MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Treatment of Anxiety Disorders in Children and Adolescents

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Disclosure

Please note that off-label medications will be discussed

Disclosures:
- MGH Psychiatry Academy: Speaking honoraria
- AACAP: Speaking honoraria

Treatment Planning Should Consider a Multimodal Treatment Approach

- Education of the parents and child about the anxiety disorder
- Consultation with school personnel and other providers
- Cognitive-behavioral interventions
- Pharmacotherapy

Treatment Planning Should Consider Severity and Impairment of the Anxiety Disorder

- Mild severity should begin with psychotherapy
- Monitor functional impairment as well as symptom reduction during the treatment process

CBT has the most empirical support for the behavioral treatment of anxiety disorders in youth

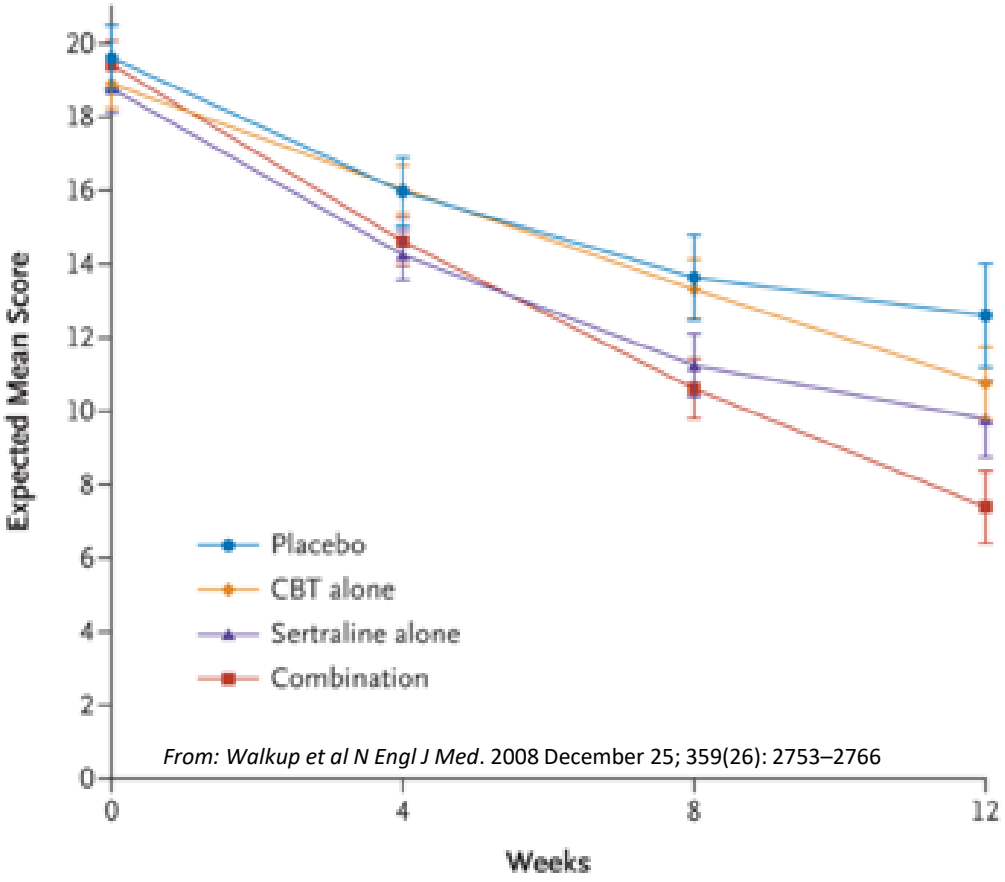
Cognitive Behavioral Therapy

- Psychoeducation (educating the patient and the family about the disorder, its course, management and treatment)
- Somatic management skills training (relaxation, diaphragmatic breathing, self-monitoring)
- Cognitive restructuring (challenging negative expectations and modifying negative self-talk)
- Exposure methods (imaginary and in vivo exposure with gradual desensitization to feared stimuli)
- Relapse prevention plans (booster sessions and coordination with parents and school)

