above average
- Height < 6 years average, but above average > 6 years
- Taller than fathers by 4-5 inches
- XXY 6 feet vs. XYY 6 ft 3 inches
- Puberty usually slightly delayed
  - Pubic hair 13.8 yrs vs. 12.4 years in male siblings
  - Growth spurt later but longer duration than siblings

Bones and Joints

- Flat Feet
  - Pes Planus
  - Treatment controversial in mild cases
    - Arch supports vs. no arch supports
    - Moderate to severe cases
      - Orthopedic Evaluation
      - Orthotics

- Elbows
  - Radioulnar synostosis
    - 2 reported cases in literature
    - 1 case in our sample
  - Inability to pronate and supinate forearm
  - Limited range of motion can interfere with fine motor skills
  - X-ray if limited range of motion
  - But, usually no treatment…
Other Medical Findings

- 52% with Clinodactyly
- 59% with Hypertelorism
- 22% Dental problems
  - Prognathic jaw with underbite and macrodontia
- 63% Hypotonia
  - Decreased strength, tone, coordination
- 52% Flat Feet

Acne

- Literature
  - 4 reports from 1970’s
  - Nodulocystic acne
  - 7/36 age 13+ (19.4%) with Mild-Moderate Acne (same as general population)
  - 0 with Severe, Cystic Acne
- Consider impact on self-esteem & peer relationships
- Treatments:
  - OTC preparations
  - Pediatricians / Dermatology
    - MANY EFFECTIVE MEDICATION TREATMENTS!

Co-Morbid Diagnoses

- 39% Asthma vs 9.6% general population
  - Asthma improves with age
  - Consider asthma diagnosis if your child has frequent respiratory infections
- 13% Seizures vs 1% general population
  - Treatment is the same as the general population
Tics

- Literature
  - Geerts et al. (2003) – 5/38 XYY males (13%)
  - Reports of Tourette’s Syndrome
- Prelim study 6/27 (22%)
- Tics
  - Motor vs. vocal
  - Occur in up to 10% of children during childhood
  - Treatment when impacting social development and self-esteem
    - No medications
    - Medications to target tics
    - Management of anxiety
  - Can be side effect of stimulant (ADHD medications)

Tremor

- Literature
  - Multiple reports of hand tremors
- Prelim study 7/27 (22%)
- Most likely to present >8-9 years, increases in adolescence
- Intention Tremor of hands
- Impacts writing and fine motor skills (self-care skills)
- Treatment:
  - Supports in school (keyboarding)
  - Weighted pens, cups, eating utensils can decrease tremors
  - Medications can be helpful if severe

Motor Tone & Coordination

- Low Muscle Tone / Hypotonia (63% cases)
  - Multiple reports in the literature
  - Consider physical therapy or activities to help with tone, coordination, and strength
- Salbenblatt et al (1987)
  - 4 males with XYY
    - Hypotonia (low muscle tone)
    - Motor planning dysfunction / dyspraxia
    - Problems with bilateral coordination
    - Problems with visual-motor integration
Motor Tone & Coordination

- MIND Institute Patients
  - Visual-Motor Coordination
  - 67% had motor coordination scores in the delayed range
- Recommendations:
  - Occupational/Physical therapy evaluations and treatments
  - Keyboarding/Assistive technology

Puberty, Testosterone, Fertility

- XYY is NOT XXY
- Most cases have normal puberty and are not infertile!!
- It is important to be aware of risks in these areas…
- PUBERTY –

Puberty, Testosterone, Fertility

- Testosterone levels in XYY – Many studies
  - Too high? Too low? Normal?
  - 39/43 normal testosterone level for age, 1 high testosterone, 1 low testosterone and delayed puberty (Bardsley et al, 2013)
- Low testosterone production = hypogonadism
  - Clinical Signs of hypogonadism
    - Fatigue, Poor endurance
    - Low body hair, decreased sexual development
    - Small penis, testicles
    - Mood instability, depression
  - Concerns?? Evaluation by endocrinologist (doctor specializing in growth and hormones)
Puberty, Testosterone, Fertility

- Fertility
  - Survey of 1,007 males with infertility
    - 3 with XYY (0.3%)
  - 28 with XXY (3%) (Other studies 2-18%)
- XYY males are at higher risk for:
  - X&Y variations in their sperm
  - Children with XXY, XYY (and others?)
- Genetic counseling prior to childbearing to discuss risks

