Social Anxiety Disorder (Social Phobia)

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Social Anxiety Disorder (SAD) Outline

- Diagnosis: DSM-V
- Epidemiology
- Neurobiology
- Comorbidity
- Treatment

Question #1

The “Performance only” subtype of Social Anxiety Disorder includes experiencing intense fear in which of the following situations:

a. athletic performance
b. musical performance
c. dancing
d. public speaking
e. urinating in a public bathroom
f. all of the above

Question #2

In general, SAD prevalence rates are higher in *females* than in *males* in the general population, but the rates are equivalent or slightly higher for *males* in clinical samples.

a. true

b. false

Question #3

Which statement is *false:*

a. Median age of SAD onset in the U.S. is 13 years
b. Onset can begin even in early childhood
c. SAD may begin following a humiliating experience
d. In the community, about 20% of people with SAD experience remission within a few years.

Question #4

U.S. epidemiological studies report which 3 psychiatric disorders are commonly associated with Generalized SAD?

a. Panic Disorder
b. Major Depression
c. Agoraphobia
d. Alcoholism
e. Somatization Disorder

Question #5

Which of the following are considered first-line treatments for SAD:

a. **SSRIs**
b. **Gabapentin/Pregabalin**
c. **SNRIs**
d. **Buspirone**
e. **CBT**

Social Anxiety Disorder Historical Perspective

Symptoms as Described by Hippocrates:

[A man who] "…through bashfulness, suspicion and timorousness, will not be seen abroad; … his hat still in his eyes, he will neither see nor be seen by his goodwill. He dare not come in company for fear he should be misused, disgraced, overshoot himself in gestures or speeches or be sick; he thinks every man observes him."

Robert Burton: Anatomy of Melancholy (1652)

Social Anxiety Disorder
Historical Perspective

Name	Author
Ereuthrophobia	Casper, 1842
Kontacktneurosen	Stockert, 1929
Tai-jin-kyofu	Morita, 1932
Social Neurosis	Shilder, 1938
Social Anxiety Neurosis	Myerson, 1945
Social Phobia	Marks, 1968

*

DSM-5 Social Anxiety Disorder (SAD)*

- Believes performance will be negatively evaluated with resulting embarrassment or humiliation
- Exposure to feared situation predictably elicits anxiety
- Avoids or endures feared social situation(s) with distress
- Fear is out of proportion to the actual threat posed
- Impairs occupational, social, or family roles
- Not better explained by drug of abuse, medication, or medical or mental disorder, e.g., major depression (social reticence), Parkinson's Disease, obesity, burns, stuttering

* Performance only: if the fear is restricted to speaking or performing in public

* SAD Differential Diagnosis

- Avoidant Personality Disorder *
- Panic Disorder / Agoraphobia
- Generalized Anxiety Disorder
- Depression-related social avoidance
- Separation anxiety disorder
- Body Dysmorphic Disorder
- Schizotypal / Schizoid Personality Disorder
- Medical conditions, e.g., tremor

* Large overlap with GSAD, but has broader avoidance pattern; Avoidant PD disappears with treatment in many patients with GSAD

* Screening for Generalized Social Anxiety
MINI-SPIN (Social Phobia Inventory)

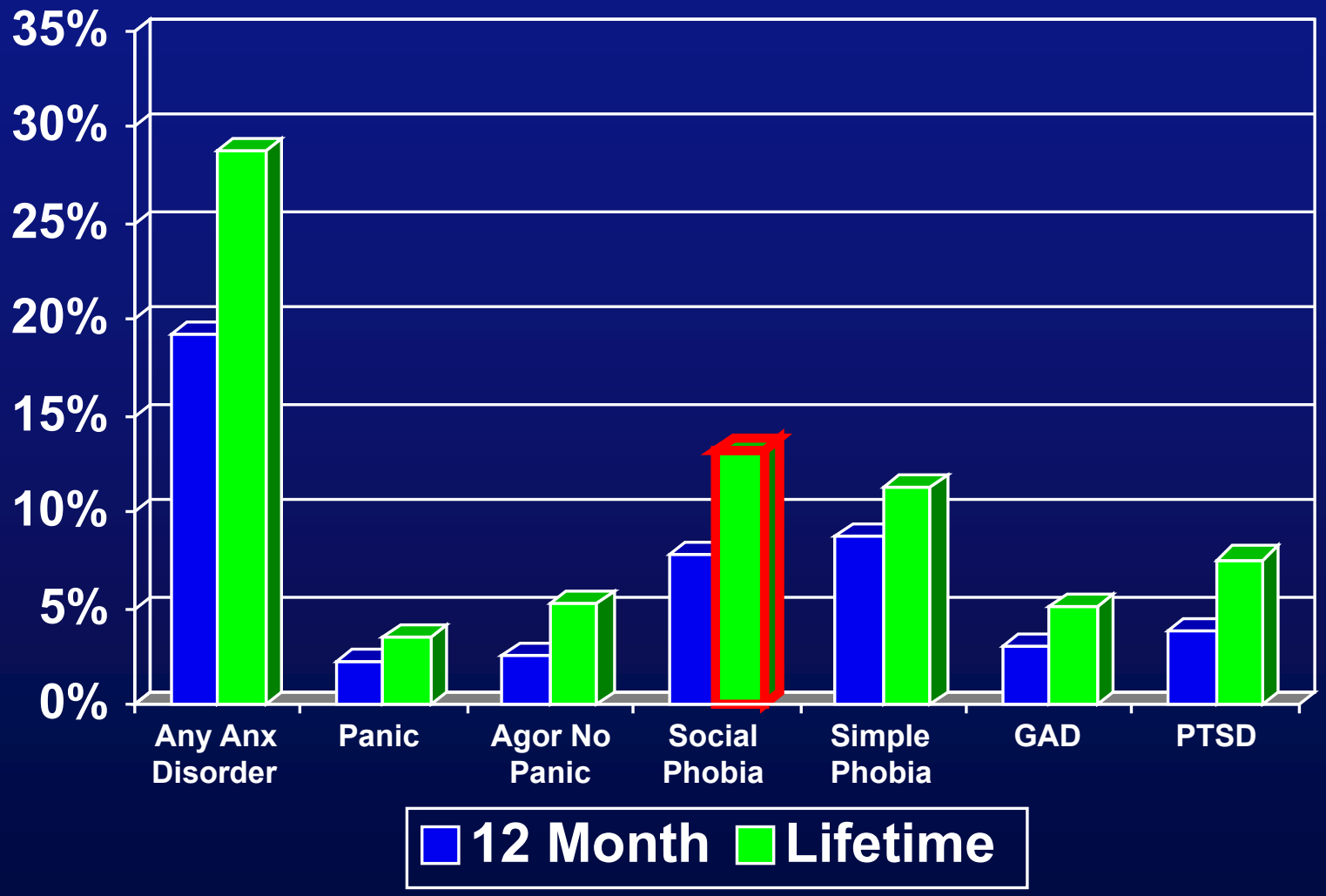
- Fear of embarrassment causes me to avoid doing things or speaking to people
- I avoid activities in which I am the center of attention
- Being embarrassed or looking stupid are among my worse fears
  - 90% accurate detection of GSAD in 344 patients

Connor KM, et al. Depress Anxiety. 2001;14:137-40.

Social Anxiety Disorder in Adolescents

- May present with or as:
  - Depression
  - Conduct Problems (truancy, etc.)
  - Substance or ETOH Abuse

SAD: Most Prevalent DSM-IV Anxiety Disorder



* Adapted from Kessler RC, et al. Arch Gen. Psychiatry. 1994;51:8-19

DSM-5 SAD Subtype Characteristics

*

Generalized (~70%)

- Pervasive social fears, avoidance
- Early onset
- Familial
- >80% comorbidity
- More impairment
- Lower remission Rate
- Extended treatment needed

DSM-5 Performance only (~30%)

- Few social fears (mostly public speaking)
- Later onset
- Not familial
- Less comorbidity
- Limited impairment
- Remission common
- PRN treatment usually adequate

Typical Feared Social Situations

Generalized

- Attending Social Events
- Conversing in a Group
- Speaking on Telephone (esp. in public)
- Interacting with Authority Figures
- Making Eye Contact
- Ordering Food in a Restaurant

Performance Only

- Public Speaking
- Eating in Public
- Writing a Check
- Using a Public Toilet
- Taking a Test
- Trying on Clothes in a Store
- Speaking up at a Meeting
- Athletic, musical, or dance performance

Performance Only subtype: 1 or 2 situations (esp. public speaking).
Generalized subtype: most interactions, aside from family and close friends

Social Anxiety Disorder Symptoms

- **Physical**
  - Tachycardia
  - Trembling*
  - Blushing*
  - Shortness of Breath
  - Sweating*
  - Abdominal Distress
  - Socially-Cued Panic Attacks

*more bothersome because they are visible to others

- **Cognitive**
  - Perceived scrutiny and certainty of negative evaluation
  - Misinterpretation or failure to note social cues
- **Behavioral**
  - Avoidance
  - Freezing

* Beidel, DC. J Clin Psychiatry. 1998;59 (Suppl 17):27-32.
van Vliet IM, et al, Psychopharmacol. 1994;115:128-34.