When to Consider Using Medication…

- Moderate-severe symptoms
- Impairment makes participation in psychotherapy difficult
- Partial response to psychotherapy
- SSRIs should be considered the first line medication for the treatment of youth with anxiety disorders

Child/Adolescent Anxiety Multimodal Study (**CAMS**)



From: Walkup et al N Engl J Med. 2008 December 25; 359(26): 2753–2766

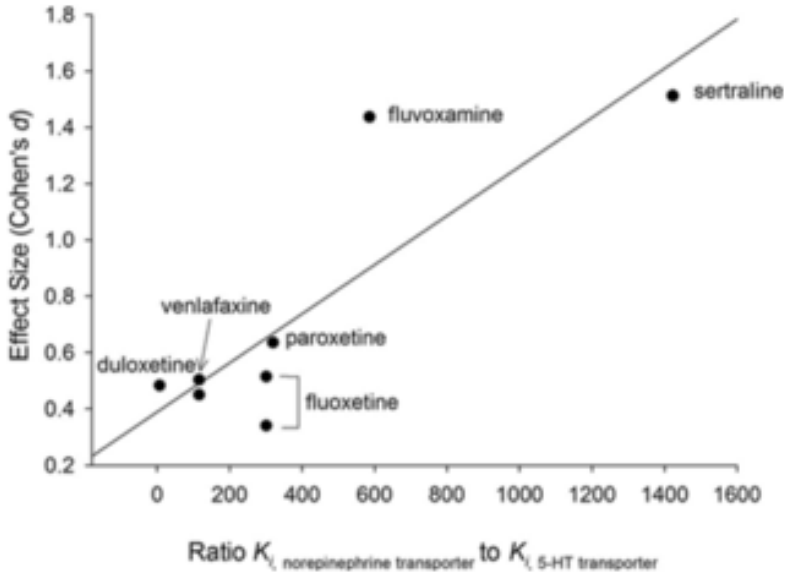
- Combined branch (sertraline and CBT) **most effective**
  - 81% responded - (CGI-I of 1 or 2)
    - (Vs ~60% CBT/SSRI; ~25% placebo)
  - 68% remitted
- Phase II: Combined treatment still most effective at 24 + 36w

Walkup et al (2008)
Compton et al (2010)

Recent Meta-analyses

Strawn et al (2015) Depress Anxiety

- 9 trials, 1,673 patients (6-17)
- 6 medications
  - Fluoxetine, duloxetine, sertraline, paroxetine, venlafaxine, fluvoxamine
- SSRI/SNRIs all showed superiority
  - "Moderate magnitude" of effect
  - Cohen's d = 0.62, p<.01
- Effect size correlated with serotonergic specificity
- Well tolerated
  - No increased risk for nausea/abdominal symptoms
- Activation trend (med vs placebo)
  - (OR: 1.86, CI: 0.98-3.53, P = .054)



Recent Meta-analyses Cont.

Wang et al (2017) JAMA Peds

- 115 studies, (7,719 patients); Medications, therapy, combination treatment
- Medications more effective compared to pill placebo:
  - Atomoxetine, duloxetine, venlafaxine, fluoxetine, fluvoxamine, paroxetine, sertraline
- TCAs - “marginally increased likelihood of treatment response”
- Benzos – no significant improvement
- CBT significantly improved symptoms, remission, response
- Combination of medication and therapy more effective than either alone

Pediatric OCD Treatment Study - POTS

- N = 112
- Ages 7-17 years
- 3 sites, 12 weeks
- CBT, Sertraline, COMB and placebo

