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Treatment of Pediatric Anxiety Disorders

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Conflict of Interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

- Toya Roberson-Moore, M.D.

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Objectives

- Discuss the role of medication in combination with psychotherapy to improve outcomes
- Describe factors affecting treatment response
- Discuss treatment of anxiety disorders with co-morbidities including OCD, Tic disorders, ADHD and Mood disorders

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Impact of COVID-19 on Child Mental Health

- **Prevalence of anxiety and depression doubled among youth worldwide during the pandemic (JAMA Pediatrics meta-analysis, 2021)**
- Study in China published in JAMA Pediatrics - 1 month lock down
  - 22.6% reported depressive symptoms
  - 18.9% were experiencing anxiety
  - Problem-focused coping style was associated with lower levels of clinical depressive symptoms
- US survey - recently published in Pediatrics, showed that since March 2020
  - 27% of parents reported worsening mental health for themselves
  - 14% reported worsening behavioral health for their children

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Anxiety Disorders

- Very common: 8-10% of youth have at least one anxiety disorder, 10-32% lifetime prevalence
- Runs in families (Genetics and modeling)
- Structural and functional alterations in frontolimbic circuitry
- Co-occur with ADHD in children, and depression and substance abuse in teens
- Can persist into adulthood
- Treatments are available and effective: Cognitive-behavioral therapy and medication
- Early identification and treatment can reduce severity and impairment in social and academic functioning

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Normal Fear vs. Anxiety Disorder

- Use judgement about whether they are above and beyond
  - Persistence and effect on daily life and functioning
  - Causing serious distress, destroy family functioning, or interfere with a child's development or education
- Significant fears may reflect an accurate assessment of a truly harmful situation or a displacement of emotion from another environmental stressor (physical or sexual abuse).

Infants:

Fear of loud noises, being dropped or startled, loss of support, separation from mother

Fear of strangers (child learns difference between others and primary caregiver)

Toddlers:

Fear of imaginary creatures (monsters), small animals

Fear of darkness

Separation anxiety

Elementary school-age:

Fear of physical injury

Fear of natural events (storms)

Fears about school

Teenagers:

Fears of social evaluation and school performance

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Common Presentations of Anxiety Disorders

- **Avoidance** — Academic and social activities may be avoided, such as school, parties, camp, sleepovers, or talking to safe strangers
- **Somatic symptoms** — Headaches, stomach aches, or dramatic presentations of pain
- **Sleep problems** — Difficulty falling asleep or waking up in the middle of the night
- **Excessive need for reassurance** — The child may seek excessive or repetitive reassurance prompted by bedtime, storms, school time, or more generally related to fears of bad things happening
- **Poor school performance** — As examples, demonstrating inattention in class or having difficulty completing tests within the allotted time
- **Explosiveness and oppositional behavior** — When such outbursts are triggered by an anxiety-provoking stimulus
- **Eating problems** — Eating insufficiently or overeating to cope with anxiety

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Anxiety Disorders	Typical Age of Onset	Physical Symptoms	Area of worry	Something unique-ish
Selective mutism	Prior to age 5	None	Specific social situations	Not talking
Separation Anxiety Disorder	7	Possible	Separation from attachment figure	Nightmares
Specific Phobia	7	Possible	One specific thing	Spiders!!! (etc)
Generalized Anxiety Disorder	7	Required	EVERYTHING! Routine situations	Muscle tension and headaches
Social Anxiety Disorder	Early adolescence	Possible	Social situations	Performance anxiety
Panic Disorder	Late adolescence	Required	Panic attacks	Panic attacks
Agoraphobia	Late adolescence	Possible	Being away from home	Won't leave the house

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Other Specified Anxiety Disorder

- Criteria is not met
- Clinician explains why in diagnosis
- Typically used when symptoms are well established but not classic
- **School Avoidance**
  - Often involves nonspecific physical symptoms
  - Commonly associated with separation anxiety disorder and/or selective mutism

