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

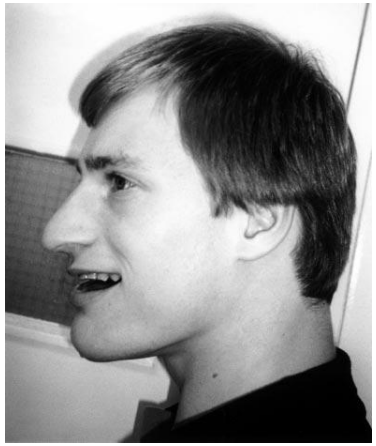
- 2006 literature review of behavior in AS
- 64 case studies of 842 subjects with AS
  - Laughing smiling 83% of subjects
  - Feeding problems (mostly in infancy) in 36% of subjects
  - Sleep disturbance in 29% of subjects
  - Restlessness/hyperactivity in 25% of subjects
  - Aggression in 6% of subjects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

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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

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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

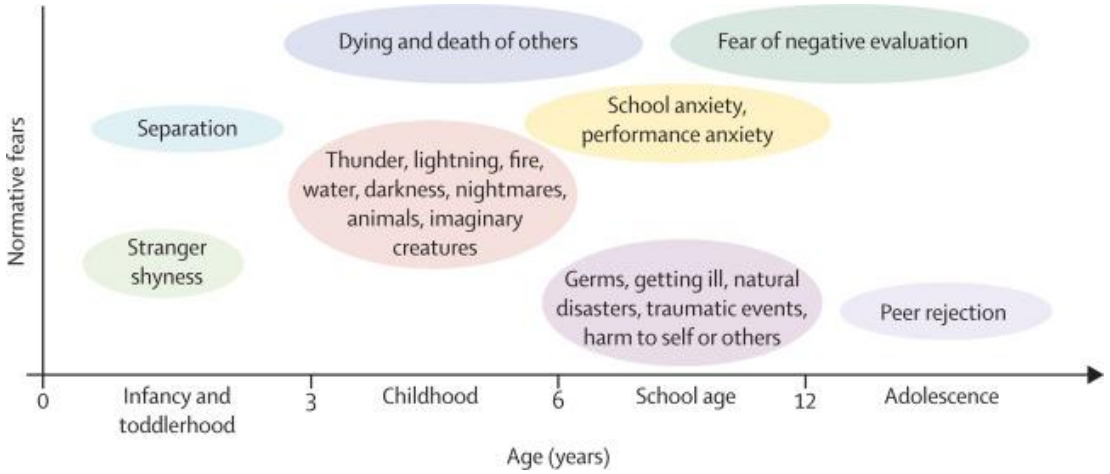

Figure adapted from Beesdo-Baum and Knappe 2012

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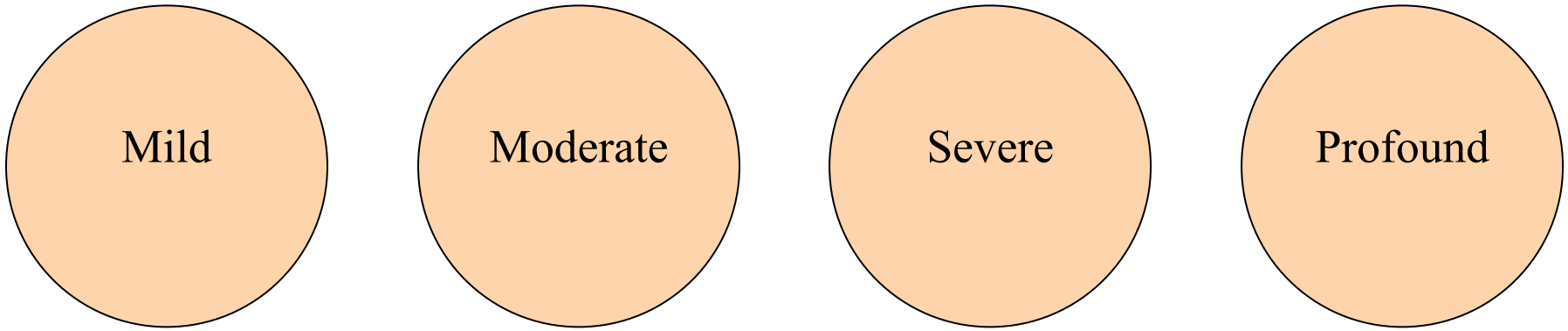
Range of intellectual disability (ID)



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

Fragile X Syndrome

Down Syndrome

Can we generalize these findings to specific genetic disorders?