The Course of SAD

- Median age at onset is 13 years
- 75% of individuals have onset between 8 and 15 years
- In the community, ≈ 30% remit within 1 year, and ≈ 50% remit within a few years
- Without treatment, the course is ≥ several years for ≈ 60% of individuals
- In Western societies, only ≈ 50% seek treatment, and tend to do so after 15-20 years of symptoms

Source: DSM-5

*

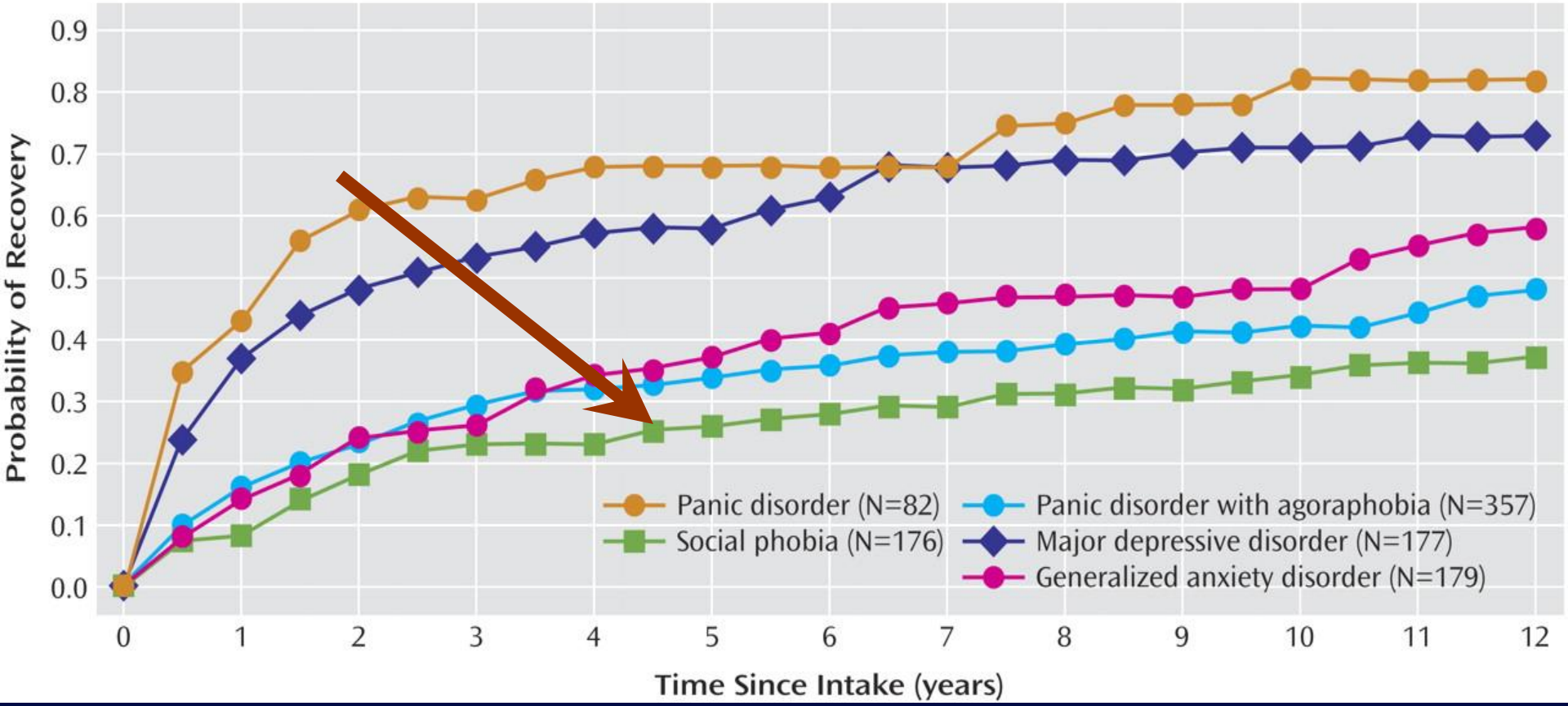
SAD-Related Impairment

- Lower educational status
  - Are less likely to graduate high school
  - Work in less skilled occupations
- Lower income and socioeconomic status
- Lower likelihood of marrying
- Higher likelihood of divorce
- Impeded leisure activities

* Magee WJ, et al. Arch Gen Psychiatry. 1996;53:159-68

SAD: 12-year Cumulative Remission Probability

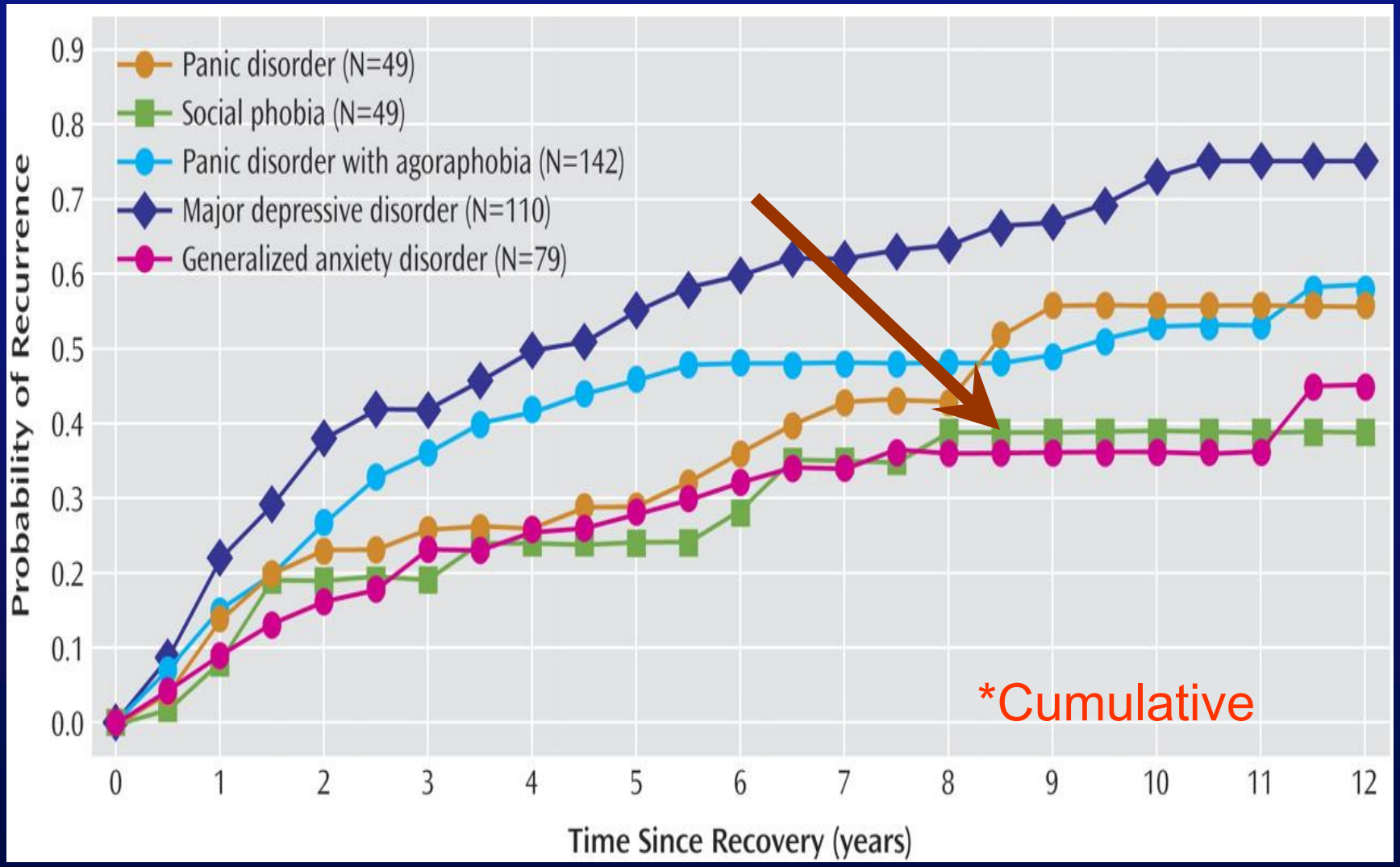
Social Anxiety Disorder had lowest rate of remission



* Bruce SE, et al. Am J Psychiatry. 2005;162:1179-87. Data are from treatment samples, not community samples, thus ascertainment bias is present.

* SAD 12-Year Probability of Recurrence after Remission

Lower rate of recurrence after remission



Bruce SE, et al. Am J Psychiatry. 2005;162:1179-87. Data are from treatment samples, not community samples, thus ascertainment bias is present.

Social Anxiety Disorder: Neurobiological Aspects

- **Familial Transmission:** GSAD risk 10x gen'l population
- **5-HT Function**
  - Genetic polymorphism in **5-HT transporter (SLC6A4)**
  - **Reduced 5-HT_{1a} receptor density**
  - **Tryptophan depletion reverses SSRI benefits**
- **DA function**
  - Low striatal dopamine D2 binding in generalized SAD (SPECT)
  - Decreased DA reuptake site density in the striatum
  - **Catechol-O-methyl transferase (COMT) polymorphism**
- **Children with Behavioral Inhibition**
  - As adults, are more likely to have anxiety, especially SAD
  - Behavioral inhibition is possibly learned from parental behavior

Fox AS, Kalin NH. Am J Psychiatry 2014;171:1162-73

Fear Circuit in SAD

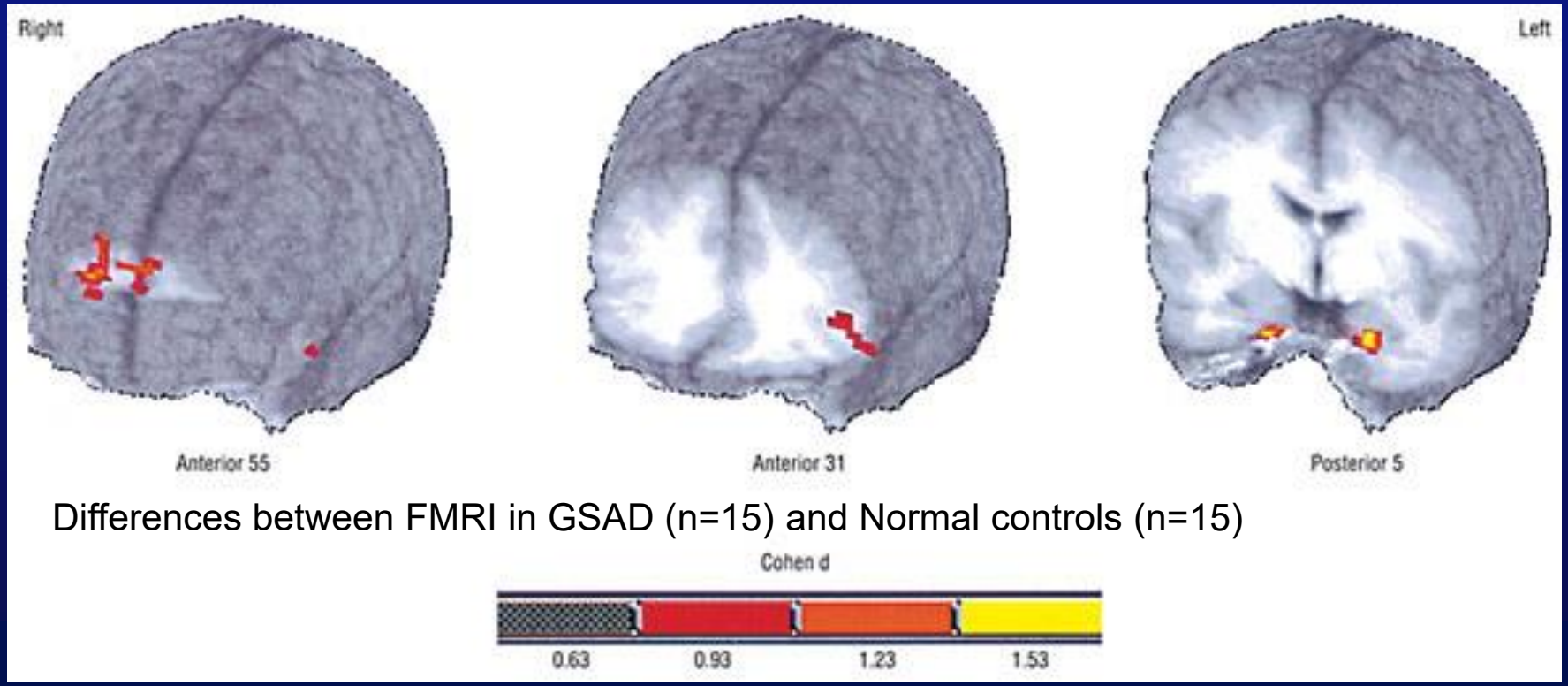
Brain areas implicated in SAD include:

