



Assessment and Treatment of Childhood Anxiety Disorders

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Disclosures for the past 12 months

John T. Walkup, MD

- Lilly, Pfizer and Abbott – free medication and placebo for NIMH-funded studies. All studies completed and manuscripts are in preparation
- Royalties from Guilford and Oxford press for books and manuals related to Tourette's syndrome.



Discussion of Off Label Use of Medications

- All medication use should be considered off label unless explicitly noted otherwise



Outline

- Review of Anxiety Disorders
- Review Treatment of Anxiety Disorders
 - OCD
 - Other Anxiety Disorders
 - CAMS
- SSRI side effects



Question 1

Approximately this percentage of children with specific phobia have another anxiety disorder?

- A) 10%
- B) 25%
- C) 50%
- D) 70%
- E) 90%



Question 2

- One of the following is a tool for assessment of childhood anxiety disorders:
 - A) SNAP-IV
 - B) CDRS
 - C) SCARED
 - D) WISC
 - E) YMRS



Question 3

Anxiety disorders in children present very commonly with:

- A) Sadness of mood
- B) Physical Complaints
- C) Aggression
- D) Hallucinations
- E) Memory problems



Anxiety Disorders in Children and Adolescents

- Specific Phobia
- OCD
- Separation Anxiety Disorder
- Generalized Anxiety Disorder
- Social Phobia
- Acute Stress Disorder
- Post-traumatic stress disorder
- Panic Disorder



Specific Phobia

- Animals, insects etc.
- Environmental - thunder, water, heights
- Blood, injection or other suspected painful event
- Situational - tunnels, bridges, elevators
- 70% have another anxiety disorder



Obsessive Compulsive Disorder

- Prominent obsessions or compulsions
 - Dirt, germs, or other contamination
 - Ordering and arranging
 - Checking
 - Repetitive acts
- Impairing or time consuming



Subtypes of OCD

- Pure Obsessions
- Contamination
 - Least likely associated with other Axis I disorders
- Symmetry/Order
- Hoarding
 - Poorer treatment response.



Separation Anxiety Disorder (SAD)

- Excessive concern regarding separation from home or from attachment figures
 - Bad things happening to parent and or child
 - Cannot be alone
 - Avoidance
 - Difficulty falling asleep or sleeping with loved ones
 - Physical aches and pains
 - Accommodation by adults
- Impairment or distress.



Generalized Anxiety Disorder (GAD)

- Excessive worry and apprehensiveness
 - Restless, keyed-up or on edge.
 - Fatigued at end of school day
 - Concentration problems “choking on tests”
 - Sleep problems (falling asleep)
 - Tense and irritable
- Unable to control the worry
- Impairment or distress



Social Phobia (SoP)

- Fear of social or performance situations
 - Specific
 - Generalized



Selective Mutism

- Ability to speak
- Not speaking in social situations
- Not part of another disorder



Acute Stress Disorder

- True stressful event – life threatening
- Re-experiencing the event
- Avoidance and numbing
- Increased arousal
- Time limited



Post-traumatic Stress Disorder

- True stressful event – life threatening
- Re-experiencing the event
- Avoidance and numbing
- Increased arousal
- Risks for enduring symptoms
 - Pre-existing mental disorder
 - Proximity
 - Post-traumatic environment



Panic Disorder

- Attacks of anxiety (Physical Symptoms)
 - ↑ Heart rate, pounding heart, palpitations
 - Hyperventilation, shortness of breath
 - Choking sensation
 - Chest discomfort or pain
 - Abdominal pain
 - Some psychological symptoms
- Worry about the next one
- Avoidance behavior related to the attacks
- Agoraphobia....



Assessment Strategies

- Multidimensional Anxiety Scale for Children (MASC) – J. March
- Screen for Child Anxiety Related Emotional Disorders Scale (SCARED) – B. Birmaher
- Achenbach Child Behavior Checklist (CBCL)



What to look for

- **Physical complaints – headaches, stomach aches, dramatic presentations of pain.**
- Problems with falling asleep and middle of the night awakening, repeated visits to parents room
- Eating problems
- Avoidance of outside and interpersonal activities – school, parties, camp, sleepovers, safe strangers
- Excessive need for reassurance – new situations, bedtime, school, storms, bad things happening
- Inattention and poor performance at school
- Not necessarily pervasive – some areas of function remain



Physical Symptoms – Provoked and Spontaneous

- Anxious children listen to their bodies
- Headache
- Stomachache – stomach and bowel problems
- Sick in the morning and can't fall asleep in the evening
- Frequent urge to urinate or defecate
- Shortness of breath
- Chest pain - tachycardia
- Sensitive gag reflex - fear of choking or vomiting
- Difficulty swallowing solid foods – growth inhibition?
- Dizziness, lightheaded
- Tension and tiredness – exhausted and irritable after a school day
- Derealization and depersonalization
- Avoidance to prevent above physical symptoms



