Anxiety in Angelman Syndrome

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Presentation Structure

• How we got interested in anxiety

• Anxiety disorders in developmental disorders

• Assessing anxiety in people with Angelman Syndrome
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History of Anxiety in Angelman Syndrome

• Anxiety not traditionally associated with Angelman syndrome (AS)

• Behavioral uniqueness
  – Frequent laughter/smiling
  – Apparent happy demeanor
  – Excitable personality
  – Hyperactive and short attention span
Behavioral Phenotype in AS

- 2006 literature review of behavior in AS
- 64 case studies of 842 subjects with AS
  - Laughing smiling 83% of subjects
  - Feeding problems (mostly in infancy) in 36% of subjects
  - Sleep disturbance in 29% of subjects
  - Restlessness/hyperactivity in 25% of subjects
  - Aggression in 6% of subjects and self-injury in 3% of subjects

- Only 1 study of the 64 reported "anxiety"

Horsler + Oliver 2006
Early signs of Anxiety as an issue

- Dr. Clayton-Smith was one of first researchers to describe anxiety:
  - "Other behaviors observed were anxiety and episodes of aggression especially if there was a disruption in routine or a change of carers"

Clayton-Smith, 2001
Behaviors concerning for Anxiety

• 2007 study of 248 subjects with AS
  – Examining for traits of autism
  – 45% became upset when routines changed

• 2007 study of 68 subjects with AS
  – 1/3 of caregivers reported individual had aversion to noise

Walz et al., 2007; Artigas-Pallarés et al., 2007
Caregivers report anxiety in AS

- Phone interview: 110 adolescents and adults with AS
  - 46% of caregivers felt the individual showed signs of anxiety
  - Sensitivity with changes in routine was consistent trend

- “Clinically referred group”

Larson et al. 2014
Next steps

• Is anxiety really this prevalent?

• If true, how severe is this problem?

• Are families describing true anxiety or other behavioral/emotional concerns?
Importance of identifying anxiety

• Anxiety linked to aggression?

• Clinical Observation: anxiety can be reported later in life

• Anxiety can limits life experiences
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Anxiety disorders: Typically developing

• Adults: prevalence 18.1% (12-month) (Kessler et al. 2005)
  – Phobias and Social Anxiety

• Kids/Teens (9–17 y/o): prevalence 9.8% (Kerikangas et al. 2010)
  – Social Anxiety (4.5%), Generalized Anxiety (3.1%) and Separation Anxiety (2.3%)

• Females > males

• Rates the same in developmental disorders?
Anxiety symptoms over time in typical development

Figure adapted from Beesdo-Baum and Knappe 2012
Range of intellectual disability (ID)

- Mild
- Moderate
- Severe
- Profound
Anxiety disorders in mild/moderate ID

- Dekker & Koot, 2003: Large community sample
  - 474 subjects (7–20 year olds)
  - Severity borderline to moderate ID
  - Prevalence 21.9% for anxiety disorder (12 month)
    - Phobias (17.5%), OCD (2.7%) and Social Anxiety (2.5%)
Anxiety Disorders in severe ID

- **Large community sample** (Cooper et al., 2007)
  - 1023 adults, full range of ID severity
  - Prevalence 3.8% for anxiety disorder
  - Lower levels in moderate to profound ID (2.4%)

- **Community sample** (Bhaumik et al., 2008)
  - 2711 adults, mostly severe to profound ID
  - Prevalence 2.4% for anxiety disorders
Can we generalize these findings to specific genetic disorders?

- Fragile X Syndrome
- Down Syndrome
- Williams Syndrome
- Prader-Willi Syndrome
Fragile X Syndrome and Anxiety

• 97 kids and adults (5–33.3 years old)
  – 82.5% had anxiety disorders. Phobia and Social Anxiety were most common

• More common among more severe ID

Cordiero et al., 2010
Williams Syndrome and Anxiety

- 119 children with Williams syndrome (4–16 years old)
  - 53.8% Phobias
  - 12% Generalized Anxiety (rates increased with age)
- Social Phobia 2.3% (low?)

- Separate study: 92 adults with Williams syndrome
  - 16.5% with Generalized Anxiety
  - 12% with Phobias

Leyfer et al., 2006; Stinton et al., 2010
Down Syndrome and Anxiety

• Meyers and Pueschel 1991: screened for psychiatric conditions in 261 children with Down syndrome
  – Anxiety disorders in only 1.5% of subjects
  – Much higher rates of hyperactivity and oppositional behavior

• Are some genetic syndromes protected from anxiety?
Genetic Mechanisms: Angelman Syndrome

Chromosome Deletion

Uniparental Disomy (UPD)

Images from Angelman Syndrome Foundation Website
Genetic Differences in AS

- Deletion genotype increased risk for more severe seizures as compared to UPD

- UPD genotype increased mobility as compared to deletion

- Will we also see behavioral differences?

Clayton-Smith & Laan, 2003
UPD = Uniparental Disomy
Prader–Willi Syndrome Genotype

• Differential risk for psychiatric symptoms between people with same condition

• Higher rates of psychosis among subjects with UPD (Vogels et al., 2003)

• Higher rates of autistic traits in UPD (Dimitropoulos & Schultz, 2007)

UPD = Uniparental Disomy
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Angelman Syndrome and Anxiety

- Wink et al. 2015: 12 subjects with AS
  - 3–29 years, mean 13.8 years variable genotype

  - Scores on anxiety measures were not elevated

  - Elevated levels of hyperactivity, irritability and sleep disorder
Why don’t we have large studies in AS?

How to identify emotions in non-verbal individuals?
Combination Assessment Tools

- Caregiver Interview
- Clinician Observation
- Assessment Tools
Parent/Caregiver Interview

• Advantages:
  – Parent/caregiver expertise

• Disadvantages:
  – Different standards for what is a problem
Clinician Observation

- Facial expression
- “Fight or flight” response
- Signs of excessive shyness
- Aversion to new environments or noise

- Such observation is used by behavioral therapists
Standardized Assessment Tools

• Advantages:
  • Standardization
  • Quantify a problem
  • Measure response to treatment

• Disadvantages:
  • Few good tools
  • Skipping certain questions can alter results
Examining Anxiety in AS is important
Examining Anxiety in AS is important

- Who is at risk for behavioral/anxiety symptoms?
- Do they get better or worse with time?
- Some seizure treatments can improve anxiety?

- Minimal treatment studies for behaviors in AS
Does your family member have a diagnosis of Angelman Syndrome?

The Massachusetts General Hospital for Children is conducting a research study at the Angelman Syndrome Clinic and the Lurie Center to characterize behavioral symptoms in individuals with Angelman Syndrome. Individuals of any age with a genetic diagnosis of Angelman Syndrome can participate in the study.

For more information, please contact Dr. Keary’s research staff at 781-860-1711 or LurieCenterResearch@partners.org.
Angelman Syndrome Clinic at Massachusetts General Hospital

Multi-disciplinary clinic focused on common care needs for children, teens and adults with AS

Neurology, Dietary, Psychiatry, Behavioral consultation, Gastroenterology, Telemedicine
Citations

- Adams & Oliver The expression and assessment of emotions and internal states in individuals with severe or profound intellectual disabilities. Clinical Psychology Review. 2011. 31;293–306.
Citations