- Amygdala
- Prefrontal cortex
- Insula
- Hippocampus
- Striatum

Fox AS, Kalin NH. Am J Psychiatry. 2014;171:1162-73

Altered Processing of Social-Emotional Cues in Generalized SAD

Differences between FMRI in GSAD (n=15) vs Normal controls (n=15)
Age, sex and handedness matched



Contemptuous or angry faces activated left amygdala, uncus, and parahippocampal gyrus more in GSAD than in normals or other stimuli (happy faces) vs. in normals

Stein MB, et al. Arch Gen Psychiatry 2002;59:1027-1034.

GSAD : ↓'d Reactivity to Public Speaking with Treatment

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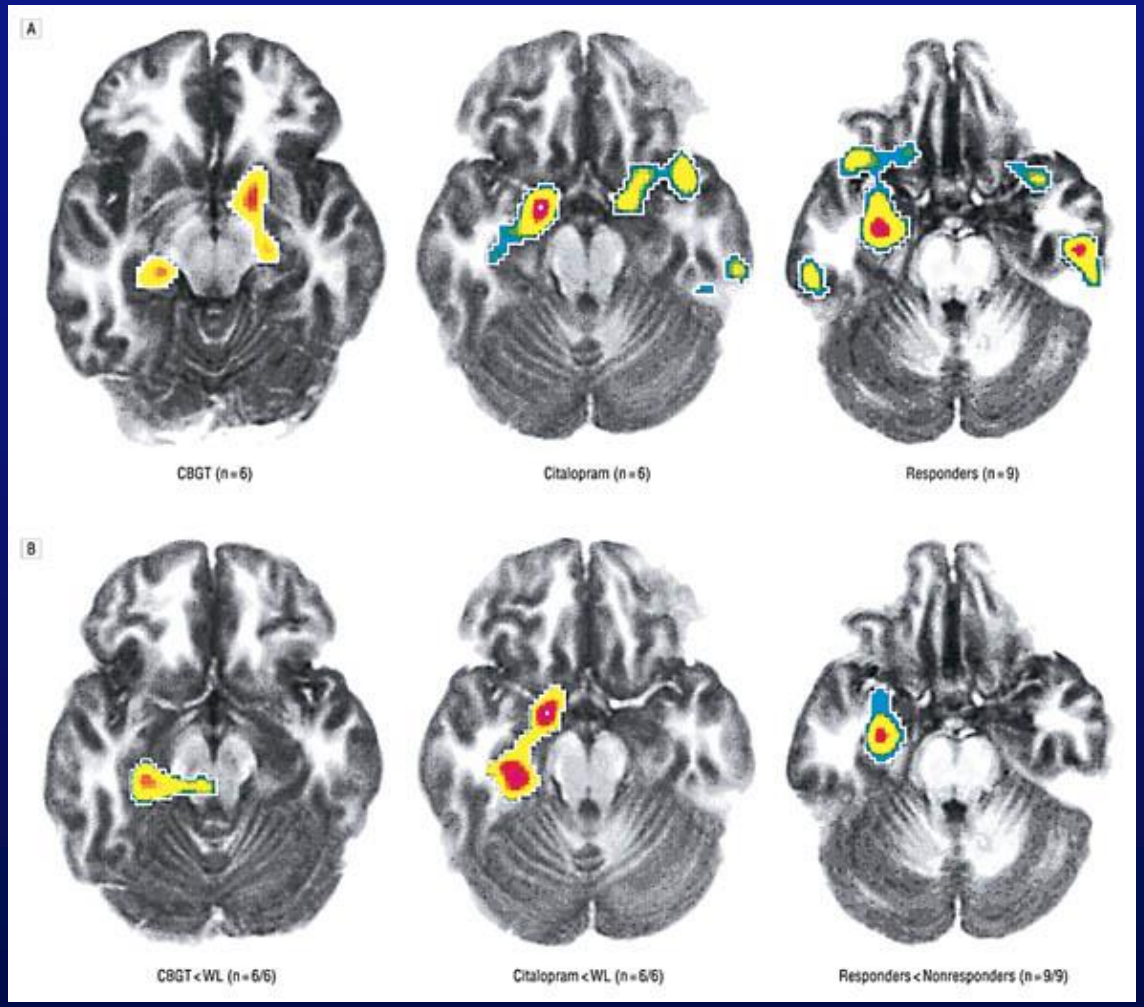
CBGT Citalopram All Responders

Pre-Treatment

Post-Treatment



Furmark T, et al. Arch Gen Psychiatry. 2002;59:425-33.
Transverse PET images superimposed on MRI reference image, showing significant decreases in regional cerebral blood flow response to anxiogenic public speaking.
CBGT = cognitive behavioral group therapy.

GSAD: rCBF Before vs. After Treatment With CBGT or Citalopram

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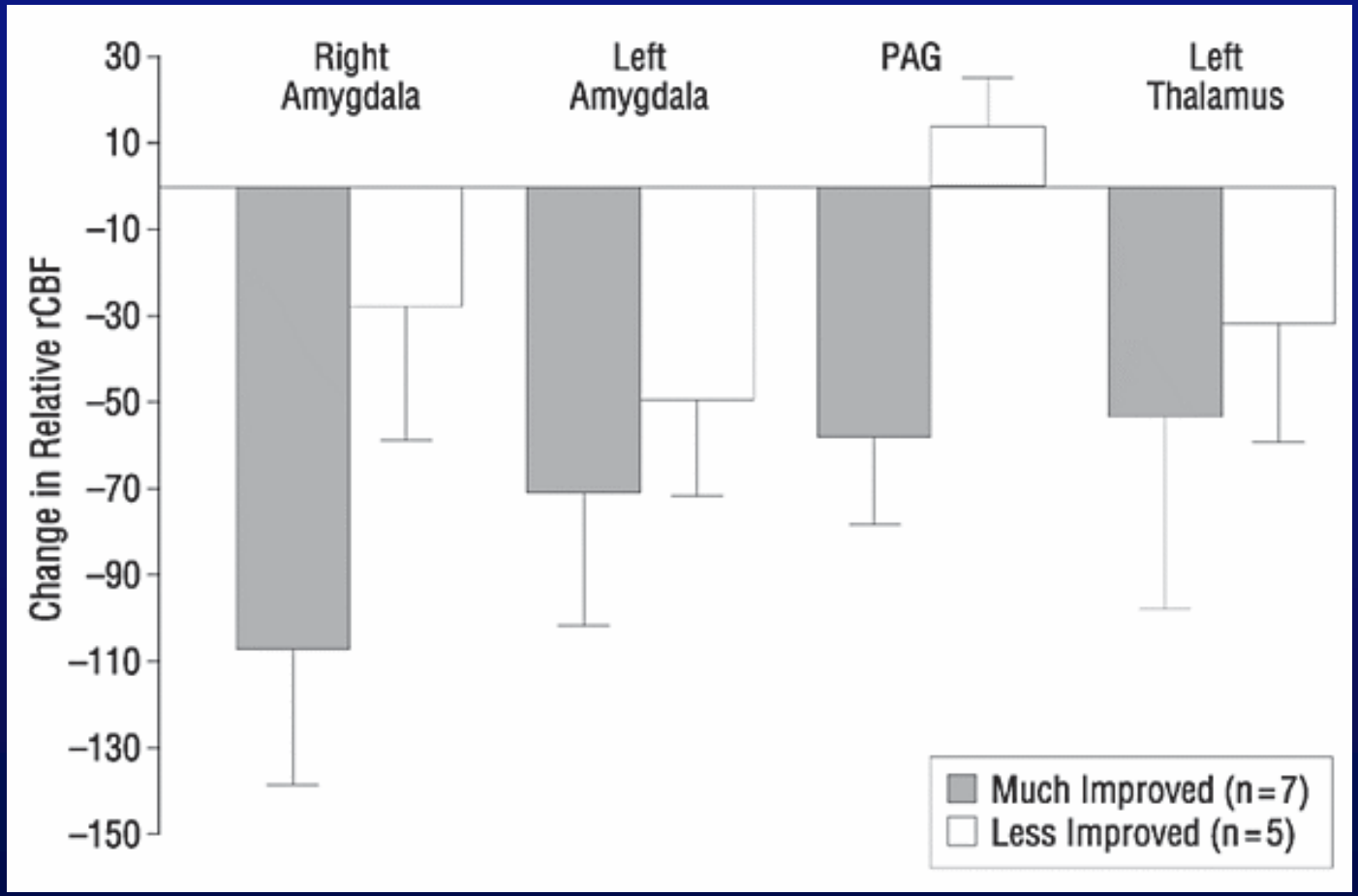


Regional cerebral blood flow (rCBF) redistribution after treatment (mean relative rCBF ± SE, after-minus-before therapy) in 4 subcortical regions. Greater initial (9-week) suppression of subcortical rCBF was associated with favorable clinical status (much vs. less improved) at 1-year follow-up. PAG = periaqueductal gray area.

Furmark, T. et al. Arch Gen Psychiatry. 2002;59:425-433.