What to look for

- Physical complaints – headaches, stomach aches, dramatic presentations of pain.
- **Problems with falling asleep and middle of the night awakening, repeated visits to parents room**
- **Eating problems – over and under**
- **Avoidance of outside and interpersonal activities – school, parties, camp, sleepovers, safe strangers**
- **Excessive need for reassurance –bedtime, school, storms, bad things happening**
- **Inattention and poor performance at school**
- **Explosive outbursts**
- **Not necessarily pervasive**



Epidemiology

- Very common up to 8-10% of kids
- Under diagnosed
- Under treated
- Need to look for it



The Treatment of OCD



Treatment of OCD

- Cognitive-behavioral therapy
- SRIs
 - Clomipramine
 - Fluvoxamine
 - Paroxetine
 - Sertraline
 - Fluoxetine
 - Citalopram
 - Escitalopram
- Combination treatment
- Deep brain stimulation



Serotonin Reuptake Inhibitors FDA Approvals

- Clomipramine - FDA approved to age 10 OCD
- Fluvoxamine - FDA approved to age 8 OCD
- Sertraline - FDA approved to age 6 OCD
- Paroxetine – effective for OCD and SoP
- Fluoxetine – effective for OCD; MDD to age 7
- Citalopram – No controlled trials in children
- Escitalopram – FDA approved for depression to age 12 years
- Venlafaxine – Effective for SoP and maybe childhood GAD (1 of 2 studies are positive)



Controlled Trials: Obsessive Compulsive Disorder

- Clomipramine - DeVeough-Geiss et al., 1992
- Fluoxetine - Riddle et al., 1992
- Sertraline - March et al., 1998
- Fluvoxamine - Riddle et al., 2001
- Fluoxetine – Geller et al., 2001
- Paroxetine - Geller et al., 2004



Sertraline In Childhood OCD

- Double-blind, placebo-controlled, 12-week, multisite trial
- N = 187; age = 6-17 years; sertraline ≤ 200 mg/d
- Sertraline > placebo
- Mild side effects
- Similar profile of response as clomipramine



Fluvoxamine In Childhood OCD

- Double-blind, placebo-controlled, multisite trial
- N = 120; age = 8-17 years; fluvoxamine 50-200 mg/d
- Fluvoxamine > placebo
- Mild side effects



Fluoxetine in Childhood OCD

- Geller et al., 2001
- N=103, ages 7-17 years
- 13 week double-blind placebo controlled trial
- Dose 10-60 mg/day
- Decrease CY-BOCS favored fluoxetine (p<.026)



Paroxetine

- Double-blind, placebo-controlled. 10 week trial
- Ages 7-17
- N=203
- Paroxetine > placebo
- Mild side effects



