Anxiety & Neurodevelopmental Disorders

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What is normative anxiety?

• 10 – 20% of children/adolescents suffer from a diagnosable anxiety disorder

BUT .....Many more children suffer with symptoms that do not meet diagnostic criteria (Walkup et al, 2008)

Some Rates:

• ~40% of grade school children have fears of separation from a parent
• ~40% of children aged 6 – 12 years have 7 or more fears that they find troubling
• ~30% of children worry about their competence and require considerable reassurance
• ~20% of grade school children are fearful of heights, are shy in new situations, or are anxious about public speaking and social acceptance (Bell-Dolan et al, 1990)
• Girls report more stress than boys – may be an artifact of social expectations
• Most of these worries and stresses are outgrown or recede as children mature and develop

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Assessing anxiety:

1. **Object:** Is this something a child of this age should be worrying about?

2. **Intensity:** Is the **degree** of distress unrealistic given the child’s developmental stage and the subject?

3. **Impairment:** Does the distress **interfere** with the child’s daily life?
   - Social functioning: unable to make friends
   - Academic functioning: failing classes
   - Family functioning: creating conflicts, limiting family choices

4. **Ability to Recover/Coping Skills:** Is the child able to **recover** from distress when the event is not present?
   - Tend to worry about future occurrences of event/object
   - Distress occurs across multiple settings

5. **For NDDs:** Do symptoms contribute to impairment and distress over and above other diagnosis?

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At different ages

• Infants
  – Fear of loud noises
  – Fear of being startled
  – Fear of strangers (around 8 – 10 months)

• Toddlers
  – Fears of imaginary creatures
  – Fears of darkness
  – Normative separation anxiety

• School-age Children
  – Worries about injury and natural events (e.g., storms, lightening, earthquakes, volcanoes)

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Anxiety at different ages

• Adolescents
  – Fears related to school
  – Fears related to social competence
  – Fears related to health issues

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The most common anxiety disorders in middle childhood and in NDDs are:

- Separation Anxiety,
- Generalized Anxiety Disorders
- Specific Phobias
Clinical Presentation

• Children with anxiety disorders may present with fear or worry but may not recognize their fears as unreasonable

• Younger kids often cannot articulate their feelings, and so we often see physical symptoms presenting first, which include:
  – Headaches, upset stomach or nausea, increased heart rate, diarrhea or constipation, sleep disturbance, increased vulnerability to common viruses, tightness in chest, tight neck or back, appetite change, fatigue & exhaustion

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What To Look For….But many features overlap with other NDDs

- Physical complaints (H/A, GI)
- Sleep (early/middle insomnia, repeated visits to parent’s room)
- Change in eating
- Avoidance of outside and interpersonal activities (school, parties, camp, slumber parties, safe strangers)
- Excessive need for reassurance (new situations, bedtime, school, storms, “is it bad?”)
- Change in attention and school performance
- Not necessarily pervasive (some areas of function remain intact)
- Explosive outbursts
Separation Anxiety Disorder
Worry about separation from parent/caregiver:

Recurrent distress (3) when
- anticipating separation from parent/caregiver,
- persistent, excessive worry about losing parent/caregiver,
- worry about experiencing an untoward event that causes separation from parent/caregiver,
- persistent reluctance or refusal to go out away from home (school refusal),
- refusal to sleep away from home,
- repeated nightmares involving the theme of separation (wont sleep alone)
- repeated complaints of physical symptoms

Commonly, the earliest age of onset among anxiety disorders
Duration: 4 weeks or more
Specific Phobias

• Fear of a particular object or situation which is avoided or endured with great distress
• Anxiety is out of proportion to the actual danger the fear or anxiety and causes clinically significant distress or impairment
• More than one phobia is common
• Adolescents and adults typically recognize that the fear is unreasonable; children may not
• Avoidance is key
• Generally begins in childhood
• Duration: 6 months

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Generalized Anxiety Disorder

- Longstanding, excessive worry in a number of areas (e.g., schoolwork, social interactions, family, health/safety, world events, and natural disasters) with at least one associated physical symptom
- Worry is most often present and not limited to a specific situation or object

Accompanying Physical Symptoms: restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension, and sleep disturbance.