SAD: Comorbidity

More often seen in generalized SAD

In the Epidemiological Catchment Area study and the National Comorbidity Survey study:

- 80% of those with DSM-III-R SAD reported at least one other psychiatric disorder
- SAD usually occurred first

SAD onset before age 15 is associated with greater risk of subsequent major depression, alcoholism, agoraphobia or generalized anxiety disorder than is onset after age 15.*

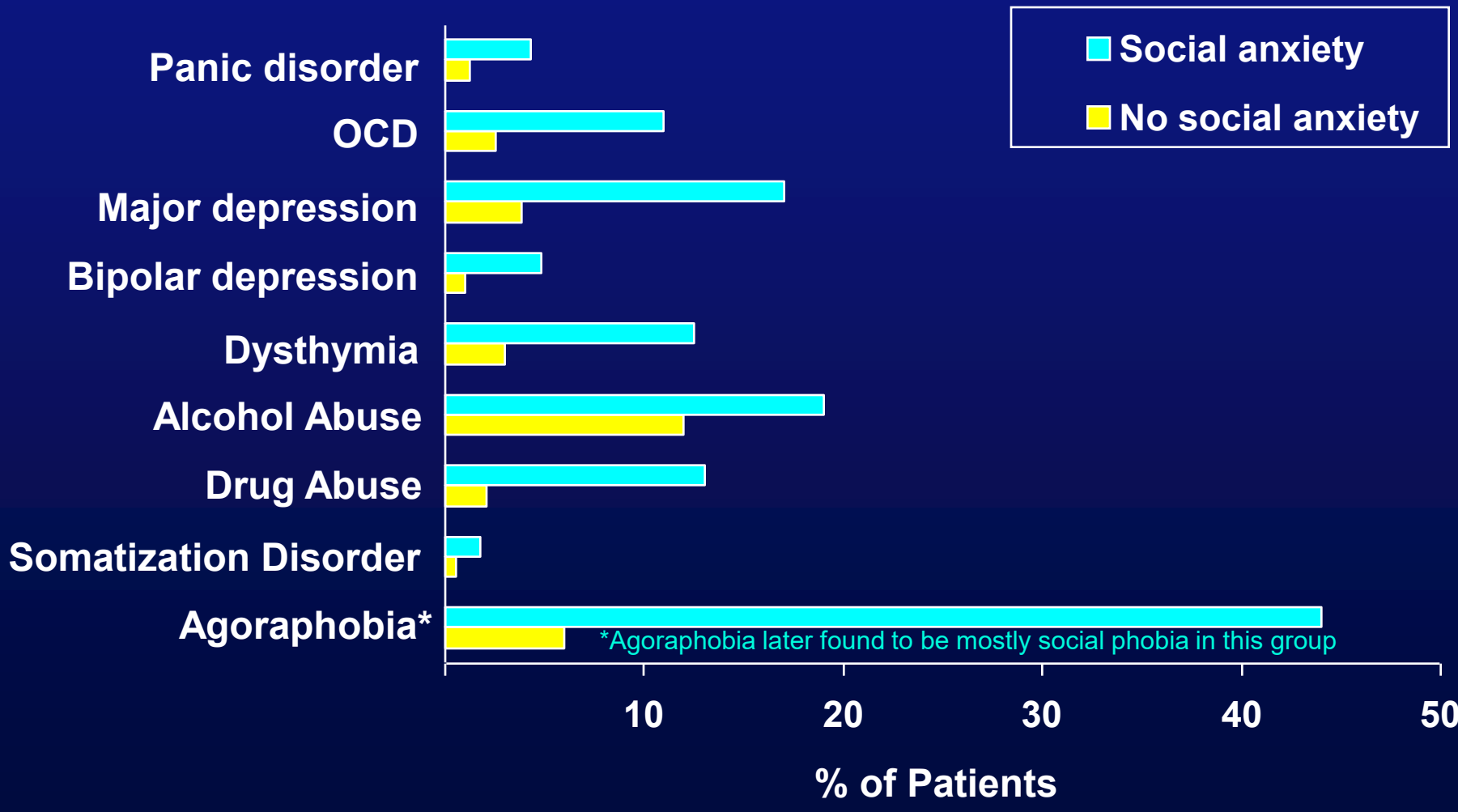
Magee WJ, et al. Arch Gen Psychiatry. 1996;53:159-68

Schneier FR, et al. Arch Gen Psychiatry. 1992;49:282-8

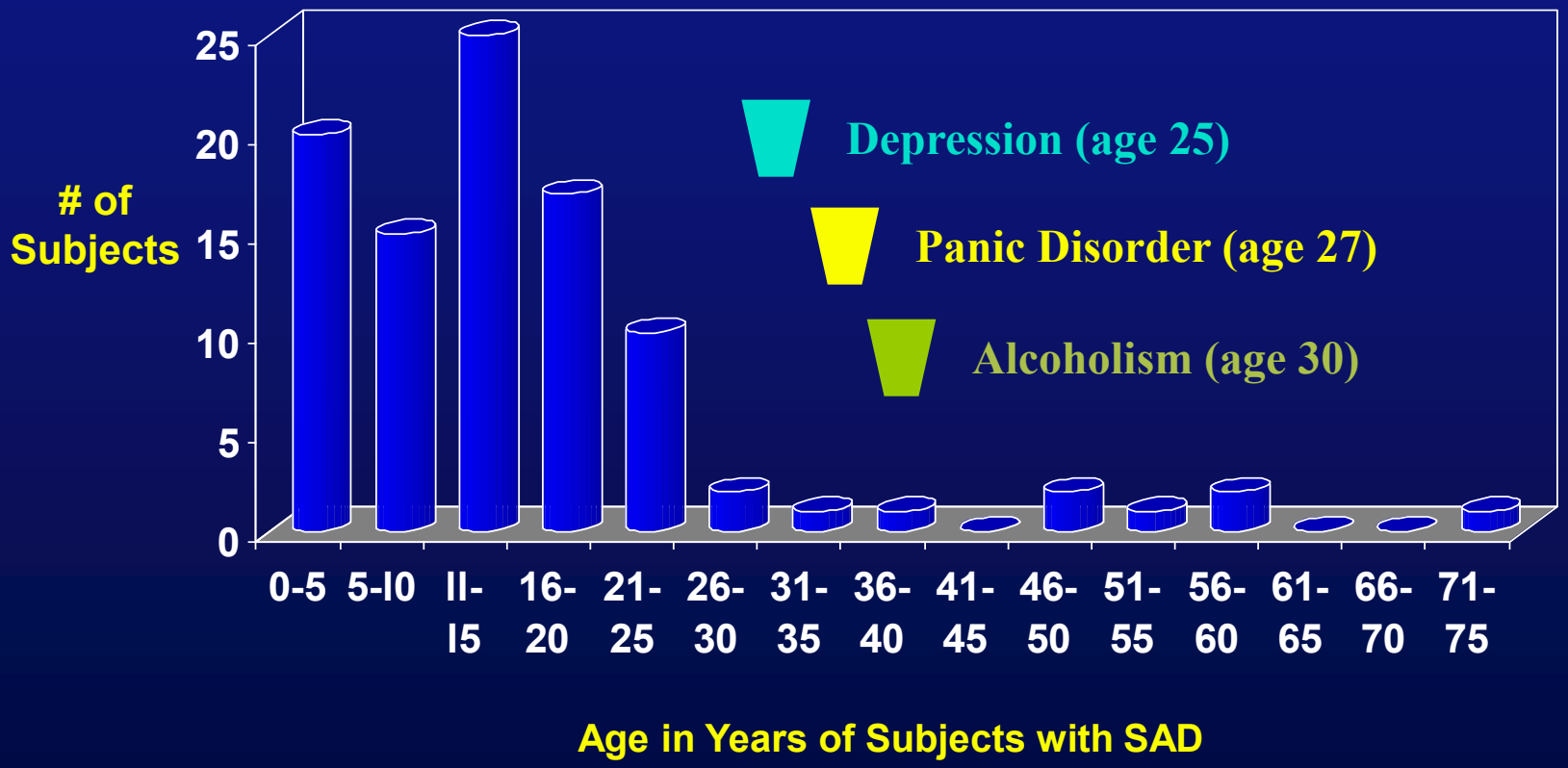
* Lecrubier Y. J Clin Psychiatry 1998;59 (suppl) 17:33-8

SAD: Comorbidity

Schneier FR, et al. Arch Gen Psychiatry. 1992;49:282-8



* SAD: Typical Order of Onset of Comorbid Disorders



Schneier FR, et al. Arch Gen Psychiatry. 1992;49:282-8

* SAD Treatment Goals

- Determine subtype: Performance only vs. GSAD
- Educate the patient about the disorder
- ↓ anxiety symptoms and distorted cognitions
- ↓ phobic avoidance
- ↓ disability and impairment
- Identify and treat comorbid disorders

Davidson JR. J Clin Psychiatry. 1998;59 (Suppl 17):47-53

SAD Assessment Tools

- **Liebowitz Social Anxiety Scale (LSAS)**

  Most often used in clinical trials; tracks well with BSPS

- **SPIN (Social Phobia Inventory)**
- **BSPS (Brief Social Phobia Scale)**
- **SPAI (Social Phobia and Anxiety Inventory)**

Liebowitz Social Anxiety Scale

Clinician -- or patient can learn to complete	Fear or Anxiety	Avoidance
1. Telephoning in public. (P)		
2. Participating in small groups. (P)		
3. Eating in public places. (P)		
4. Drinking with others in public places. (P)		
5. Talking to people in authority. (S)		
6. Acting, performing or giving a talk in front of an audience. (P)		
7. Going to a party. (S)		
8. Working while being observed. (P)		
9. Writing while being observed. (P)		
10. Calling someone you don't know very well. (S)		
11. Talking with people you don't know very well. (S)		
12. Meeting strangers. (S)		
13. Urinating in a public bathroom. (P)		
14. Entering a room when others are already seated. (P)		
15. Being the center of attention. (S)		
16. Speaking up at a meeting. (P)		
17. Taking a test. (P)		
18. Expressing a disagreement or disapproval to people you don't know very well. (S)		
19. Looking at people you don't know very well in the eyes. (S)		
20. Giving a report to a group. (P)		
21. Trying to pick up someone. (P)		
22. Returning goods to a store. (S)		
23. Giving a party. (S)		
24. Resisting a high pressure salesperson. (S)		