Other Medical Problems

<table>
<thead>
<tr>
<th>Medical Issues</th>
<th>Prenatal</th>
<th>Postnatal</th>
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<tbody>
<tr>
<td>Hypotonia</td>
<td>51%</td>
<td>71%</td>
</tr>
<tr>
<td>Clinodactyly</td>
<td>46%</td>
<td>57%</td>
</tr>
<tr>
<td>Dental Problems</td>
<td>29%</td>
<td>18%</td>
</tr>
<tr>
<td>Flat feet</td>
<td>44%</td>
<td>59%</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>9%</td>
<td>16%</td>
</tr>
<tr>
<td>Motor Delay/dyspraxia</td>
<td>23%</td>
<td>18%</td>
</tr>
<tr>
<td>Low musculature</td>
<td>20%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Outline

- Medical Problems in XYY
- Development and Neurodevelopmental Disorders in XYY
**XYY and Development**

AT RISK FOR:
- Speech and Motor delays
- Learning Disabilities
  - Verbal
  - Reading
- Short attention span
- Impulsivity
- Social Skills problems
- Sensory Integration Problems
- Anxiety, Depression, Mood Disorders

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**XYY Syndrome**

(2003) Geerts et al, Genetic Counseling

<table>
<thead>
<tr>
<th></th>
<th>PRENATAL DX (n=12)</th>
<th>POSTNATAL DX (n=26)</th>
</tr>
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<tbody>
<tr>
<td>Normal IQ</td>
<td>100%</td>
<td>92%</td>
</tr>
<tr>
<td>FSIQ</td>
<td>95.8</td>
<td>89.9</td>
</tr>
<tr>
<td>Special Ed</td>
<td>8%</td>
<td>50%</td>
</tr>
<tr>
<td>Speech delay</td>
<td>50%</td>
<td>77%</td>
</tr>
<tr>
<td>Motor delay</td>
<td>25%</td>
<td>85%</td>
</tr>
<tr>
<td>PDD</td>
<td>0%</td>
<td>19%</td>
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</tbody>
</table>

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Source: Adapted from Randy Ross, M.D.
### XYY Syndrome (Bardsley, 2013)

<table>
<thead>
<tr>
<th></th>
<th>PRENATAL DX (n=36)</th>
<th>POSTNATAL DX (n=44)</th>
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</thead>
<tbody>
<tr>
<td>Full Scale IQ</td>
<td>102</td>
<td>85</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>101</td>
<td>82</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>107</td>
<td>90</td>
</tr>
<tr>
<td>Special education</td>
<td>23%</td>
<td>52%</td>
</tr>
<tr>
<td>OT or PT</td>
<td>59%</td>
<td>70%</td>
</tr>
<tr>
<td>Speech therapy</td>
<td>64%</td>
<td>94%</td>
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### XYY Syndrome

<table>
<thead>
<tr>
<th></th>
<th>PRENATAL DX (n=15)</th>
<th>POSTNATAL DX (n=25)</th>
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<tbody>
<tr>
<td>CBCL behavior total</td>
<td>63</td>
<td>66</td>
</tr>
<tr>
<td>Internalizing total</td>
<td>61</td>
<td>62</td>
</tr>
<tr>
<td>Externalizing total</td>
<td>57</td>
<td>60</td>
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</tbody>
</table>

Most severe behavioral issues for both groups:
- Internalizing behaviors (withdrawn, somatic complaints, anxiety/depressed, social problems, thought, attention)

### XYY Syndrome

<table>
<thead>
<tr>
<th></th>
<th>PRENATAL DX (n=35)</th>
<th>POSTNATAL DX (n=55)</th>
</tr>
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<tbody>
<tr>
<td>ADD or ADHD</td>
<td>40%</td>
<td>60%</td>
</tr>
<tr>
<td>Verbal and motor tic</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Oppositional defiant</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Depression</td>
<td>11%</td>
<td>15%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>17%</td>
<td>31%</td>
</tr>
<tr>
<td>Autism/Pervasive</td>
<td>11%</td>
<td>40%</td>
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</table>
Behavioral Profiles - BASC
- Behavioral Assessment System for Children (n=31)

Sensory Integration Dysfunction
- Difficulty processing information from the senses (touch, movement, smell, taste, vision, and hearing) and responding appropriately to that information.
- One or more senses that either over- or underreact to stimulation.
- Sensory processing disorder can cause problems with a child’s development and behavior
  - Withdraw when touched.
  - Refuse to eat certain foods because of how the foods feel when chewed.
  - Oversensitive to odors.
  - Hypersensitive to certain clothes
  - Dislike getting his or her hands dirty.

