Family genetic background contributes to phenotypic variability in sex chromosome variations and other neurodevelopmental conditions

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June 25, 2017
Disclosures

- Consultant, Board of Directors National Fragile X Foundation
- Consultant, Labcorp

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Clinical Variability in SCV

- Wide variability in physical and developmental symptoms
- Increased chance for social difficulties, language impairments, learning differences
- Implications for:
  - Prognosis
  - Intervention
  - Family Stress
**Quantitative Traits**

*Quantitative trait:* a measurable characteristic that depends on the cumulative actions of many genes and the environment. These traits vary among individuals, over a range, to produce a continuous distribution (curve).

Examples include height, weight, blood pressure, certain personality traits, motor skills, and learning abilities.
Height as a Quantitative Trait
Human quantitative traits tend to be highly heritable

Michael Jordan  6’6”

Lindsey Vonn  5’10”
Family Study of Quantitative Traits

- Study of heritability of quantitative traits that influence learning and behavior
- Impact of family background on symptom variability in people with SCV and other genetic conditions
- Studying unaffected parents and siblings, as well as the person with SCV, to look for family background contributors to symptom variability
- Direct testing and online assessments of quantitative traits in person with SCV and unaffected family members
IQ as a Quantitative Trait

![IQ Curve Diagram](image)

- Intellectual Disability
- IQ Curve
- "Gifted"
IQ as a Quantitative Trait

Tartaglia et al, A Review of Trisomy X, OJRD, 2010
Social Responsiveness as a Quantitative Trait

Social Responsiveness Scale (SRS-2), Constantino, 2012
Social Responsiveness in 16p11.2 deletion

- Individuals with deletion
- Siblings
- Parents

Moreno-De-Luca et al., *JAMA Psychiatry* 2015:72:119–126
Child with Genetic Variant

Family B

Decreasing Social Responsiveness
RESEARCH OPPORTUNITY!

Look for the Geisinger Autism & Developmental Medicine Institute table to participate or learn more!

When you have Klinefelter Syndrome, you hear a lot about that extra X...

We want to learn about ALL of your chromosomes!

By studying the impact of family background, we hope to better understand and personalize interventions for boys with Klinefelter Syndrome!
Family Studies in SCV

- Social responsiveness
- Language
- Cognitive functioning
- Multisensory integration (MSI)
  studying how information from different senses may be integrated by the central nervous system

  (McGurk effect, flash – beep integration, temporal binding window)
Conclusions and Implications

• Family genetic background known to contribute to variability in symptoms in genetic conditions
• Family studies of quantitative traits (IQ, social abilities, language skills, motor skills) could allow more accurate prediction of prognosis in SCV
• Ability to more precisely predict specific strengths and weaknesses in children with SCV may allow more focused recommendations for interventions
• Future importance for measuring effectiveness of targeted pharmaceutical and behavioral treatments for SCV

Acknowledgements

**SCV Project**
- Marissa Mitchel
- Lauren Kasperon
- Karahlyn Troutman

**Bucknell University**
- Aaron Mitchel (Co-PI)

**Geisinger Faculty**
- David H. Ledbetter
- Christa L. Martin
- Thomas D. Challman
  - Christopher Chabris
  - Andrew Michael
  - Scott M. Myers
  - Cora M. Taylor
  - Vanessa Troiani
  - Karen Wain

**Team ADMI!**

Autism & Developmental Medicine Institute
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**Grant Support**
- Bucknell-Geisinger Research Initiative
- National Institute of Mental Health
- Simons Foundation

...and the many families who make our work possible