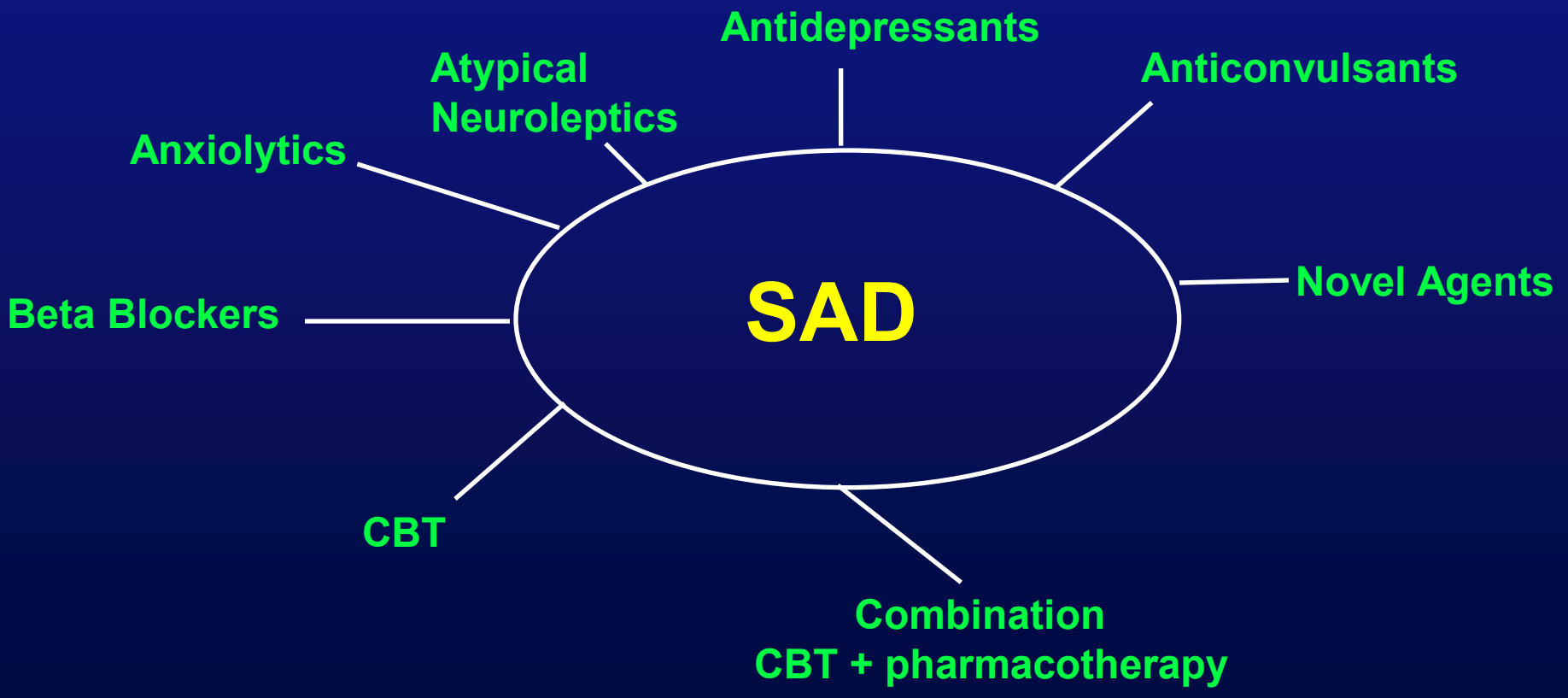
Liebowitz, MR. Mod Probl Pharmacopsychiatry 1987; 22:141-73

LSAS Interpretation

- Score each item 0-3 for degree of fear and avoidance
- Decrease of 30% over 8-12 weeks is considered ‘response’ in clinical trials
- Normals’ total score is <30
- ≥80: Severe
- 60-80: Moderate
- ≤30: Remission

Liebowitz, MR. Mod Probl Pharmacopsychiatry 1987; 22:141-173

Social Anxiety Disorder Treatment Options



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* SAD – Performance Only Subtype Treatment

Performance situations are usually predictable

- Therefore, prn medication is often sufficient

- Beta-blockers
- Benzodiazepines (use short-acting)
  - alprazolam, lorazepam)

CBT is also effective

* Beta Blockers for Performance Only SAD

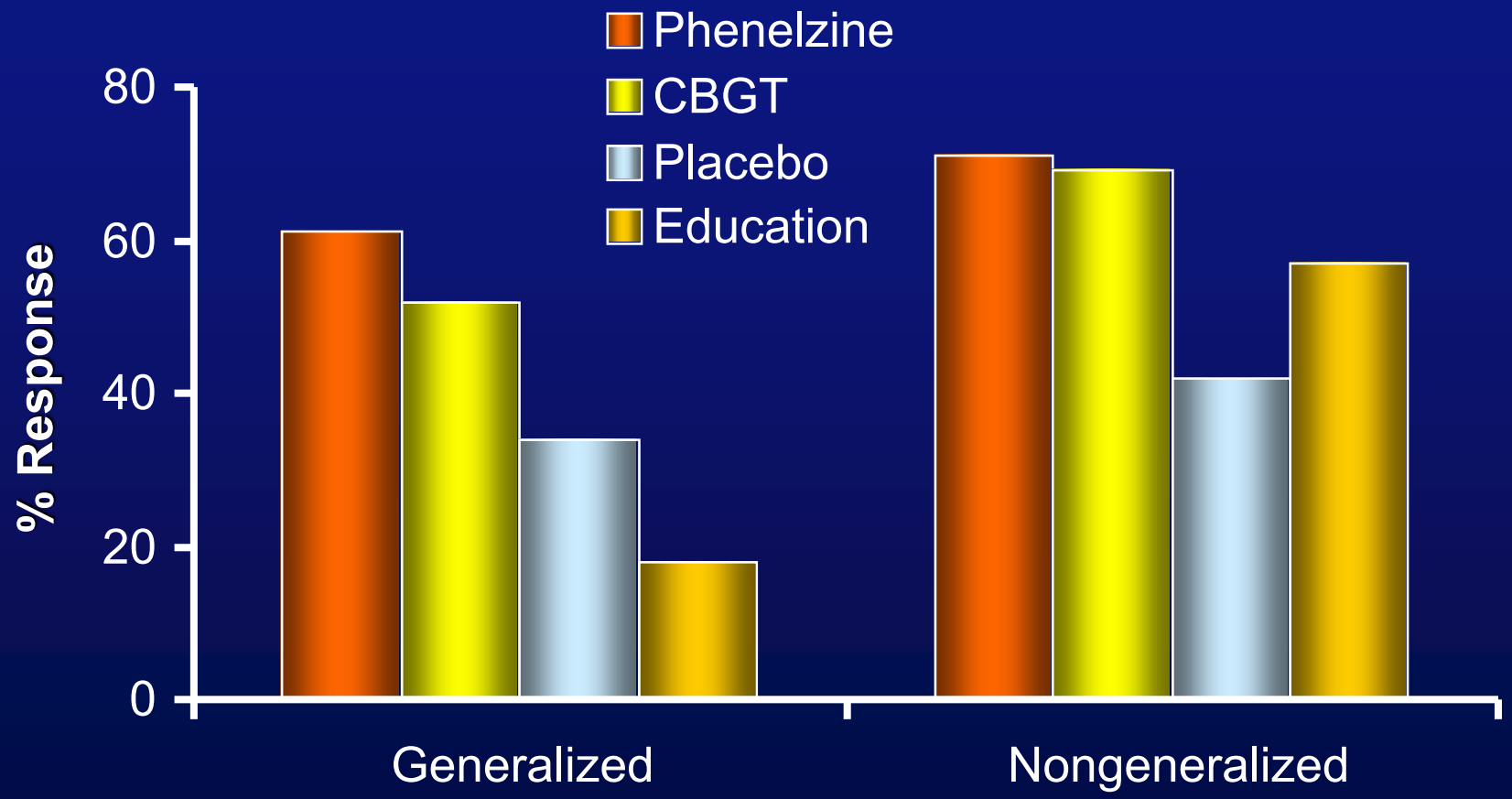
Propranolol: 10 - 40 mg PO

Atenolol: 50 - 150 mg PO

Not Effective for Generalized SAD, Major Depression or Other Comorbidities

- Decrease physiologic arousal (tremor, palpitations) more than subjective anxiety
- Administered 1- 2 hours before planned event

Social Anxiety Disorder Response by Subtype to CBGT *



*Intent to treat. N=30-35 per group. CBGT=cog-behav group therapy

Heimberg RG, et al, Arch Gen Psychiatry 1998;55:133-41

Generalized SAD Pharmacotherapy:

- Advantages
  - Works quickly
  - More robust initial response
  - May treat comorbid conditions
- Disadvantages
  - Patient concerns about taking medication
  - Cost
  - Side Effects
  - Drug interactions
  - Relapse rate after D/C

Drug Selection Considerations

- Evidence for Efficacy
- Safety
- Tolerability
- Half-Life
- Drug-Drug Interactions
- Protein Binding
- Comorbid psychiatric disorders
- Comorbid medical conditions

Generalized SAD – Treatment Overview (1)

Placebo-controlled studies support *acute efficacy* of:

Escitalopram
Fluoxetine
Fluvoxamine
Paroxetine
Sertraline

Alprazolam
Clonazepam

Phenelzine
Venlafaxine
Duloxetine

Gabapentin (weak)
Pregabalin (weak)

CBT

Baldwin DS, et al. J Psychopharmacol. 2005;19:567-96

Generalized SAD – Treatment Overview (2)

Placebo-controlled studies support *long-term* efficacy of:

Escitalopram
Fluvoxamine
Paroxetine
Sertraline

Phenelzine

Venlafaxine

CBT

Baldwin DS, et al. J Psychopharmacol. 2005;19:567-96

Generalized SAD – Treatment Overview (3)

Placebo-controlled studies support *relapse prevention* efficacy of:

- Escitalopram
- Paroxetine
- Sertraline
- Clonzepam
- CBT

Baldwin DS, et al. J Psychopharmacol. 2005;19:567-96

Agents with Limited or No Proven Efficacy in Generalized SAD

Bupropion

Buspirone

TCAs

Nefazodone

Levetiracetam

*Adapted from: Lydiard RB. In: *Textbook of Anxiety Disorders*. Washington, DC:American Psychiatric Press, Inc; 2002