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Screening Forms

- **Screening for Child Related Anxiety Disorders** (SCARED)
  http://www.midss.org/content/screen-child-anxiety-related-disorders-scared
  - F8 and up, parent and child versions
  - Subscales
- **Spence Children's Anxiety Scale**
  https://www.scaswebsite.com/1_1_.html
  - Validated for preschoolers, parent and child versions
  - Subscales
- **Multidimensional Anxiety Scale for Children** (MASC)
  - 8 and up, parent and child versions
  - Subscales
  - proprietary

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Differential: Psychiatric

- ADHD
  - restlessness, inattention
- Psychotic disorders
  - restlessness, social withdrawal
- Autism Spectrum
  - social awkwardness, social communication deficits, repetitive behaviors, adherence to routines
- Learning Disorder
  - worries about school performance
- Bipolar disorder
  - restlessness, irritability, insomnia
- Depression
  - poor concentration, sleep problems, somatic complaints

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Differential: Other Physical

- **Physical conditions** with anxiety-like symptoms
  - Hyperthyroidism
  - Migraine
  - Seizure disorders
  - Lead intoxication
  - Pheochromocytoma
  - Arrhythmias
- **Medication side effects**
  - Prescription – albuterol inhalers, steroids, any sympathomimetic
  - OTC - cold medicines, antihistamines, caffeine
- **Somatic symptoms** commonly associated with anxiety
  - consider mental health assessment early in medical evaluation

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Initial PCP In Office Interventions

- Psychoeducation - with the child and parents about the illness and principles of treatment
- Parent training - To establish daily structure, expectations, **positive reinforcement**, monitoring of symptoms and progress at home
- Case management that includes contact with the mental health professionals and referrals

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Talking with Families about Anxiety Disorders

- Children with anxiety problems see the world in a different way
- They think up lots of ways that things can go wrong:
  - Biases in attention
    - Remember the bad forget the good
  - Misinterpretation of stimuli
    - "Hear noise at night = burglar!"
  - Negative self-talk
    - "I won't be able to do this"

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FAMILY FACTORS THAT INFLUENCE DIAGNOSIS

- Cultural and social background influence:
- Symptom Expression
- Problem Definition
- Problem Interpretation
- Timing of caregiver help seeking

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Alarms and False Alarms

- Alarms (anxiety) can protect us from danger
  - A problem when timing or intensity does not fit danger or stimulus
- Anxiety disorder: Alarm a little too sensitive
- False alarms: Alarm goes off too much

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Treatment Planning

- Age, **severity**, impairment, and comorbidity
- Older youth with depression and social withdrawal often need more intensive treatment
- Involve child and family in treatment planning

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Severity

- **Mild:** Start with education and relaxation techniques, if persistent Consider CBT (Cognitive Behavioral Therapy) first
- **Moderate:** Start as above with CBT and consider medications for:
  - Acute relief of anxiety
  - Partial response from other treatment
  - Comorbid disorders that may benefit from meds and multimodal approach
- **Severe:** Combination intensive treatments with therapy and medications may be necessary

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Goals of CBT for Anxiety

- Teach skills to identify when danger is not real and when anxiety is not needed
- Identify accurately when situations are safe
- Shrink or eliminate tension, worry, fear, panic
- Encourage hope and confidence "I can do it!"
- Reduce avoidance, increase opportunities for corrective experiences (Exposures).

