Psychiatric and Neurodevelopmental Comorbidities in XXY

ERIN TORRES MSN, CRNP-PMH
DEVELOPMENTAL NEUROGENOMICS UNIT, NIMH
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD, USA

SRISHTI RAU, PHD
CHILDREN’S NATIONAL HEALTH SYSTEM
DEVELOPMENTAL NEUROGENOMICS UNIT, NIMH
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD, USA
Objectives

- Briefly review what previous research has demonstrated regarding rates of neurodevelopmental and psychiatric diagnoses in XXY
- Provide preliminary results from our sample of individuals with XXY in order to:
  - Discuss the variability in symptomatology among individuals with XXY
  - Underscore the need for multidisciplinary and comprehensive evaluation, and treatment
- Briefly provide guidance regarding key professionals and types of services that may support areas of struggle
Sex Chromosome Aneuploidy

- Typically there are 22 pairs of chromosomes plus one pair of sex chromosomes (X,Y)
- 47, XXY-males have an extra X chromosome
XXY

• Also known as Klinefelter’s Syndrome
• Occurs between 1 of 500 and 1 of 1000 live male births
• Many men with XXY go undiagnosed
  • This is changing with an increase in prenatal testing
• Physical features can include:
  • Tall stature, broad hips
  • Smaller testes
  • Difficulty with fertility
    • Most common genetic cause of male infertility
• #1 rule – great variability in XXY!
• There is an increased risk of impairments with
  • Language
  • Executive functioning
  • Social cognition
  • Emotion regulation
• Struggles in these areas contribute to higher rates of a number of neurodevelopmental and psychiatric diagnoses
Intellectual functioning (IQ)

- IQ falls in the average to low average range
- Typically not in the range of Intellectual Disability
- At younger ages, some studies indicate relatively stronger visual thinking skills relative to verbal reasoning abilities
ADHD rates amongst 5-20 yr olds with XXY
- 36% (20 out of 56)
  - 95% (19 of the 20) with ADHD – Inattentive subtype
  - 5% (1 of the 20) with ADHD – Combined subtype
- ADHD was diagnosed 5.6 times more often in adult men with XXY compared to men with XY
- Impacts grades and academic achievement
Learning Disorder (LD)

- Reading disability in XXY: 50-75%
- Literacy and spelling especially impacted, but struggles are not limited to these areas
- Pace of acquiring academic skills can be slower relative to unaffected classmates
- Struggles can persist into adulthood
Autism Spectrum Disorder (ASD)

- ASD rates vary depending on the method of diagnosis
  - Screening measures alone and/or parent interview: 12-47%
  - Comprehensive assessment: 5-10%
- ASD diagnosed 6.2 times more often in men with XXY compared to XY
Mood/ Depression

- Different Mood disorder subtypes
  - Major Depressive Disorder
  - Dysthymia
  - Disruptive Mood Dysregulation Disorder
- 300 million ppl suffer from depression
  - Lifetime prevalence – 11% amongst 13-18 yr olds
- Rates of depressive disorder in XXY 12-24%
Anxiety

- Common subtypes of anxiety disorder
  - Generalized Anxiety Disorder
  - Social Anxiety Disorder
  - Phobia
- Rates of anxiety disorder in XXY range from 14-32%
Additional comorbid diagnoses seen in XXY

- Psychosis
- Bipolar Disorder
- Obsessive Compulsive Disorder (OCD)
- Tourette’s / Tic Disorder
X And Y Chromosome Variation Development Study At NIH
We all have our own strengths and weaknesses

Can you solve this Fruit Math equation?

\[
\begin{align*}
\text{apple} &= 7 \\
\text{blackberry} + \text{apple} &= 5 + 1 \\
\text{apple} + \text{banana} &= ?
\end{align*}
\]
Demographic characteristics of Participants seen to date