*

Generalized SAD: Pharmacotherapy

Recommended First-Line = **SSRI** or **SNRI**

- Initial dose for 2-4 weeks, then ↑ if needed
- Should see some benefit in 2 - 4 weeks
- May require up to 2x dose needed for MDD
- 40-60% respond to any one SSRI / SNRI

*

*

After 6-8 weeks…

- For partial response to SSRI-
  - Increase dose as tolerated
  - augment with BZ or CBT
- For non-response
  - Try a second SSRI
  - Switch to an SNRI
  - Switch to CBT

Monotherapy may be insufficient (See notes for this slide)

*

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Generalized SAD: Pharmacotherapy

- **Typical pattern:**
  - **Continued improvement over several months**
  - **May take ≥ 1 yr for optimal response**
- **Continue medication after gains maximized to allow for resumption of psychosocial development**
- **Relapse after D/C medication alone is high**

Ravindran LN, Stein MB. J Clin Psych 2010; 71:839-54

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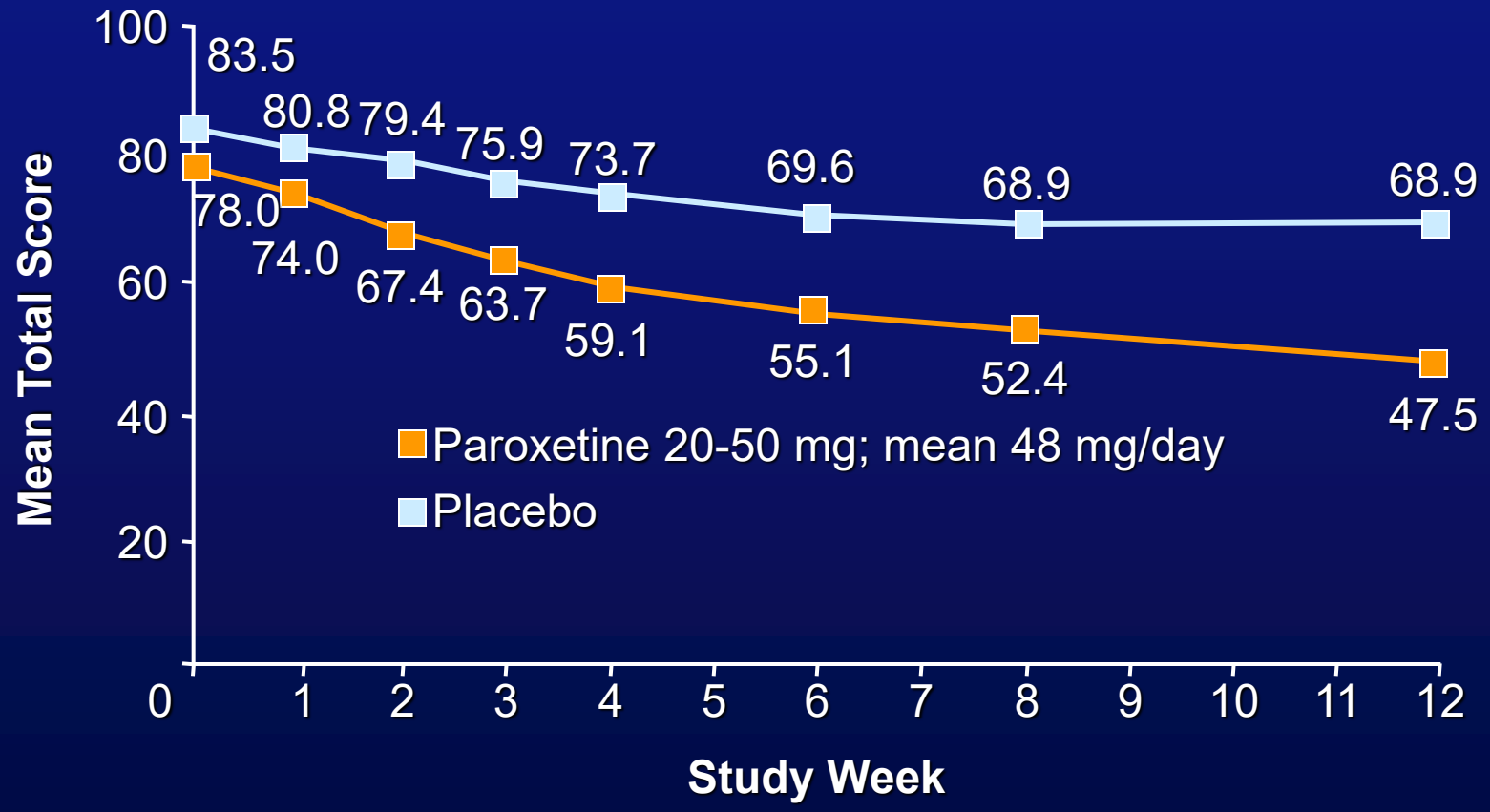
Typical SSRI vs. Placebo in SAD

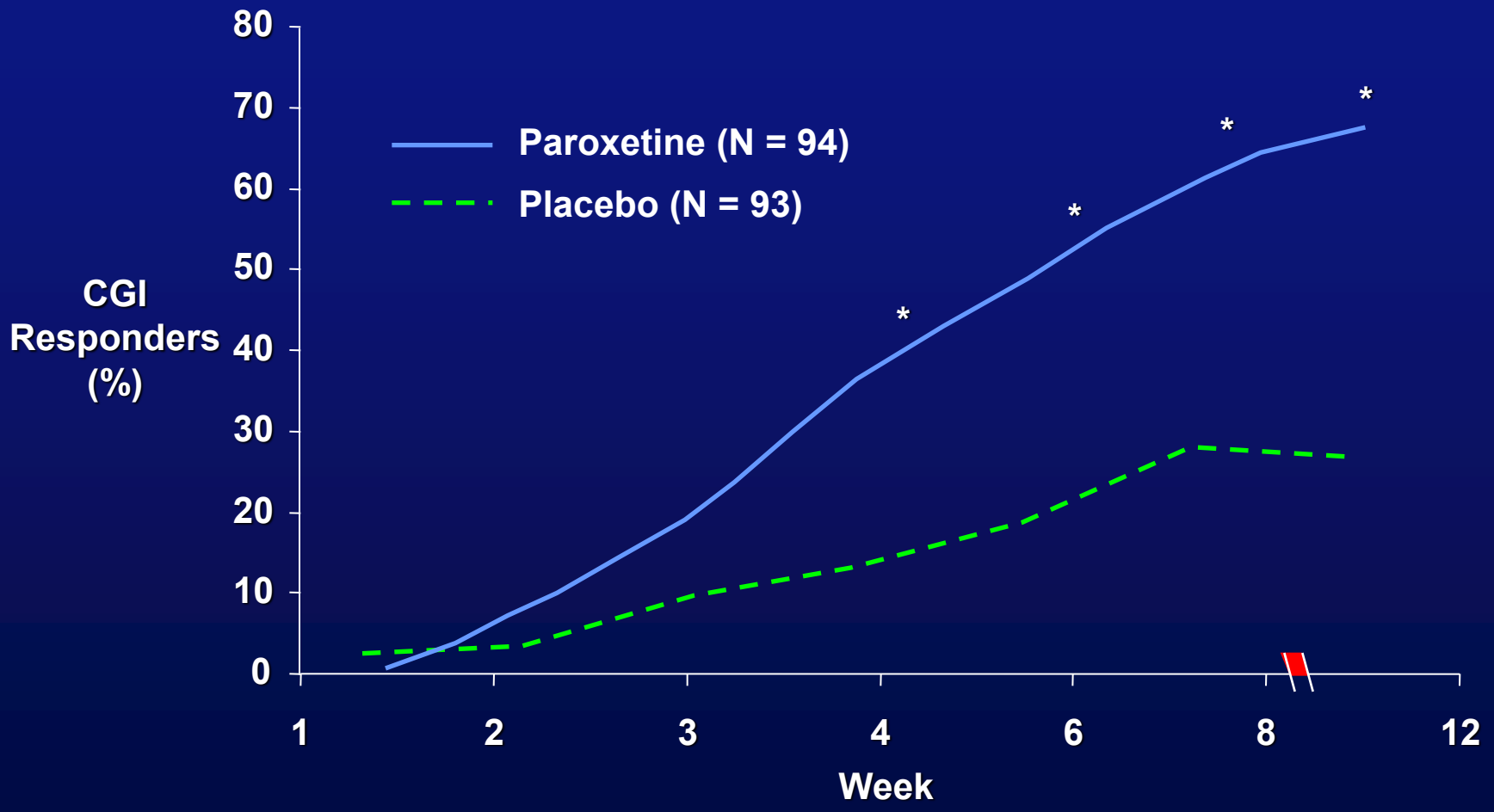
Paroxetine -- Total Change in LSAS score