Duration: 6 months or more

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Social Phobia

- Feeling scared or uncomfortable in one or more social settings (discomfort with unfamiliar peers and not just unfamiliar adults) or performance situations (e.g., sports, music)
- Associated with a fear of scrutiny and of doing something embarrassing in social settings such as classrooms, restaurants, or extracurricular activities
- May have difficulty answering questions in class, reading aloud, initiating conversation, talking with unfamiliar people, and attending parties and social events
- Anxiety dissipates when away from a social situation (unlike GAD)
  The social situations almost always provoke fear, the fear is out of proportion to the actual threat posed by the social situation, the fear is persistent
- Duration: 6 months or more

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Rates of anxiety disorders in NDDs

- CDC report between 1/3 to 1/5 children with ADHD have a diagnosed anxiety disorder (Sep, GAD, Social) (Danielson J Clinical Child & Adolescent Psychology 2016)

- ~30% of children and adolescents with OCD also meet criteria for another anxiety disorder (31%) - separation anxiety disorder common (Boileau 2011 Dialogues Cl Neuroscience)

Limited studies in intellectual disability (7 total) rates between 3-22% (Reardon Res Rev Disabil 2015)
## Studies Assessing Psychiatric Comorbidity in ASD

<table>
<thead>
<tr>
<th>Study</th>
<th>DSMIV</th>
<th>Sample Origin</th>
<th>N</th>
<th>Age</th>
<th>Assessment</th>
<th>Comorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joshi JADD (2010)</td>
<td>AuD, PDD-NOS</td>
<td>Referred to Psychiatric Care</td>
<td>217</td>
<td>9.7 (3-17)</td>
<td>KSADS-E</td>
<td>83% ADHD, 73% ODD, 22% CD, 56% MDD, 31% Bipolar D, 61% multi-anxiety, 37% enuresis, 22% encopresis 23% Tic Disorders</td>
</tr>
<tr>
<td>Simonoff JAACAP 2008)</td>
<td>AuD, PDD-NOS</td>
<td>Population Cohort</td>
<td>112</td>
<td>11.5 (10-14)</td>
<td>CAPA</td>
<td>71% had one comorbidity 29%SocP, 28%ADHD, 28%ODD, 13% GAD, 10% Panic 11% enuresis</td>
</tr>
<tr>
<td>Matilla JADD (2010)</td>
<td>AS/HFA</td>
<td>Community + Clinic</td>
<td>50</td>
<td>12.7 (10-16)</td>
<td>KSADS-PL</td>
<td>~75% with comorbidity 19 (38%) ADHD 21 (42%) Any anxiety (14 SpecificP, 11OCD) 13 (26%) Tic Disorder 18 (36%) insomnia</td>
</tr>
<tr>
<td>Mazefsky J Clin Child Adolesc Psychol. (2012)</td>
<td>HF-ASD</td>
<td>Clinic</td>
<td>35</td>
<td>13 (10-17)</td>
<td>ACI</td>
<td>51% with comorbidity 10 MDD, 13 Anx, 1 OCD, 4 ODD, 12 ADHD</td>
</tr>
<tr>
<td>Skokauskas JIDR (2012)</td>
<td>Any ASD</td>
<td>Clinical Sample</td>
<td>67</td>
<td>12.7</td>
<td>CBCL/6-18</td>
<td>45% Cl. significant ADHD 46% Cl. Significant anxiety</td>
</tr>
<tr>
<td>Van Steensel, FJ Clin Child Fam Psychol Rev (2011)</td>
<td>Any ASD</td>
<td>Meta-Analysis of studies assessing anxiety prevalence</td>
<td>2,121</td>
<td>&lt;18</td>
<td>Any Stndrdzd.</td>
<td>40% with anxiety dis. 30% Specific P, 17% OCD, 16% SocP, 15% GAD, 9% Sep, 2% panic</td>
</tr>
</tbody>
</table>
In ASD

• Recent meta-analysis (n>2000 C&A)
  1. Specific phobia (30%)
  2. OCD (17%)
  3. Social anxiety (16%)
  4. Generalized anxiety (15%)
  5. Separation anxiety (9%)
  6. Panic disorder (2%)

<table>
<thead>
<tr>
<th>CMHC in Autism</th>
<th>Meta-Analysis Results</th>
<th>General Population Prevalence Estimates</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Overall Prevalence (95% CI)</td>
<td>Population/Registry Studies (95% CI)</td>
</tr>
<tr>
<td>ADHD</td>
<td>33% (29-37%)</td>
<td>26% (21-33%)</td>
</tr>
<tr>
<td>Anxiety Disorders (based on DSM-IV, DSM-5, or ICD-10)</td>
<td>23% (19-27%)</td>
<td>17% (12-22%)</td>
</tr>
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</table>

Lai, Kassee, Szatmari, Ameis et al In preparation
Lifespan development of CMHC in people with ASD

**Childhood**
- NDDs (ADHD, Tics, LD, DCD, OCD)
- Anxiety
- Ext; “ODD/CD”

**Adolescence**
- NDDs
- Anxiety
- Depression
- Suicide

**Emerging Adulthood**
- NDDs
- Anxiety
- Depression
- Suicide
- Bipolar disorder
- Psychosis spectrum

**Late Adulthood**
- NDDs?
- Anxiety?
- Depression?
- Suicide?
- Bipolar disorder?
- Psychosis spectrum?
- Dementia

Courtesy of Meng-Chuan Lai
Identifying Psychiatric Comorbidity in NDDs: Diagnostic Challenges

Standardized diagnostic interviews in general child/adult population may not be validated

Few specialized interviews exist

Language impairments lead to challenges with communicating regarding thoughts and feelings. May need to assess based on behaviour.