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

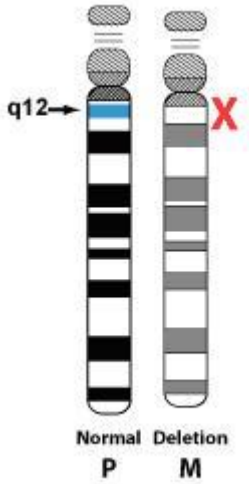
Leyfer et al., 2006; Stinton et al., 2010

Down Syndrome and Anxiety

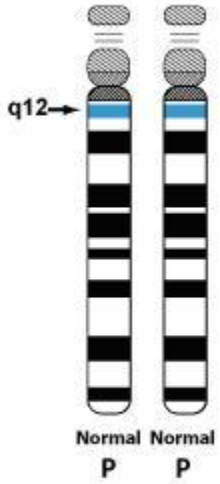
- Meyers and Pueschel 1991: screened for psychiatric conditions in 261 children with Down syndrome
  - Anxiety disorders in only 1.5% of subjects
  - Much higher rates of hyperactivity and oppositional behavior

- 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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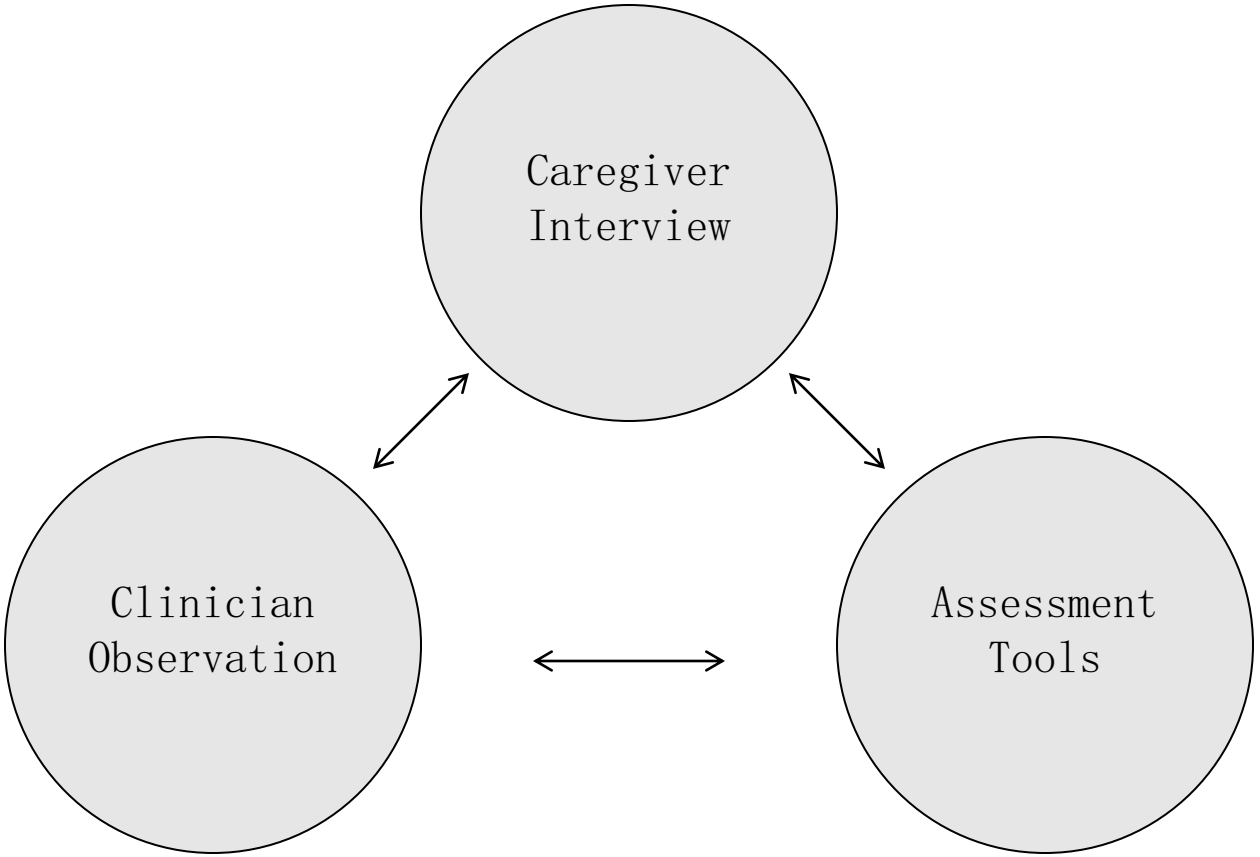
Angelman Syndrome and Anxiety

- 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



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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**

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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

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