***P*<.05 versus placebo**

* Stein MB, et al. JAMA. 1998;280:708-13

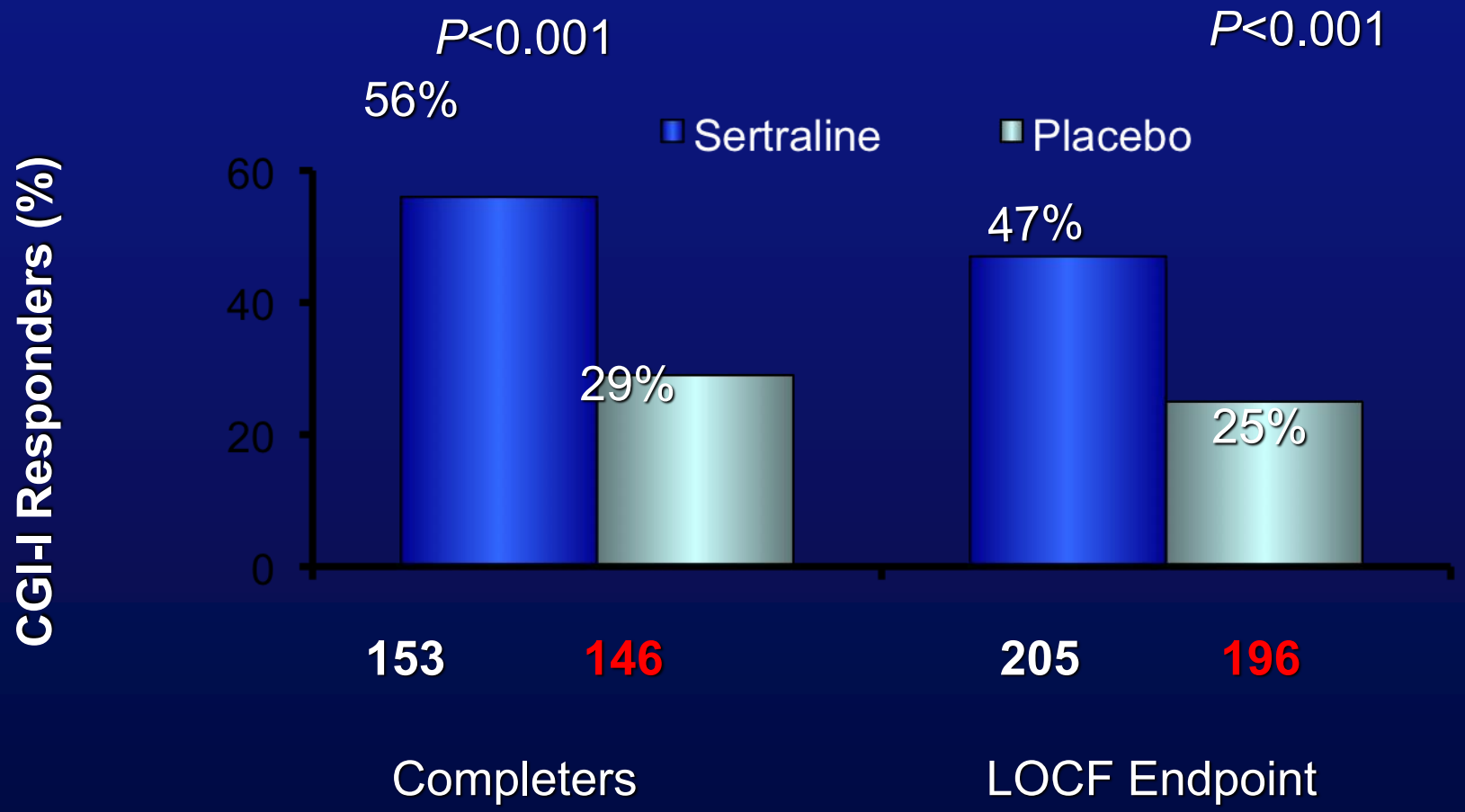
Paroxetine Treatment Of SAD



* P≤.001 vs placebo – visit-wise data set.

Stein MB, et al. JAMA. 1998;280:708-13

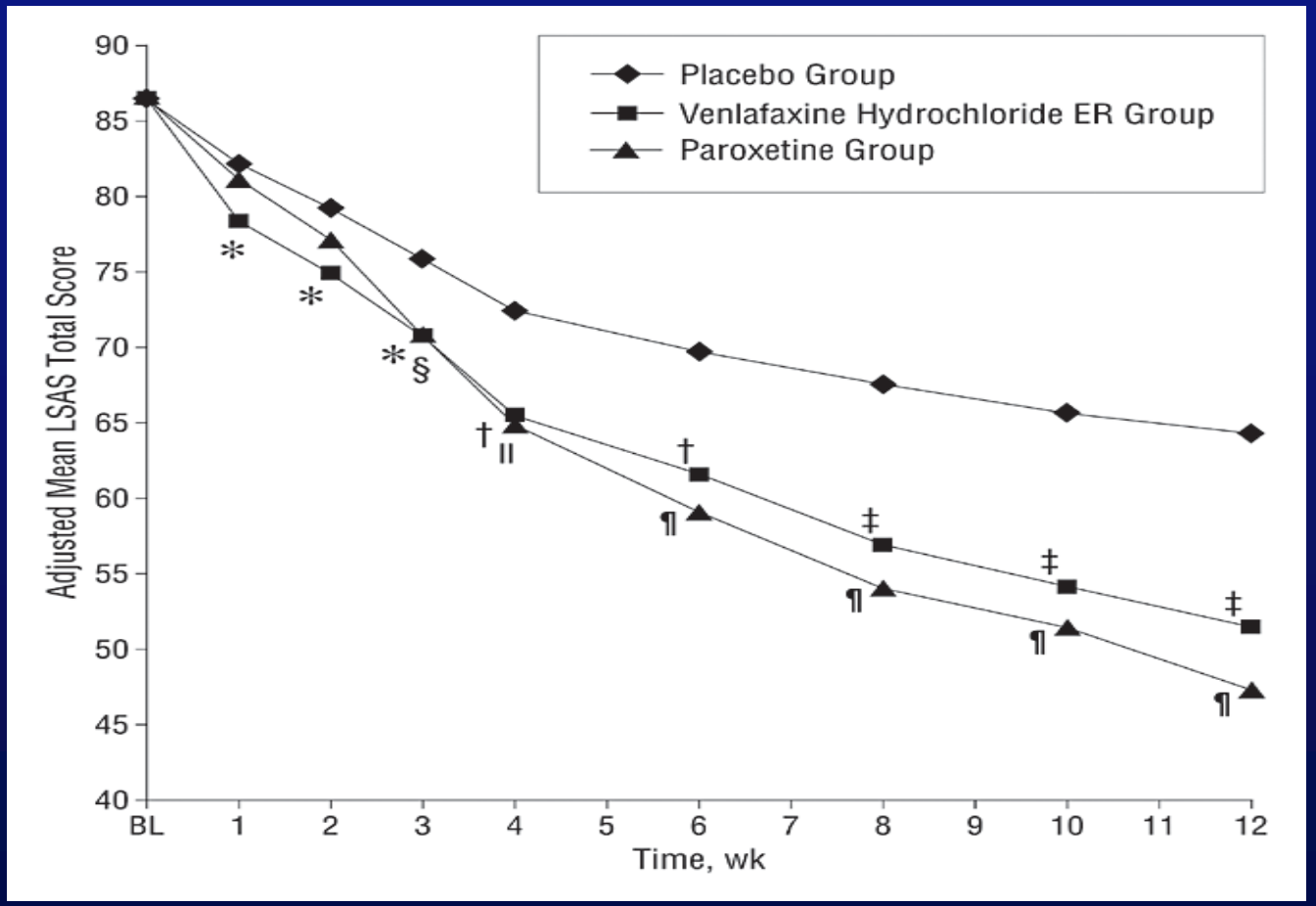
Sertraline in Social Anxiety Disorder: CGI-I Responders* at Week 12 Endpoint



*ITT Responder: CGI-I ≤2.

Liebowitz MR, et al. J Clin Psychiatry. 2003;64:785-92

GSAD: SNRI vs. SSRI vs. Placebo
Flexible Dose - Venla 75-225 mg, Parox 20-50 mg



Venla n =146; Parox n=147; PBO n=147.