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Riding the Anxiety Wave

- CBT provides coping skills so that child can ride the anxiety wave long enough and see that anxiety will go down
  - When child avoids anxiety trigger then wave goes down, but next time may be higher for same anxiety stimulus
- If wave is too high, medications reduce severity of anxiety symptoms so child can use CBT and ride the wave

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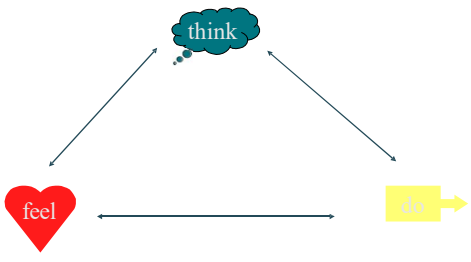
The Cognitive Triangle



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Social Anxiety Disorder

think: "I am going to embarrass myself"

feel: Increased heart rate, shaking, sweating, hyperventilation, dizziness

do: Avoidance of feared social situations, such as school refusal

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Separation Anxiety Disorder

think: "Something bad is going to happen to my mom if I am not with her"

feel: Nausea, vomiting, headaches

do: Avoidance of leaving mother, such as school refusal; increases sick days; tantrums when separated

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Cognitive Behavioral Therapy

think: Challenge automatic thoughts: is it the truth or am I just accepting it because I think it?

feel: Relaxation techniques, medications

do: Exposures and habituation

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Common Cognitive Distortions

- All or Nothing Thinking
  - "It wasn't perfect so I failed"
- Overgeneralization
  - "bad things always happen to me"
- Negative filtering/Discounting positives
- Jumping to conclusions
  - Mind reading: "I know they will make fun of me"
  - Fortune/future telling: "I know I will fail"
- Should statements
- Labeling/Personalization/Blame:
  - "I am stupid"
- Emotional Reasoning
  - "I feel stupid, therefore I must be stupid"

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Relaxation Skills Training

1. Healthy lifestyle (optimal nutrition, daily exercise)
2. Deep breathing/diaphragmatic breathing
3. Cuddle
4. Stretch
5. Listen to music
6. Meditation/Mindfulness and Yoga
7. Laugh
8. Progressive Muscle Relaxation
9. Guided Imagery
10. Toe Tensing

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Exposures for School Avoidance

- Progressively plan to attend school for longer and longer periods of time
  - Initially work on preparing for going to school (depending on severity of fears) with live and imaginal exposures (driving past school, walking on school grounds, entering school)
  - Increasing time at school, not necessarily in classroom
  - Work up to part of day and eventually full day
- Start with most comfortable setting/activity in classroom
- Set up rewards for each step
- Be careful not to start exposures close to vacations or holidays

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Take Home Points: Psychopharm

- 80% of Rx are not approved by the FDA for use in children [1]
- Fewer evidence-based studies in children than adult psychiatry
  - Often have to use your best judgment based on adult literature and clinical experience (or can look at recommended practice parameters/guidelines) [1]
- Pharmacotherapy plus psychotherapy tends to have better results than pharmacotherapy alone
- Stigma against using medications in treating mental illness, more so for pediatric patients
- Placebo effect is greater in kids than adults which blunts the effects seen in short term studies.

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Suicidality in Children/ Adolescents

- Suicide is the 2nd leading cause of death in ages 10-24 [23]
- 90% of suicides in youth are associated with psychiatric illness [6]
- Only 2% of youth who have committed suicide are actually taking any kind of psychiatric medications [6]
- Most of these children who committed suicide sought out treatment only 1 month prior to the event [6]
- 35-50% of depressed children receiving care have made or will make a suicide attempt [6]
  - 2-8% completing within a 10 year period in adults
- In 2003, early warnings from the UK appeared
  - "3.2% risk of self-harm and potentially suicidal behavior in paroxetine- treated patients vs. 1.5% in placebo"
- Warnings expanded over the next year, encompassing more antidepressants and leading to Black Box Warning (2004)

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Pharmacokinetics in Pediatrics

Lipophilic Medications:

- Most psychotropic medications are highly lipophilic
- The percentage of total body fat increases during the first year of life, then decreases gradually until puberty [4]
- Children have different volumes of fat for drug storage at different ages.

CYP/Metabolizing enzymes:

- Both CYP450 and phase II drug metabolizing enzymes generally are absent in infancy, though rapidly develop over the first few years of life.
- Toddlers and older children may have levels of these drug-metabolizing enzymes which exceed adult levels!
- These decline until puberty, where they generally remain the same until adulthood.