Autistic Features
- Pervasive Developmental Disorders or Autism Spectrum Disorders
  - Autistic Disorder
    - Impaired Communication
    - Impaired Social-Emotional Reciprocity
    - Restricted Interests or Stereotyped Routines
  - Asperger’s Syndrome
  - PDD-Not Otherwise Specified (PDD-NOS)
Autism Spectrum Disorders

<table>
<thead>
<tr>
<th></th>
<th>XXY</th>
<th>XYY</th>
<th>XXYY</th>
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<tbody>
<tr>
<td>N</td>
<td>20</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Mean Age</td>
<td>9.13</td>
<td>9.45</td>
<td>12.19*</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>XXY</td>
<td>XYY</td>
<td>XXYY</td>
</tr>
<tr>
<td>Prenatal</td>
<td>8</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Postnatal</td>
<td>12</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>VIQ</td>
<td>102.3</td>
<td>90.4</td>
<td>76.75</td>
</tr>
<tr>
<td>PIQ</td>
<td>104.3</td>
<td>102.5</td>
<td>89.1</td>
</tr>
<tr>
<td>FSIQ</td>
<td>103.6</td>
<td>95.2</td>
<td>81.2</td>
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ADHD

- 33 males age 6-20 with XYY
- 76% of males with XYY Syndrome met DSM-IV diagnostic criteria for ADHD.
- 49% Predominantly Inattentive Symptoms
- 24% Combined Inattentive and Hyperactive/Impulsive Symptoms
- 3% Predominantly Hyperactive – Impulsive symptoms
- Prenatal 64% vs. Postnatal 82%
Attentional Problems

- Not all attentional problems are AD/HD
- Main features of Attention Deficit/Hyperactivity Disorder
  - Inattention
  - Hyperactivity
  - Impulsivity

ADHD Symptoms in Children

- Inattention
  - Difficulty sustaining attention in tasks or play activities
  - Difficulty organizing tasks or activities
  - Distracted by extraneous stimuli
  - Loses things necessary for activities (toys, school assignments, pencils)
  - Does not follow through on instructions

ADHD Symptoms in Children

- Hyperactivity & Impulsivity
  - Fidgets with hands or feet, squirms in seat
  - Is “on the go” or “driven by a motor”
  - Blurs out answers
  - Has difficulty awaiting turn, butts into conversations/games
  - Often runs around, climbs excessively when inappropriate
ADHD in Children

3-8% of children,
Male:female 3:1

ADHD – Combined Type
ADHD – Predominantly Inattentive Type
ADHD – Predominantly Hyperactive Type

It’s not always ADHD…

- All complaints of Inattention or Hyperactivity are NOT necessarily ADHD
- Other considerations:
  - Learning Disability
  - Dyslexia
  - Auditory Processing Disorder
  - Anxiety
  - Sensory reactivity/Sensory Integration Disorder
  - Seizures
  - Sleep Disorder, Obstructive Sleep Apnea
  - Mental Retardation
  - Diagnosis of ADHD by professional

Treatments for ADHD symptoms

- Behavioral Interventions
  - Strategies to support ADHD symptoms
  - Strategies to improve executive function
  - School accommodations
- Medications
Medications for psychological or behavioral problems in X&Y chromosome variations

- Not everyone will need medications
- Medical treatment of abnormality in brain development caused by genetic condition
- Medication treatment should always accompany behavioral therapies
- Criteria to consider treatments: (Only 1 needed)
  - Child expresses distress about symptoms
  - Interferes with learning, academic progress
  - Interferes with social development
  - Interferes with overall home life/general functioning
- If your child seems “drugged,” it is the wrong medication

Positive Response to ADHD Medications (n=101)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>XXY</td>
<td>73%</td>
</tr>
<tr>
<td>XYY</td>
<td>79%</td>
</tr>
<tr>
<td>XXX</td>
<td>75%</td>
</tr>
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</table>

Medications

- ADHD Medications:
  - Stimulants
    - Methylphenidate (Ritalin, Concerta, Metadate, Focalin, Daytrana, etc.)
    - Adderall
    - Side effects: decreased appetite, sleep disturbance, tics, agitation
    - Benefits: They work the day you give them, can use as needed
  - Nonstimulants - Effects generally not as strong as stimulants, but can also help with anxiety in some children
    - Strattera (atomoxetine)
    - Side effects: sedation, agitation
  - Alpha Agonists:
    - Guanfacine: Intuniv (long acting), Tenex (twice per day)
    - Clonidine: Kapvay (long acting)
    - Side effects: sedation
Other Medications in XYY

- Medications to target Anxiety, Mood Swings, Outbursts, Tantrums
  - Anxiety / Depression
    - SSRIs (Zoloft, Celexa, Prozac)
  - Atypical Neuroleptics
    - Abilify, Risperdal
    - Can also help with atypical thoughts, paranoia, psychotic symptoms
  - Sleep (Melatonin, Trazodone)

Questions???