Symptoms may be overlapping and difficult to distinguish
Assessment Principles in NDDs

Do symptoms contribute to dysfunction over and above other NDD diagnosis?

Objective rating helpful and can be tracked

Supplement history & observation with collateral information (what interferes at school, in Rx)
Assessment Principles: Differentiating ASD Sx from psychiatric comorbidity

Clarify longstanding/baseline Sx/behaviors consistently present (i.e., restricted interests, repetitive behavior, baseline affect)

Differentiate longstanding from new onset or sudden change in behavior

Determine symptom duration, relationship with recent stressors (new teacher, change in environment) & effect on functioning (change in interest, self care, initiative).

Collateral information from teachers, therapists, etc.
Do symptoms interfere significantly with functioning across different contexts
Treatment of Anxiety Disorders in Children (Psychotherapy)

• Cognitive Behavioural Therapy (CBT)
  – Indications: OCD and phobias (with ERP), Panic, GAD, SAD

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What happened?
My friend Emma hasn't spoken to me as much as usual over the past week.

My Thoughts
I thought: “Emma hasn’t talked to me much this week. She must be mad at me.”

Because I was upset I ignored Emma and avoided her at school.

My Actions
I felt sad and hurt.

My Feelings

Just because you have a thought doesn't mean it's true. Your thoughts are guesses about why something happened, or about something that might happen. Coming up with new thoughts will help you see a situation differently.
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<th>New Feelings</th>
<th>New Actions</th>
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<td>“Emma might be upset with me, but maybe not. I don’t know.”</td>
<td>Concerned that Emma <em>might</em> be upset, but I’m not as sad as I was.</td>
<td>Ask Emma if she is mad at me, or if she has another problem.</td>
</tr>
<tr>
<td>“Emma has probably been busy with school or something else.”</td>
<td>Disappointed I haven’t talked to Emma, but understanding.</td>
<td>I’ll stay friendly with Emma, as usual. I’ll be sure to say “hi” anyway.</td>
</tr>
<tr>
<td>“Maybe Emma is upset about something unrelated to me.”</td>
<td>Worried about how Emma is feeling.</td>
<td>Ask Emma what’s going on, and if she needs help.</td>
</tr>
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</table>
Treatment of Anxiety Disorders in Children (Medication)

- SSRIs have been shown to be efficacious in numerous studies
- Zoloft has the best safety data in children and adolescents (studies extend two years)
- FDA approval only for OCD:
  - Fluoxetine (Prozac®) 7 – 17 y/o
  - Sertraline (Zoloft®) 6 – 17 y/o
  - Fluvoxamine (Luvox®) 8 – 17 y/o
  - Clomipramine (Anafranil®) 11 – 17 y/o

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Child and Adolescent Anxiety Multimodal Study (CAMS) (Walkup et al, 2008).

- Compared CBT, medications, and combined treatment
- Randomly assigned 488 children and adolescents with Separation Anxiety Disorder, Social Phobia, or Generalized Anxiety Disorder, aged 7 to 17 years, to one of four treatment groups for 12 weeks.
  - CBT for 14 sessions
  - Sertraline up to 200 mg/day
  - CBT + Sertraline
  - Placebo (PBO)
- Over 80% of children who received combined treatment improved, as opposed to 60% receiving CBT only and 55% receiving medication only; although there was no statistical separation between the CBT and medication groups
- All treatments more effective than PBO (24% improved)

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Clinical Practice Implications:

• A number of studies have found positive evidence that CBT undertaken in children/adolescents with ASD, without intellectual disability, and with a variety of anxiety disorders leads to clinical improvement in anxiety symptoms and should be pursued when clinically significant symptoms of anxiety.

• Clinicians should exercise caution when prescribing SSRIs, TCAs or other agents for the treatment of mood or anxiety symptoms as a target in individuals with ASD, using objective tools to screen for treatment targets and monitor benefits and side-effects as trials focused on treatment of this target in ASD are lacking.
THANK YOU

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TherapyAid.com

Colleagues: Drs. Meng-Chuan Lai and Yona Lunsky
Social Processes Initiative in Neurobiology of Autism-spectrum and Schizophrenia-spectrum Disorders (SPIN-ASD)
REB#: 005/2018

What is the study about?

We are interested in understanding more about how the brain works in Autism Spectrum Disorder (ASD), and how brain properties (e.g. structure, function) relate to behaviour. This is an imaging study, which means if you decide to participate you will have a brain scan, and we will also ask you to complete some assessments in person.

Current Diagnosis of ASD, 18-29 year olds,

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