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Pharmacokinetics in Pediatrics

Liver mass effects:

- Relative to body weight, the liver mass of a toddler is 40-50% greater than an adult. A 6 year old is 30% greater than an adult.
- Children tend to clear drugs more rapidly than adults
- Children may require higher mg/kg concentrations to achieve the same plasma levels.

Renal filtration:

- By age 1, GFR and renal tubular mechanisms for secretion have reached adult levels
- However, fluid intake may be greater in children relative to adults
- Therefore, medications have a more rapid renal clearance in children compared to adults

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Anxiety Disorders Treatment (Non-OCD)

- Duloxetine (e.g. Cymbalta) is the only FDA approved medication for children and adolescents for non-OCD anxiety disorders.
- Approximately 10-20% of children have an anxiety disorder such as GAD, Separation Anxiety Disorder, or Social Phobia.
- Children and adolescents with mild to moderate anxiety do best in combined therapy in which CBT and medications are prescribed.

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Anxiety Disorders (Non- OCD)

- While sertraline does not have FDA approval for treatment of anxiety disorders in children, there is good evidence for its efficacy.
- Medications should be dosed at rates done in clinical trials.
- Typical dosages for sertraline based on CAMS study are 100-150 mg by week 12.
- Typical dosage for fluoxetine are based on TADS and TORDIA studies and show need to titrate up to 40 mg by week 12.

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Anxiety Disorders (Non- OCD)

- Childhood-Adolescent Anxiety Multimodal Study (CAMS)
  - CBT + Sert>Sert=CBT>placebo
  - Combo superior at 2 and 3yr f/u
  - Overall 80% of responders were in remission
  - At 6yr f/u 50% were still in remission
- Social Effectiveness Therapy for Children (SET-C) + fluoxetine
  - Both fluoxetine and SET-C improved anxiety symptoms relative to placebo

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Anxiety Disorders (Non- OCD)

Medications:

- **SSRI's**: first line (fluoxetine, sertraline, escitalopram) Other SSRI's (paroxetine e.g. Paxil, fluvoxamine)
- **SNRI**: duloxetine (e.g. Cymbalta)
- **TCA's** (clomipramine for OCD)
- **Venlafaxine** (2nd or 3rd line for panic, GAD, social anxiety)
- **Buspirone** (no positive studies, but can use as 2nd or 3rd line for GAD)
- **Hydroxyzine**
- **Benzo** (clonazepam short term for school refusal, social anxiety, panic to allow kid to utilize CBT skills/don't use in preschool age).

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Secondary SSRI effects

- SSRIs have distinct secondary effects on the body producing slightly different side effect profiles (i.e. stimulating vs. sedating)
- Can be advantageous or disadvantageous
  - Activating effects helpful with extreme psychomotor retardation
  - Activating effects can lead to added distress in patients with anxiety or panic
- **Consideration of possible differences in secondary effects lead to more favorable matches for UC vs. OC Depression**

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SSRI-Induced Activation Syndrome in Children and Adolescents

Signs and symptoms:	irritability
	Agitation
	somatic manifestations of anxiety
	panic attacks
	restlessness
	hostility
	aggression
	Insomnia

Time of onset: during first 2 or 3 weeks after SSRI administration

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SSRI-Induced Activation Syndrome in Children and Adolescents

- **Relationship to drug dose: most studies suggest higher doses associated with higher rates of activation**
- **Biological susceptibility**
  - Twice as common in adolescents
  - Naturalistic study- every 1-year increase in age associated with 27% decrease in probability of severe event
  - Supported by preclinical studies
- Rating scale: Treatment-Emergent Activation and Suicidality Assessment Profile (TEASAP)
  - Parent rating scale
  - Currently being used in two prospective, randomized controlled trials of escitalopram in youth with depression and anxiety at risk for BPD

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SSRI-Induced Activation Syndrome in Children and Adolescents