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total participants seen</td>
<td>60</td>
</tr>
<tr>
<td>Age (years)</td>
<td>Mean=16.8; Median= 17.5; Range= 7-25</td>
</tr>
<tr>
<td>Number diagnosed prenatally or at birth [n (%)]</td>
<td>22 (37%)</td>
</tr>
<tr>
<td>Number diagnosed postnatally [n (%)]</td>
<td>38 (63%)</td>
</tr>
<tr>
<td>Age at postnatal diagnosis (years)</td>
<td>Mean=10.6; Range= 0.5-20</td>
</tr>
</tbody>
</table>
Prenatal versus Postnatal Diagnosis

Diagnosis Prenatally or at Birth: 37%
Diagnosis Postnatally: 63%

Age Distribution

Histogram of VISIT_AGE with Frequency counts.
ADHD

- 57% (N=34) with ADHD
  - Majority with ADHD Inattentive Presentation

No Diagnosis, no problems? Not quite…

- Clinically elevated challenges in those without ADHD (N=25):
  - Attention (12%)
  - Executive functioning (20%)
Autism Spectrum Disorder (ASD)

- Comprehensive assessment
- 12 (20%) had a prior ASD diagnosis
  - 2 with prior diagnoses did not meet criteria for ASD
  - 10 ASD diagnoses maintained
- 48 (80%) came in without prior ASD
  - 8 were diagnosed with ASD for the first time
- Total rate in our sample is 30%**
  **Interim rate; data collection ongoing

- Clinically elevated challenges in those without ASD
  - 35% with Social Skills
  - 50% with Executive functioning

[Pie chart showing distribution between ASD and No ASD]
K-SADS

- Schedule for Affective Disorders and Schizophrenia for School-Aged Children
- Assessment completed with parent/guardian
- Current Diagnoses
- Past Diagnoses
Mood

Met criteria for MDD
- 11.7% met criteria for any mood disorder
  - MDD 3.3%
  - Dysthymia 3.3%
  - DMDD 5%

Difficulties amongst those without a depressive disorder
- 28.8% CBCL internalizing

No Depression Diagnosis
MDD
DMDD
Dysthymia
Anxiety

KSADS
- 20% met criteria for an anxiety disorder per the KSADS
- 11.7% met criteria for GAD
- 6.7% met criteria for Social Anxiety

Difficulties amongst those without an anxiety diagnosis
- 17% CBCL internalizing
Prenatal vs. Postnatal

- **ASD**
  - **Prenatal**: [counts]
  - **Postnatal**: [counts]

- **ADHD**
  - **Prenatal**: [counts]
  - **Postnatal**: [counts]

- **Depressive Disorder**
  - **Prenatal**: [counts]
  - **Postnatal**: [counts]

- **Anxiety**
  - **Prenatal**: [counts]
  - **Postnatal**: [counts]
Take home points

- Individuals with KS are at greater risk for a number of neurodevelopmental and psychiatric diagnoses
- If you have concerns about a child’s development, seek (or refer for) evaluation and treatment
- Symptoms should not be attributed to their genetic diagnosis alone
- Symptoms can improve with appropriate interventions
- Often a diagnosis can aid in getting to the right intervention
Types of supports

- Speech-language
- ABA
- Social Skills group
- IEP/504 plan
- Academic interventions
- Psychotherapy
- Psychiatry
- Endocrinology
- Transition supports
  - AXYS resources
  - Statewide agencies
Our Team

Developmental Neurogenomics Unit

Armin Raznahan, MD, PhD
Cassidy McDermott, BA
Ajay Nadig, BA
Jonathan Blumenthal, MA
Srishti Rau, PhD
Marissa Miller, PhD
Lauren Kenworthy, PhD
Erin Torres, MS, CRNP-PMH
Francois Lalonde, PhD
Liv Clasen, PhD
Kathleen Wilson, BA
Ethan Whitman, BS
Allysa Warling, BA

Will join in September 2019:

Christy Casnar, PhD
Kim Schauder, PhD
Thank you!

Questions?

If interested in learning more about or joining our study, please contact Jonathan Blumenthal, MA at jb364e@nih.gov

Flyers with study details are also available at our table.
References