Augmentation Strategies for OCD

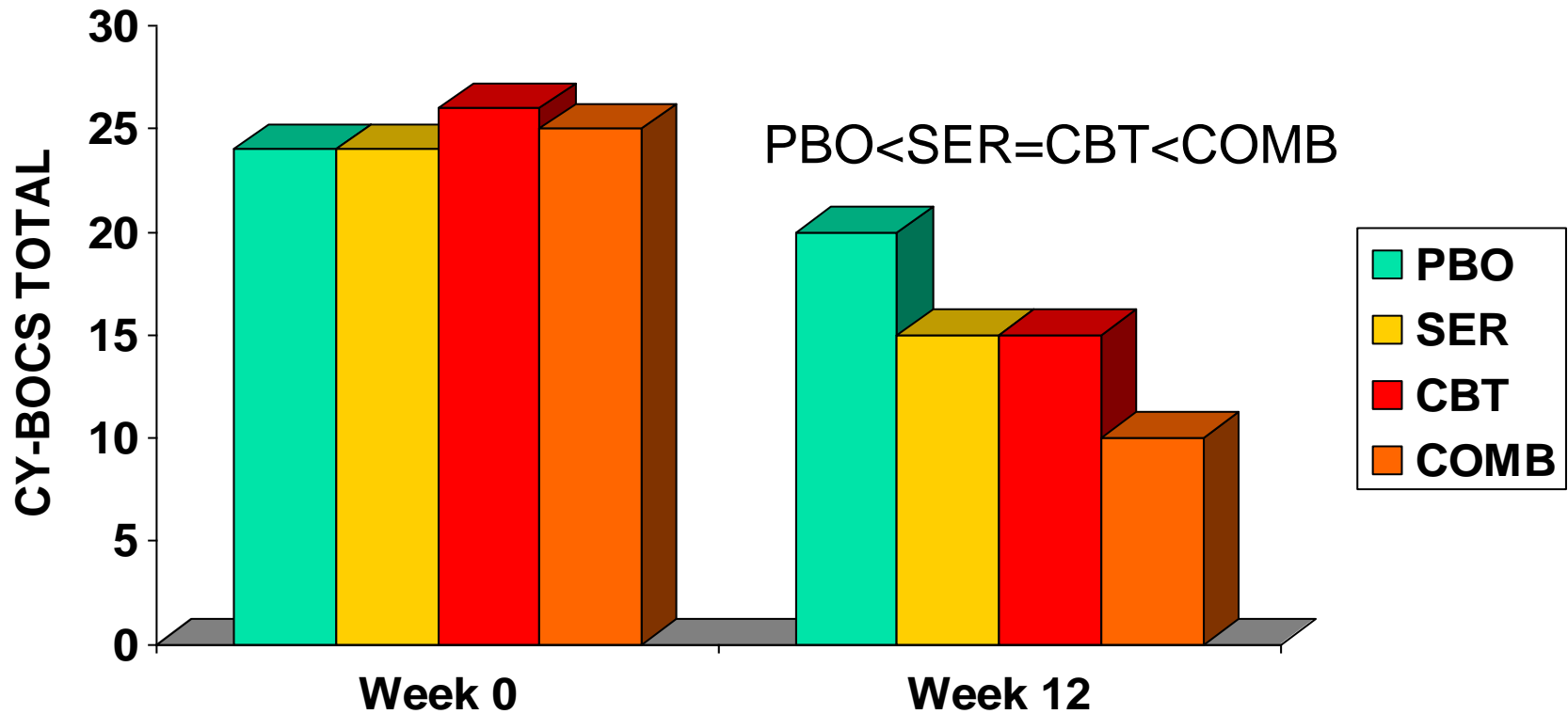
- Clomipramine
- Clonazepam
- Antipsychotics
- IV Clomipramine
- Buspirone
- Add second SSRI
- Lithium
- Stimulants
- Others



Pediatric OCD Treatment Study - POTS

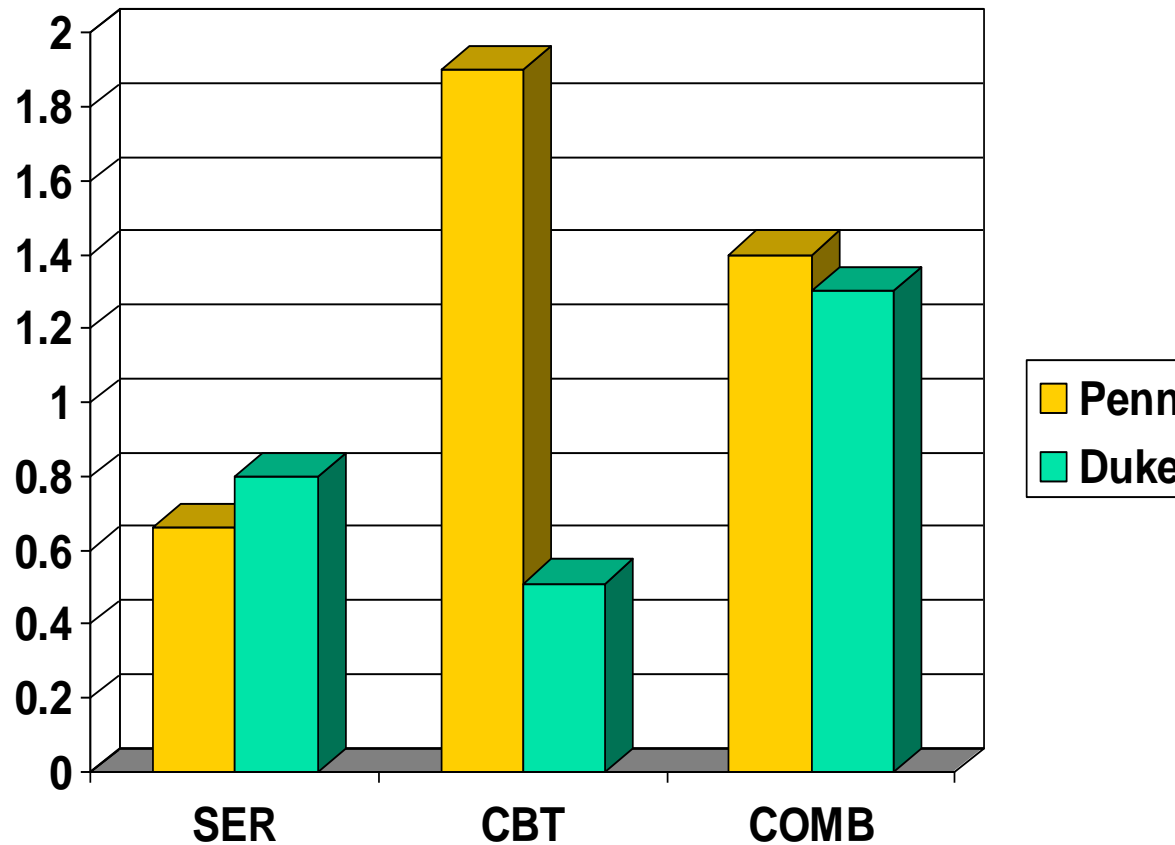
- N = 112
- Ages 7-17 years
- 3 sites, 12 weeks
- CBT, Sertraline, COMB and placebo