- Mania
  - data suggests behavioral activation might represent subsyndromal manic symptoms or unrecognized bipolar disorder
  - Some stress SSRI-induced manic symptoms and activation syndrome should be distinguished since mania spectrum involve grandiosity and euphoria
  - Younger pts more likely to experience SSRI-induced mania
- Activation in ADHD
  - risk may be increased in youth with ADHD
  - Amphetamine derivatives ➔increased irritability (via meta-analysis)
  - Methylphenidate based ➔decreased irritability
  - DB study methylphenidate w/fluvoxamine-activation rates not higher compared to stimulant with placebo

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SSRI-Induced Activation Syndrome in Children and Adolescents

- Suicidality
  - 2004 "black box" warning
  - Limited evidence that activation syndrome may be related to suicidality; need to clarify possible association. TADS says no
  - Antidepressant treatment studies may under-represent the presence of activation in youth with anxiety disorders
  - Activation syndrome vs. energizing phenomena
  - Need to appropriately dose SSRI's in order to lower the risk of SSRI-induced activation syndrome

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SSRI-Induced Activation Syndrome in Children and Adolescents

- Risk Factors
  - Risk of activation did not differ among trials involving depressed and anxious youth
  - SSRI – related restlessness less common in older children compared to younger children
  - Higher plasma concentrations of SSRIs and rapid increases in plasma concentrations
  - Significant Ethnic and and inter-individual variability, polymorphisms in cytochromes associated with altered clearance
  - Dose titration: to date, only one DB-RCT of youth examined dose of SSRI on activation. Activation occurred at similar rates in both groups

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SSRI-Induced Activation Syndrome in Children and Adolescents

Pharmacokinetcs and pharmacogenetics

- Slow hepatic biotransformation
- Serotonin transporter polymorphism
  - SLC6A4 or 5-HT exists as long or short variant
  - Short allele may be assoc with increased risk of depressive and anxiety disorders and decreased response to SSRIs (Wehry et al, 2017)
  - Open label study in youth with citalopram three polymorphisms analyzed; only 5-HTR1DB G861C was associated with increased risk of activation; **CC genotype significantly more activation**

Pathophysiology

- Switch to a variant of a manic or mixed state possible explanation
- Changes in the regional brain 5-HT2 or 5-HT3 receptor sensitivity might be involved
- **Activation-related disinhibition may lead to impulse control problems**

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SSRI-Induced Activation Syndrome in Children and Adolescents

Biological Predictors

- MiRNAs as potential biomarkers

Medication Factors

- early onset of activation may be linked to 5HT1A-associated depression of 5-HT release
- Paradoxical decreases in seroternergic tone associated with impulsive and violent behaviors
- **Dietary deficits in omega-3 polyunsaturated fatty acids may promote behavioral activation in response to SSRI treatment**
  - Youth with MDD exhibit blood omega-3 fatty acid deficit
  - Increasing blood levels of omega-3 found to promote SSRI response
  - SSRI treatment associated inflammation – induced irritability in human subjects with TNF-a polymorphism

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SSRI-Induced Activation Syndrome in Children and Adolescents

- **Management**
  - In youth with UC Depression, start SSRIs at low doses with slow, planned titrations
  - **start SSRIs at low doses with slow, planned titrations**
  - Decreasing daily dose or stopping the medication
  - Youth who experience activation with one agent may be more likely to experience activation again on another agent
  - Treating insomnia with melatonin
  - **Assess med adherence- withdrawal symptoms may mimic symptoms seen in activation syndrome**
  - In youth with GAD and comorbid ADHD consider starting low dose and titrate up more slowly

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Anxiety Disorders (non-OCD)

Guanfacine or **Clonidine**

- one controlled study for anxiety disorders
- Consider w/ SSRI when anxiety w/ significant autonomic arousal and/or restlessness
- Baseline EKG, BP and pulse monitoring
- Severe rebound hypertension with abrupt discontinuation
- Tourette's, ADHD, Trichotillomania, other impulse-control disorders, Bipolar, PTSD (prazosin)

B-Blockers

- Consider for focused performance anxiety (No trials in youth)

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Buspirone (GAD)

No positive published controlled studies.