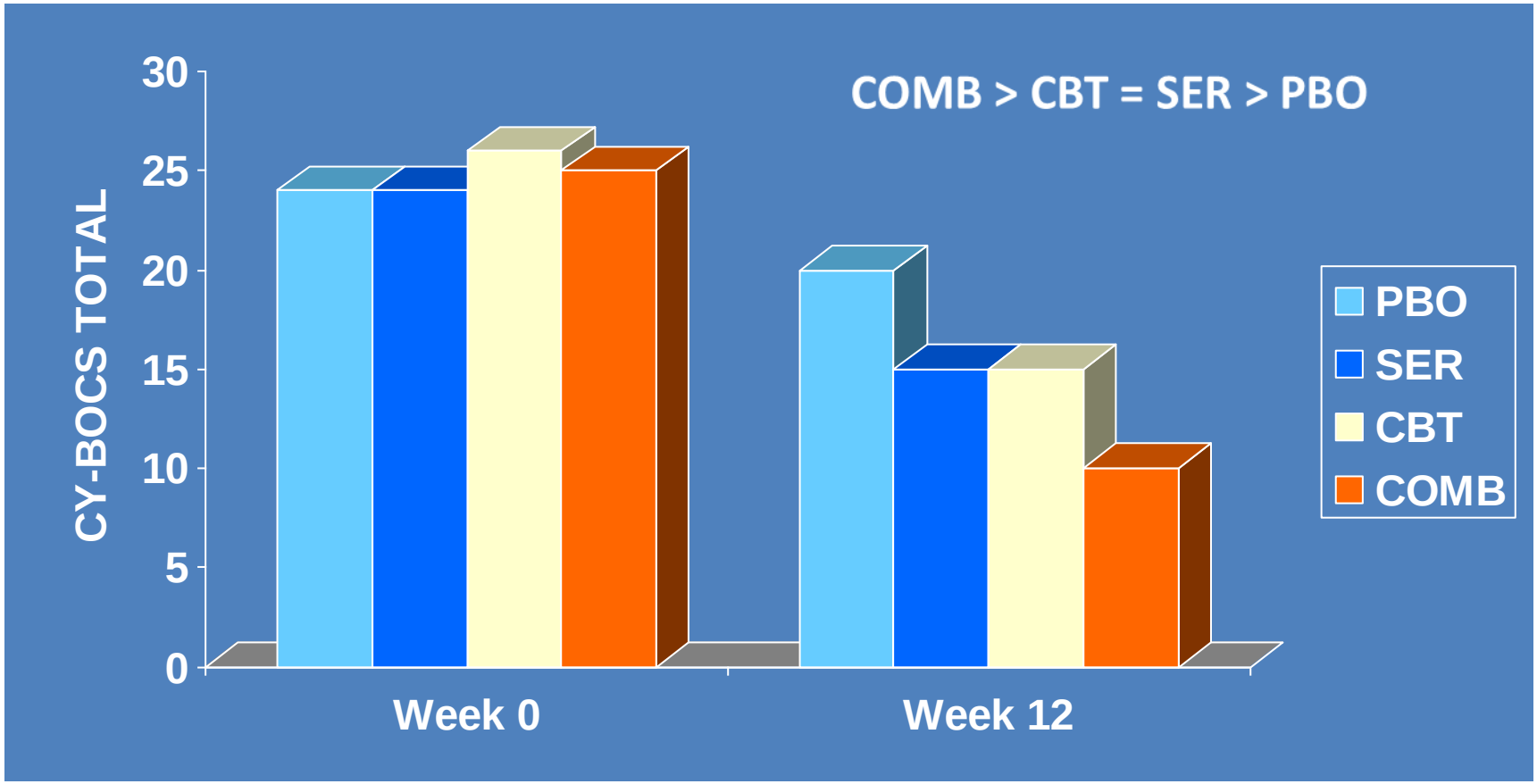
Pediatric OCD Treatment Study (POTS)

- Combination therapy (CBT and medication) is most effective for moderate-severe OCD (aiming for CY-BOCS<11)
  - Combined: 53.6%
  - CBT: 39.3%
  - Sertraline: 21.4%
  - Placebo: 3.6%

- POTS II: For children/adolescents who are partial responders to SRIs
  - Weekly CBT with antidepressant (69% improvement)
  - Instructions on CBT and antidepressant (34% improvement)
  - Antidepressant alone (30%)

Garcia et al, JAACAP, 2010: Pediatric OCD Treatment Study (**POTS**)

CY-BOCS ITT Outcomes



Pediatric OCD Study Team (2004) *JAMA*.