CY-BOCS ITT Outcomes



Pediatric OCD Study Team (2004) *JAMA*.

Site x Treatment Interaction



Pediatric OCD Study Team (2004) JAMA.



Deep Brain Stimulation

- Indicated for Parkinson's, tremor and pain
- Humanitarian exemptions for dystonia and OCD
- Small number of subjects world wide for refractory depression and Tourette's syndrome



PANDAS

- **P**ediatric **A**utoimmune **N**europsychiatric **D**isorders **A**ssociated with **S**treptococcal infections
- Not a validated disorder
- Treatment outpaced our knowledge of the disorder
- Most treatments should be done as a part of a research trial
- 'Epi'-studies suggest a small group of kids may be at risk.



PANDAS

- Suspected cases
 - Throat culture
 - If positive – treat
 - Do not get spot titers
 - Probably no role in non-research settings for other immunologically-based treatments



Controlled Trials: “Separation Anxiety Disorder”

- Imipramine - Gittelman-Klein et al., 1971, 1973, 1992
- Clomipramine - Berney et al., 1981
- Alprazolam and imipramine - Bernstein et al., 1990
- Bernstein et al., 1999, 2000, 2001
- Clonazepam - Graae et al., 1994



SAD, GAD and SoP

- Pharmacotherapy
 - RUPP trial, 2001
 - Birmaher et al., 2003
- Psychotherapy
 - Kendall, 1994
 - Kendal et al., 1997
 - Many others