- Adverse side effects: lightheadedness, headache, dyspepsia.
- Higher peak plasma levels in children vs adolescents. May be tolerated at 5-30mg in teens and 5-7.5mg in children, twice daily
- May be an alternative to SSRIs for GAD in youth. Controlled studies needed.
- May augment SSRIs

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Benzodiazepines

- **Clonazepam:** benzo most used in youth
- Small controlled studies did not show efficacy
- Short-term use for school refusal, SAD, Panic disorder to supplement SSRI or allow acute participation in CBT(exposure)
- Risks of dependence long-term, half-life
- Contraindication in teens w/ substance abuse
- Side effects: sedation, disinhibition, cognitive impairment, difficulty with discontinuation
- Long-term use in GAD or severe chronic anxiety if other alternatives exhausted

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Atomoxetine (RCT)

- Selective norepinephrine reuptake inhibitor
- Youths with **ADHD and comorbid anxiety** disorder : SAD, GAD and/or social anxiety dis (Geller et al., 2007).
- Randomly assigned to 12 weeks of atomoxetine (n = 87) versus placebo (n = 89). Using last observation carried forward, the atomoxetine group compared with the placebo group was significantly improved on both anxiety and ADHD symptoms.
- These findings are encouraging because approximately **one fourth of children with ADHD have comorbid anxiety disorders.**

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Management of PTSD

- **Treat significant depression and anxiety**
- **Increased risk for suicide**
- **SSRI's** (Antidepressants)
  - For anxiety, depression, core symptoms
- **Guanfacine or Clonidine**
  - For hyperarousal, impulsivity, startle
- **Neuroleptics** (such as Risperidone)
  - For dissociation, brief psychosis, severe aggression
  - (monitor AIMS or DISCUS, glucose, weight)
- **Meds can reduce severity of symptoms so child can engage in therapy and exposures**

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Medications for Comorbidity

- **Depression**: Impairment, SSRI, monitor suicidal risk, CBT (Fluoxetine recommended)
- **ADHD**: First choice stimulants and behavioral tx. If stimulants exacerbate insomnia or anxiety, Atomoxetine second line, also Buproprion and Venlafaxine. Guanfacine or clonidine (get EKG) for hyperactivity/ impulsivity and sleep struggles.
- **Alcohol Use Disorder**: Caution against benzos
- **Bipolar disorder**: SSRIs may exacerbate, but can be introduced at low doses once stable

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OCD

- **FDA approved medications for treatment of OCD**
  - Clomipramine ≥ 10 y/o
  - Fluvoxamine ≥ 8 y/o
  - Sertraline ≥ 6 y/o
  - Fluoxetine ≥ 7 y/o
- Pediatric OCD Treatment Study (POTS)[42]
  - Sert+CBT>CBT=Ser>placebo
- Medication Augmentation: Clomipramine, Clonazepam, Neuroleptics (risperidone, haldol), 2nd SSRI, Lithium [16]
- Ask about any recent Group A beta hemolytic strep infections (if OCD or tics/ tourette's symptoms)
  - Pediatric Autoimmunie Neuropsychiatric Disorder Associated with Strep (PANDAS/ PANS)--Immune mediated antibodies at Basal Ganglia?
  - Modifications in Treatment Plan

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Management of Treatment Refractory OCD

- Titrating SSRI dose upward toward maximum tolerated range is advisable
- Continue SSRI for at least 1 year after successful response to SSRI
- No discontinuation trials in peds; taper off slowly and during periods of low stress; consider CBT booster sessions during SSRI discontinuation period
- Some experience remission by adolescence unrelated to pharmacotherapy
- SSRI less effective with co-morbid tic disorders

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Management of Treatment Refractory OCD

Neuroleptic augmentation:

- Reasonable option based on strong evidence in adults
- Only consider initiating after multiple failed adequate SSRI trials and CBT
- Adult RCT for risperidone, haloperidol, quetiapine, olanzapine, Abilify; no significant differences in efficacy between them (RCT)
- Discontinue if no noticeable improvement after 6-12 weeks due to long-term metabolic side effects
- ****CBT outperformed antipsychotic augmentation in recent RCT in adults**

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Management of Treatment Refractory OCD

Glutamate-Modulating Agents

- Neuroimaging studies show higher levels of glutamate in the caudate nucleus in treatment- naïve children with OCD
- Riluzole: DBPC trial in 60 children with OCD failed to demonstrate benefit compared to placebo; case reports of pancreatitis in children
- Should only be an option in children who have failed to improve on other evidence based tmts for OCD

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Management of Treatment Refractory OCD

- **Ketamine**- NMDA receptor antagonist, no studies in peds, In adult studies, extremely short-lived benefit of ketamine observed for OCD (hours-days)
- **Memantine** – case report-level data in children with refractory OCD; potential option in children who have failed all other evidence based
- **Topiramate** – inhibits AMPA/kainate glutamate receptors; safety profile well known in children but few data regarding efficacy in children with OCD (conflicting results in adult RCT)
- **N-Acetylcysteine (NAC)- glutamate-modulating agent**; Adult RCT showed effectiveness; clinical trials currently underway for use in pediatric OCD; consider in families who are opposed to using prescription medication; well tolerated in previous peds trials in autism, trichotillomania and cannabis dependence

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Management of Treatment Refractory OCD

- **Benzodiazepines**

  RCT in adults with OCD have failed to demonstrate efficacy compared to placebo

  Use in pediatric OCD not supported by the literature
- **Neurosurgical techniques:** currently no published controlled studies for ablative procedures; DBS crossover trials demonstrate efficacy in adults
- **Neurostimulatory techniques:** rTMS targeting of supplemental motor cortex has demonstrated efficacy in one sham-controlled study in treatment refractory adults with OCD; but a RCT of rTMS over R dorsolateral prefrontal cortex and bilateral SMA showed no significant difference between active and sham treatment

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Drug Name	Starting Dose to Maximum Dose (mg/day)		
	Young Child (age 4-6)	Pre-adolescent (age 6-12)	Adolescent (age 12 to 17)
Fluoxetine	1-2mg (5-10mg)	2.5 to 5mg (20-40mg)	5 to 10mg (40-60mg)
Sertraline	5mg (50 to 75mg)	10 to 12.5mg (100-150mg)	25 mg (150-200mg)
Fluvoxamine	5mg (50 to 75mg)	12.5 to 25mg (100-150mg)	25 to 150mg (150-300mg)
Citalopram	No data	5 mg (20-40mg)	10mg (20-40mg)
Escitalopram	1-2mg (5-10mg)	2.5mg (10-20mg)	5-20mg (30mg)
Venlafaxine	No data	37.5 (75-112.5mg)	37.5 (150-225mg)
Buspirone	No data	5-7.5mg BID	5-30mg BID

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Alternatives to medication

- Combining **nutraceuticals** with psychotherapy may lead to better outcomes
  - Omega-3 Fatty Acid (3 positive RCT)
  - Omega-3 Fatty Acid + Inositol (1 positive double-blind placebo controlled RCT)
- **Exercise** improves depressive symptoms in adolescents (Metanalysis of depressive symptom score. Carter, et al. JAACAP 2016)
- **Repetitive transcranial magnetic stimulation (rTMS)**. Several studies including (*Wall, 2016*).

