Anxiety Disorders in Children and Adolescents

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Disclosure

- Neither I nor my spouse has a relevant financial relationship with a commercial interest to disclose.

Most Prevalent Mental Illness in Youth

- ADHD (6.8%)
- Conduct Disorder (3.5%)
- Anxiety (3.0%)
- Depression (2.1%)
- ASD (1.1%)
- SUD (in prior year – 4.7%)
- Alcohol Abuse (in prior year – 4.2%)
- Nicotine Dependence (prior month – 2.8%)
- Suicide is the second leading cause of death in youth (Accidental death is leading cause)

DSM V Anxiety Disorders

- Separation Anxiety Disorder
- Selective Mutism
- Specific Phobia (snakes, heights, etc)
- Social Anxiety Disorder (Social Phobia)
- Panic Disorder
- Panic Attack (specifier)
- Generalized Anxiety Disorder
- Substance/Medication-Induced Anxiety Disorder
- Anxiety Disorder Due to Another Medical Condition
- Other Specified Anxiety Disorder
- Unspecified Anxiety Disorder

DSM V Obessive-Compulsive and Related Disorders

- Obsessive-Compulsive Disorder
- Body Dysmorphic Disorder
- Hoarding Disorder
- Trichotillomania (Hair-Pulling Disorder)
- Excoriation (Skin-picking) Disorder
- Substance/Medication-Induced OC and Related Disorder
- OC and Related Disorder Due to Another Medical Condition
- Other Specified OC and Related Disorder
- Unspecified OC and Related Disorder

Pediatric Anxiety Disorders

- Anxiety disorders present a great social and economic burden
  - US National Comorbity Survery: Anxiety disorders are the most prevalent class
  - Cost the US more than $42 billion/year – almost 1/3 of the total US mental health bill
- OCD is fourth most common mental illness
  - Under recognized and under-reported
  - Top 10 leading global causes of disability affecting children, adolescents, adults

Risk Factors

- Temperamental
  - Behavioral Inhibition
    - Consistent tendency to show marked behavioral restraint or fearfulness with unfamiliar people, situations, or events
- Family Genetic
  - Rates in *at-risk* offspring of parents with AD range from 21-68% vs offspring of controls 0-26%
  - Exposure to maternal AD predicts childhood AD
    - Particularly GAD

Risk Factors

- Combining data from 14 studies, 37% of *at-risk* offspring of anxious parents had AD compared with 15% of controls

Weissman 1984; Turner 1987; Sylvester 1988; Biederman 1991, 2001, 2006; Mufson 1992; Warner 1995; Capps 1996; Beidel 1997; Unnewehr 1998; Merikangas 1998; Black 2003; Johnson 2005

Risk Factors

- Non-genetic factors
  - Non-heritable etiological factors are as great or greater than genetic factors for risk of developing OCD
  - Many if not most cases of OCD arise *without* a positive family history of the disorder
  - Studies have focused on
    - Perinatal (intrauterine, birth, and postnatal)
    - Adverse psychosocial experiences
    - Immune mediated neuropsychiatric models of illness (PANDAS = pediatric autoimmune neuropsychiatric disorders associated with streptococcus; PANS= pediatric acute- onset neuropsychiatric syndrome)

- Adverse Psychosocial Events
  - the majority of pediatric OCD case do not give a clear history of prescipitating adverse psychosocial stress and have a subclinical onset
    - Exception is….PANDAS/PAN which is characterized by acute onset
    - Central hypothesis of PANDAS derives from neurobehavioral disturbances accompanying Sydenham's chorea that leads to an immune response to group A beta-hemolytic streptococcus (GABHS)
    - PANDAS remains controversial issue

  - In many adult studies and one pediatric case series (LeFleur et al, 2011), there is a significant and frequent relationship between OCD and PTSD

Assessment of Childhood Anxiety Disorders

- Structured Interviews (K-SADS, ADIS-C)
- Self- report instruments (R-CMAS, MASC, SCARED, STAI-C, FSSC-R, PARS)
- Parent ratings (CBCL, PARS)
- Teacher Ratings (TRF)
- Behavioral Observations
- Anxiety Ratings ("Fear Thermometer)
- Family Assessment (FES)

Assessment cont'd

- Evaluate concurrent disorders
  - Psychiatric comorbidity is the rule
  - Response rates in patients with comorbid disorders are significantly lower
  - Comorbidity is also associated with a greater rate of relapse following treatment (Geller et al, 2009)

Components of the Diagnostic Process

- Psychiatric assessment (structured, semi-structured)
- Cognitive assessment
- Assessment of school functioning
- Psychosocial assessment
- Laboratory assessments (when indicated)

Psychosocial evaluation

- Family Environment
  - Marital discord
  - Parenting difficulties
  - Separation and divorce
  - Custodial parent
  - Guardianship
  - Potential issues of abuse/neglect
  - Low SES
  - Family conflit
  - Single parent homes
  - Parently psychopathology

- Social Functioning
  - Relationship with peers
  - Relationship with parents
  - Use of leisure time

Laboratory Assessment

- Blood Chemistries
  - CBC, LFTs, Renal panel, Thyroid Panel, Drug of abuse screening, Therapeutic drug monitoring
- Cardiovascular Assessments
  - ECG, BP, HR
- Other assessments
  - Height, weight

Treatment

- Pharmacotherapy
- Psychotherapy
- Pharmacotherapy + Psychotherapy (best outcomes)

Psychotherapy

- Should be recommended as part of the treatment of all childhood anxiety disorders and OC disorders
  - Exposure-based CBT has most empirical support
  - 5 CBT components
    - Psychoeducation
    - Somatic management skills training (relaxation)
    - Cognitive restructuring (e.g. challenging negative expectations and modifying negative self-talk)
    - Exposure methods (exposure w/ desensitization)
    - Relapse prevention plans (booster/maintenance)