SAD, GAD and SoP – RUPP, 2001

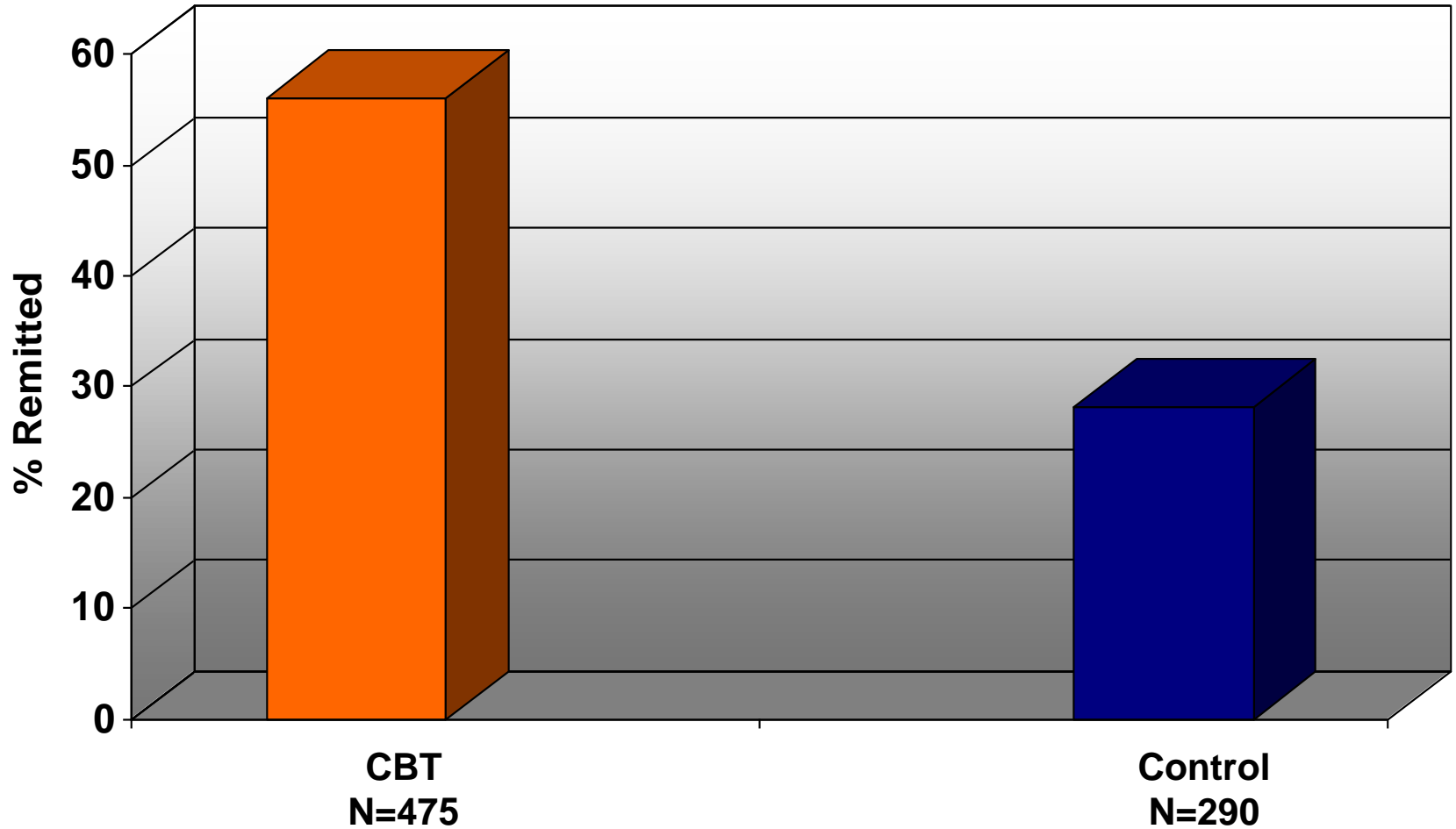
- Ages 6-17 years old
- N=128
- Fluvoxamine up to 250-300 mg/day
- Randomized double-blind, placebo-controlled
- 8 weeks.
- RESULTS:
 - Fluvoxamine > placebo on CGI-I
 - 76% (48/63) > 29% (10/65)
 - Pediatric Anxiety Rating Scale
 - Fluvoxamine 18.7 to 9.0 > 50% change
 - Placebo 19.0 to 15.9 = No Change



SAD, GAD and SoP

- Ages 7-17 years old
- N=74
- Fluoxetine 20 mg/day
- Randomized, double-blind, placebo controlled
- 12 weeks.
- Results
 - Fluoxetine 61% vs Placebo 35%

CBT for Child Anxiety (ITT Outcomes)





Social Phobia

- 16-week, randomized, double-blind, placebo-controlled, flexible-dose, parallel-group,
- N= 322 children (8-11 years of age) and adolescents (12-17 years of age) with social anxiety disorder
- Medication: paroxetine 10-50 mg/d or placebo.
- RESULTS:
 - Response: 77.6% vs. 38.3%
 - CGI-I = 47.8% vs. 14.9%.



Other Important Studies

- Sertraline in GAD - Rynn et al., 2001
- Venlafaxine in GAD, Rynn et al., 2007
- Venlafaxine in SoP, March et al., 2007
- Buspirone in GAD, unpublished



CAMS

- Aim: to compare sertraline and CBT, alone and in combination, to PBO.
- N=488 subjects with separation anxiety disorder, generalized anxiety disorder, or social phobia
- Age: 7-17 years
- Duration- 12-week trial



CAMS

- All 3 active treatments demonstrated efficacy
- 81% response to COMB, 61% CBT, 56% sertraline, 26% PBO
- COMB > CBT=Sertraline > PBO



Adverse Events

- Activation is common: 10-15% difference between groups
- Bipolar switches uncommon <1%
- Frontal lobe symptoms at higher doses
- GI issues early
- Easy bruising and bloody noses
- Some case reports about growth



Suicidality

- Risk Difference for Efficacy
 - MDD - 11.0% = NNT of 10
 - OCD - 19.8% = NNT of 5
 - Non-OCD anxiety disorders - 37.1% = NNT of 3
- Risk Difference for Suicidality 1-2%
- Overall - 0.7% = NNH of 143
 - But not for individual disorders
 - MDD - 0.9%; NNH ~100
 - OCD - 0.5%; NNH ~200
 - non-OCD anxiety disorders - 0.7% ; NNH ~140



Summary

- Anxiety is common
- Anxiety is easy to miss
- Anxiety disorders are responsive to treatment
- Side effects with meds are minimal and can be managed with good monitoring



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Answers

1) D

2) C

3) B