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Genetic Testing

- In general, gives information regarding tolerability but not effectiveness
- Intended to provide information regarding genetic variants that may play a role in the metabolism of some medicines. However, FDA have required that the test label make clear that it is not intended to provide information on a patient's ability to respond to any specific medication.
- Some utility in individuals with mixed racial/ethnic background and atypical pharmacologic response
- Pharmaceutical Propaganda

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Summary: Treatment of Anxiety Disorders (AD) in Childhood

- Routine screening to identify AD early from several sources: child, parent, teacher.
- Comprehensive assessment to rule out other medical causes, identify specific AD, severity & impairment. Note somatic sx. Partner with specialist if concerns.
- Consider comorbid conditions in treatment planning
- **LEVEL 1**: If mild to moderate AD, cognitive behavioral therapy (CBT) with qualified therapist if available/feasible or at least psychoeducation re:CBT
- If inadequate response to CBT or AD mod to severe, consider monotherapy with SSRI (RCT's for : Fluoxetine, Sertraline first-line, then Fluvoxamine).
- For moderate to severe AD, combined therapy with CBT and SSRI medications can improve results

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Summary: Treatment of Anxiety Disorders

- Maximize dosing, increase dosing monthly if needed.
- If initial SSRI failed, try another SSRI in monotherapy and consider family history and response to SSRIs
- Paxil is not recommended due to side effect concerns. Consider if strong family history of success, after other SSRIs tried, w/ close monitoring
- **LEVEL 2**: If Level 1 failed, treat with Venlafaxine
- **LEVEL 3**: Consider other medication options as monotherapy or as adjunctive treatment with SSRIs (Buspirone, Benzodiazepines, TCAs, Clomipramine)
- Monotherapy with benzodiazepines is not recommended, but rather short-term use as SSRIs takes effect or to address anxiety related to brief medical or dental procedures.

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Red Flags: Treatment of Childhood Anxiety Disorders

- Starting medication trial without discussion of CBT as part of psychoeducation with child & family, whether or not CBT locally available
- Using paroxetine as first-line med for AD in youths
- Using benzodiazepines as single agent, long-term medication for childhood AD without trial of SSRI or venlafaxine
- Committing to long-term polypharmacy prior to maximizing initial medication.
- Starting young children on higher medication dosing more appropriate for adolescents or adults.
- In child with comorbid anxiety and bipolar, initiating SSRI treatment prior to stabilizing bipolar disorder

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CBT Anxiety Therapy Manuals

DON'T FORGET THE POWER OF PSYCHOTHERAPY!!!

- Foundational: Diaphragmatic breathing, progressive muscle relaxation
- **Coping Cat** (Phillip Kendall, 1990, 2000) and **CAT** (for adolescents)
- How I Ran OCD Off My Land (John March)
- Blink, blink, clop, clop (OCD)
- Meeky Mouse Therapy Manual: CBT Program for Selective Mutism (D. Fung, A. Kenny & S. Mendlowitz)
- Social Effectiveness Training for Children (SET-C: Beidel & Morris) - for Social Anxiety Disorde
- Modular Cognitive Behavioral Therapy for Child and Adolescent Anxiety Disorders
  (Bruce Chorpita, 2001)

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Resources

National Child Traumatic Stress Network www.musc.edu/tfcbt; www.nctsnet.org

American Academy of Child & Adolescent Psychiatry www.aacap.org

Anxiety Disorders Association of America www.adaa.org

SM Group- Child Anxiety Network www.selectivemutism.org

Association for Behavioral and Cognitive Therapies www.abct.org
Obsessive Compulsive Foundation www.ocfoundation.org

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References for Parents &Teachers

- **My Anxious Mind: A Teen's Guide to Managing Anxiety and Panic (Tompkins et al, 2010)**
- Helping Your Anxious Child (Rapee, Wignall, Spence, Cobham, 2008)
- Keys to Parenting Your Anxious Child (Manassis, 2008)
- Freeing Your Child from Anxiety (Chansky, 2004)
- Freeing Your Child from OCD (Chansky, 2001)
- **Helping Your Child with Selective Mutism (McHolm et al, 2005)**
- When Children Refuse School: Parent Workbook (Kearney & Albano, 2007)

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THANK YOU

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