Dose Range for SSRI's in Preadolescents and Adolescents with Obsessive Compulsive Disorder

Medication	Start Dose Preadolescent	Start Dose Adolescent	Typical Dose Range (Typical Mean Dose)
Prozac (F.D.A. Approved)	5-10	10-20	10-80 (25)
Zoloft (F.D.A. Approved)	12.5-25	25	50-200 (178)
Luvox (F.D.A. Approved)	12.5-25	25-50	50-300 (165)
Anafranil (F.D.A. Approved)	12.5-25	25	50-200

Adapted From Martin A. Pediatric Psychopharmacology:Principles and Practice (2003)

Guidelines for Using SSRI's in OCD

- Rate of response
  - Will see ~2/3 of response in first 2-4 weeks
  - 12 weeks for maximal response at any particular dose
  - Balance need for higher doses with response to medication
- Expect partial response
  - 25%-40% improvement
  - Full remission is rare
  - 25% fail clomipramine or SSRIs
- Continue effective medication for ≥1 year

SSRI Dosing table for GAD, SP, PTSD and Panic Disorder

SSRI	Starting Dose*	Increment	Max Daily Dose	Contraindicated Meds	Available Doses	Generic available
Fluoxetine (Prozac)	10mg qd/od**	10-20mg	60mg	MAOIs	10 mg tablets 10,20,40 mg pulvules 90mg weekly pulvule and liquid form	Y
Sertaline (Zoloft)	25mg qd/od**	12.5-25mg	300mg	MAOIs	25, 50, 100 mg tablets and liquid form	Y
Citalopram (Celexa)	10mg qd/od**	10mg	60mg	MAOIs	20, 40 mg tablets and liquid form	Y
Escitalopram (Lexapro)	5mg qd/od**	5mg	20mg	MAOIs	5, 10, 20 mg tablets and liquid form	N
Fluvoxamine (Luvox)	25 mg qd/od, ** then bid	25 mg	250mg	MAOI's, terfenadine, astemizole, pimozide	25, 50, 100 mg tablets and liquid form	Y
* Start with lower doses for younger children; **qd = od = every day;						

Pharmacotherapy in Pediatric Anxiety

- Typically developing children/adolescents, **SSRIs** and SNRIs are effective in treating pediatric anxiety disorders (and OCD) compared to placebo
  - SSRIs are associated with greater and faster improvement compared to SNRIs
  - "Sertraline has the greatest evidence of efficacy [in pediatric anxiety]" (p. 6, Strawn et al, 2017)

Strawn et al (2018) *JAACAP*
Strawn et al (2017) Curr Probl Pediatr Adolesc Health Care
Strawn et al (2015). Depression Anxiety.
Wang et al (2017). JAMA Peds

Adverse Effects

Mills and Strawn (2020) *JAACAP*

- Meta-analysis of adverse events, suicidality and AE-related discontinuation in youth with GAD and OCD
  - 18 trials, ~2500 patients, 7 medications
- SSRIs associated with greater likelihood of:
  - AE-related discontinuation, activation, sedation, insomnia, abdominal pain, headache
  - Activation was more common in SSRIs compared to SNRIs (p=0.007)
  - Neither SSRI nor SNRIs associated with treatment-emergent suicidality

Antidepressants and Black-box Label

- Black-box warning on antidepressants (2004)
- "Did not observe an increased risk of treatment-emergent suicidality in youth with anxiety disorders" (Strawn et al 2015, p.154)
  - Venlafaxine and paroxetine

Off-label Pharmacological Treatments

- Tricyclic antidepressants (TCAs)
- Benzodiazepines
- Buspirone
- Alpha-agonists
- Pregabalin
- Natural supplements / Cannabis

When/How to Stop the Medication

- Solid response
  - No breakthrough symptoms
  - No seasonal slumps
- Trial of CBT
- Take it down slow
- Watch carefully for year

Summary

- **Most common childhood psychiatric disorder**
- Behavioral and pharmacotherapy options both effective
  - Combined approach is best
  - SSRIs > SNRIs
- Watch for common co-morbidities (ADHD, depression)
- Watch for ‘specific to pediatric’ presentation (e.g. somatic and oppositionality)
- They are treatable!

Thank you!

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