AACAP guidelines: Connolly & Bernstein, 2007; Albano and Kendall, 2002

CBT interventions

- At least 20 controlled trials of CBT for childhood AD (excluding studies of treatment of specific fears/phobias)
- All but two show efficacy for exposure-based protocols in reducing symptoms and diagnoses
- Limited by tendency to lump together different diagnoses

- CBT is first line treatment for mild to moderate cases of OCD in children (AACAP Practice Parameter for OCD, 2012)
- ***Informed consent for pharmacotherapy is not "informed" without a discussion of CBT!***

Pharmacotherapy

ALL ARE OFF LABEL AS THERE ARE NO FDA-APPROVED MEDICINES FOR ANXIETY IN CHILDREN

- First Line – SSRIs, venlafaxine, duloxetine
- Second Line – buspirone, benzodiazepines, and TCAs
- Third Line – mirtazapine, GABA-ergic anticonvulsants, propranolol, alpha agonists
- Fourth Line – low dose atypicals

Meta-analysis of (non-OCD) Anxiety RCTs

- Randomized placebo controlled trials of antidepressants in youth; 6 trials; N-1136
- GAD
  - Rynn et al 2001 (sertraline to 50mg)
  - Rynn et all 2007 (venlafaxine to 225mg)
- SAD/Social Phobia
  - Wagner et al 2004 (paroxetine to 50mg)
  - March et al 2009 (venlafaxine to 225mg)

Bridge et al, 2007

Meta-analysis cont'd

- Social Phobia/Separation/GAD
  - Rupp 2001 (fluvoxamine to 300mg)
  - Bimaher et al 2003 (fluoxetine to 20mg)
- 2-4 months duration
- Pooled rates of response
  - 69% in antidepressant-treated participants
  - 39% in those receiving placebo
- All studies favored antidepressant treatment, yet large variation in the degree of benefit across trials

Bridge et al, 2007

C/A Anxiety Multimodal Study (CAMS)

- Randomized, controlled trial of 448 children (7-17 yrs)
- Separation, GAD, social phobia
  - 14 sessions of CBT
  - Sertraline (to 200mg/day)
  - Combined CBT and sertraline
  - Placebo for 12 weeks

Walkup et al, NEJM 2008

CAMS: response

- Sertraline (N=133)
  - 4 wk =19%; 8 wk = 47%; 12 wk =55%
- CBT (N=139)
  - 4 wk=9%; 8 wk= 30%; 12 wk = 60%
- Combination (N=140)
  - 4 wk = 21%; 8 wk =54%; 12 wk = 81%
- Placebo (N=76)
  - 4 wk – 7%; 8 wk = 22%; 12 wk – 24%

Pharmacotherapy for OCD

- For moderate to severe OCD medication is indicated
- SSRIs are the first line and should be used following the AACAP guidelines to monitor response, tolerability, and safety

Pharmacotherapy Safety and Tolerability

- In general, SSRI medications are well-tolerated and safer than their predecessor TCAs
- Behavioral side effects are more likely in younger children and may be a late-onset effect. Usually sensitive to dose adjustment
- Most commonly described AE of SSRIs
  - CNS – headache, tremor, drowsiness, insomnia, sexual, disinhibition, agitation, hypomania
  - GI – nausea, loose or looser stools

General Principles of Pharmacotherapy in C/A

- Use of psychotropics should follow a careful evaluation of child, including family history
- Prior to beginning treatment, parents and child (keep age appropriate) need to be familiarized with the risks/benefits of such intervention
- Treatment should be started at the lowest possible dose with FREQUENT reevaluation during the initial phase of treatment (weekly)

- Following sufficient period of clinical stabilization (12 months for first treatment episode) it is prudent to reevaluate the NEED for continued psychopharmacologic intervention
- Certain adverse effects can be anticipated based on known properties of the drug/drug class while others, generally rare, are unexpected and are difficult to anticipate

What is an adequate drug trial?

- Adequate dosage and duration (10-12 weeks) needed to determine response to a given SSRI
- Relatively high doses of SSRIs have been used in published studies

Indications for Combined Pharmacotherapy

- Comorbidity
  - High rates of psychiatric comorbidity in childhood psychiatric disorders
  - Irrespective of etiology, different disorders require different treatments

Combined Pharmacotherapy

- Treatment resistant cases
  - Augmentation
  - Less than satisfactory response to a single agent
  - Potential synergy of combined agents for certain disorders
    - Combined tx may permit the use of lower doses of two agents reducing the adverse affect profile associated with higher doses of a single agent

Combined Pharmacotherapy

- Vast array of potential combinations
- Clinicians should become familiar with potential psychopharmacological combination regimens
  - Adverse effects (i.e. excessive sedation)
  - Drug-drug interactions (i.e. fluoxetine plus TCAs)

Combined Pharmacotherapy

- Simple cases: monotherapy could be sufficient and should be preferred
- Complex cases: monotherapy may be insufficient and combined therapy should be considered

Clinical Take-home…

- Psychiatric Disorders do run in families…
  BUT not everyone will manifest the same symptoms or even the same disorder!
- Genes are not (necessarily) destiny: environment matters! E + G
- No validated genetic tests for common psychiatric disorders…yet.

Clinical take-home…

- Retrospective studies suggest that untreated anxiety disorders are persistent
- 12 prospective studies found that having a childhood AD increased the risk of developing AD in later childhood, adolescent, or adulthood
  - Costello, 2003: Kim-Cohen, 2003; Gregory, 2007
- Do not memorize CYP450 interactions…
  - Good current resource: http://medicine/iupui.edu/clinpharm/ddis/main-table/

Questions?