* Liebowitz MR, et al. Arch Gen Psychiatry. 2005;62:190-8

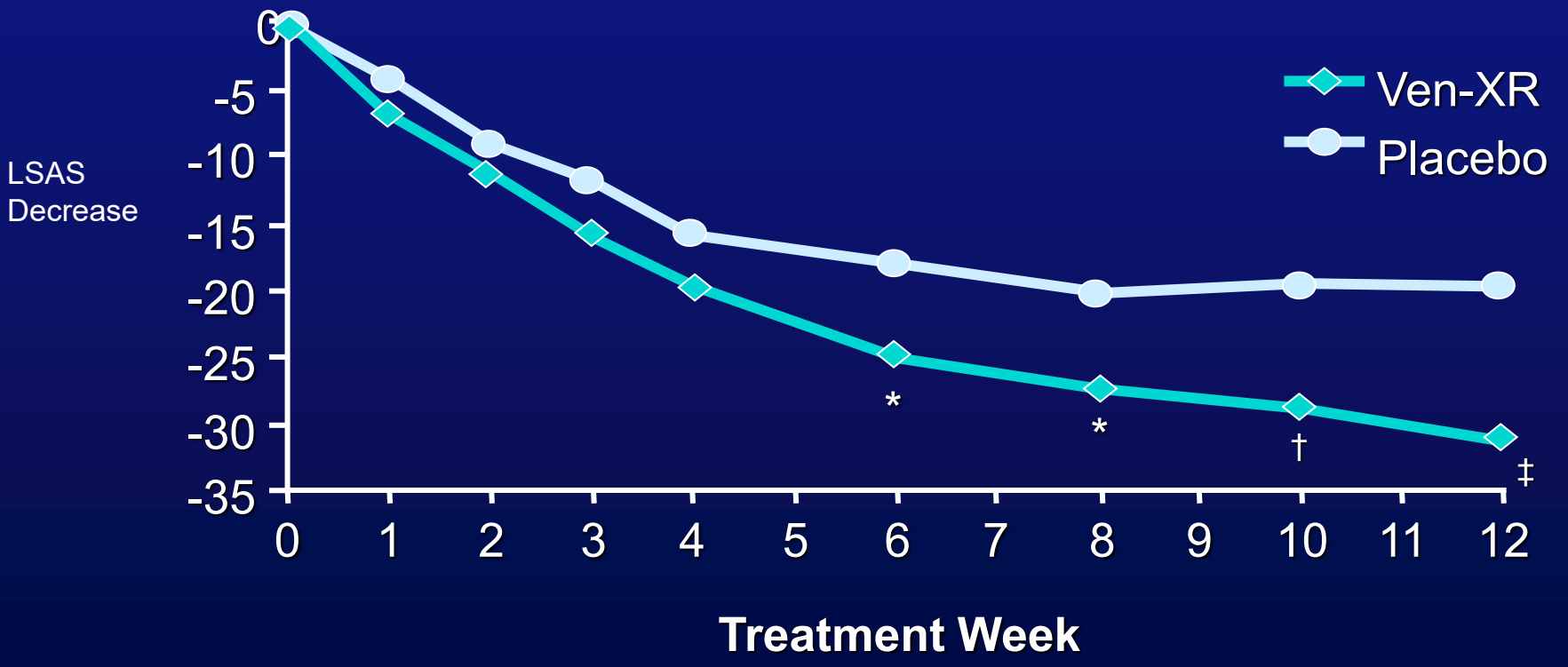
SNRI: Venlafaxine XR vs. PBO

Flexible Dose 75-225 mg/day

*

271 randomized, 173 completed

Response: Venla XR 44%; PBO 30%. Remission: Venla XR 20%; PBO 7 %

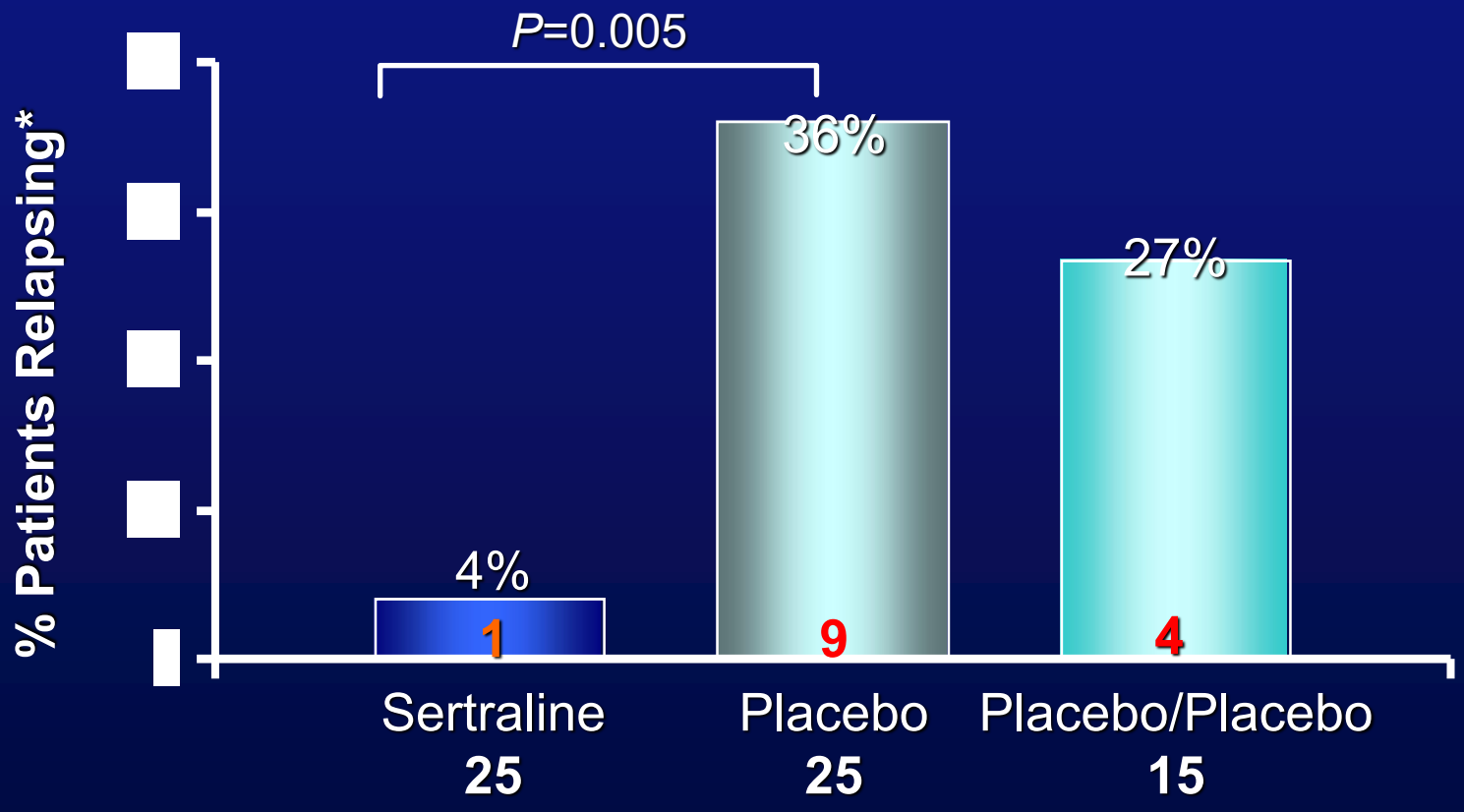


*P = 0.022; †P = 0.003; ‡P = 0.0002.

ITT Population, LOCF Analysis. Liebowitz MR, et al. J Clin Psych 2005;66:238-47

Sertraline: Relapse* Prevention in Social Anxiety Disorder

Proportion of Patients Relapsing During 24 Weeks of Double-Blind Treatment



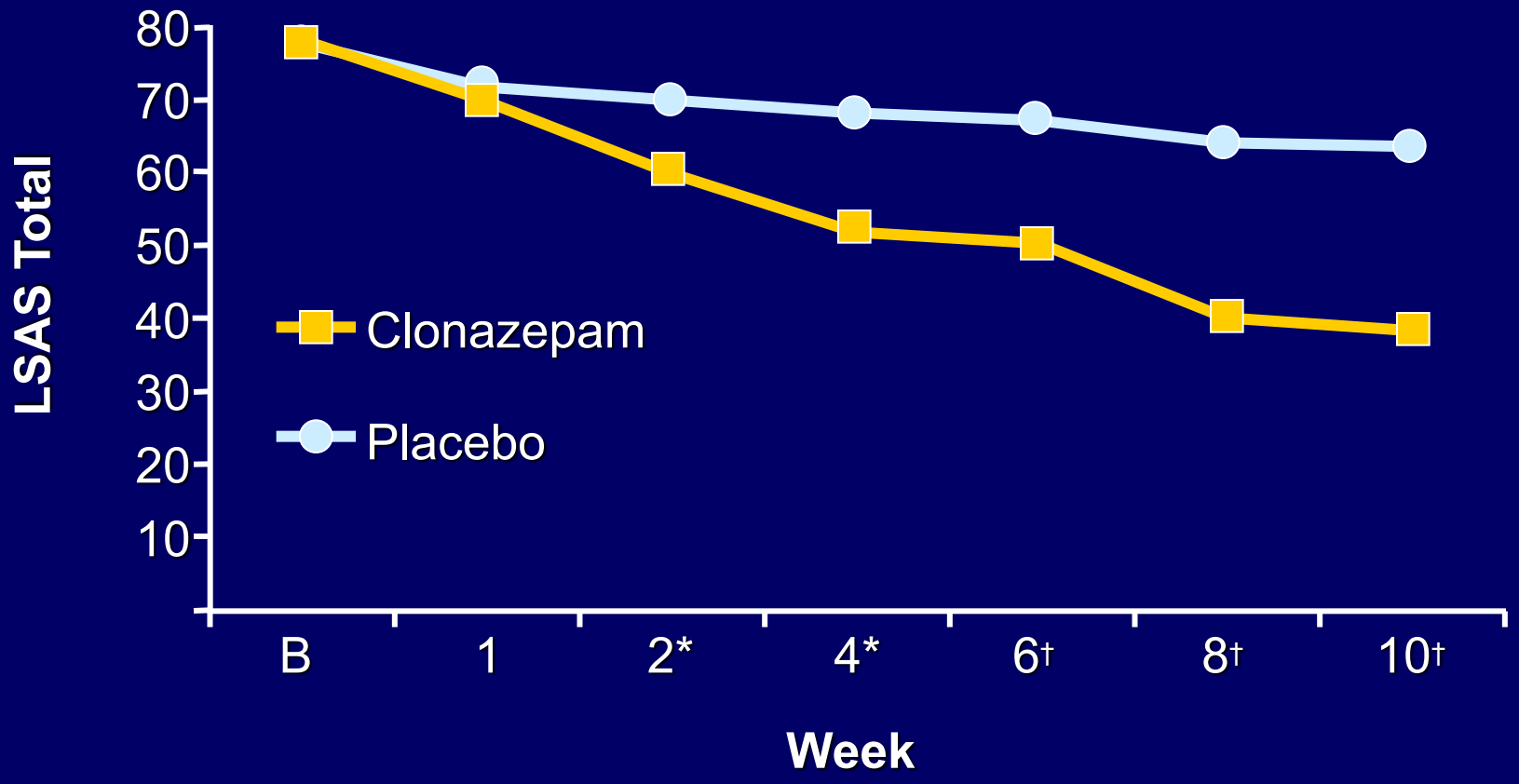
*Relapse = CGI-S ↑ ≥2 from continuation baseline or D/C for lack of efficacy.

Walker JR, et al. J Clin Psychopharmacol. 2000;20:636-44

Benzodiazepines in Treating Generalized SAD

- Disadvantages include:
  - Cognitive impairment
  - Sedation
  - Incoordination
  - Dependency/withdrawal symptoms
  - Lack of antidepressant effect
  - Need to avoid use in patients with alcohol/durg abuse history

Benzodiazepines: Clonazepam in Social Anxiety Disorder



* $P \leq .01$; † $P \leq .0001$ (LOCF MANCOVA).

Davidson JR, et al. J Clin Psychopharmacol. 1993;13:423-8.

Long-term Clonazepam Rx of GSAD: Discontinuation vs. Maintenance

- Patients stable on clonazepam for 6 months
  - Continuation treatment x 5 months versus
  - Double-blind substitution @ 0.25 mg/wk to placebo
- At 11 months
  - Continued clonazepam relapse = 0%
  - Discontinued clonazepam relapse = 21%
- But, significant gains were maintained by many
  - ~80% did well off drug!
- Supports long-term Rx with clonazepam

Connor KM, et al. J Clin Pychopharmacol. 1998;18: 373-8

Augmentation vs. Switch for SAD

- Double-blind, 12-wk: sert. + clonazepam [3 mg] vs. sert. + placebo vs. switch to venlafaxine [225 mg]. N=181 non-responders to 10 weeks of sertraline alone
- Remission: sert. + clonazepam 27%, sert. + placebo 17% (p=ns), venlafaxine 18%
- Response (LSAS≤50): sert. + clonazepam 56%, sert. + placebo 36% (p=.03); venlafaxine 46% (p=ns vs. sert. + placebo)

Pollack MH, et al. Am J Psychiatry 2014;171:44-53

Monoamine Oxidase Inhibitors Treatment Of SAD

- Irreversible (nonselective: Phenelzine, Tranylcypromine)
  - Supported by well-controlled trials
    - Poorly tolerated (postural hypotension, sexual SE, weight gain, sleep disturbance)
    - Interaction with tyramine - diet limitations required

- Reversible Inhibitors of Monoamines (RIMAs)
  - Selective for MAO-A
    - Well tolerated
    - Not generally available in the US
      - » Moclobemide: Weak response in US studies
      - » Brofaromine: 5-HT reuptake (-); inhibits MAO-A
      - » Deprenyl (Ensam) in US for depression; selective at doses < 20 mg/day p.o.

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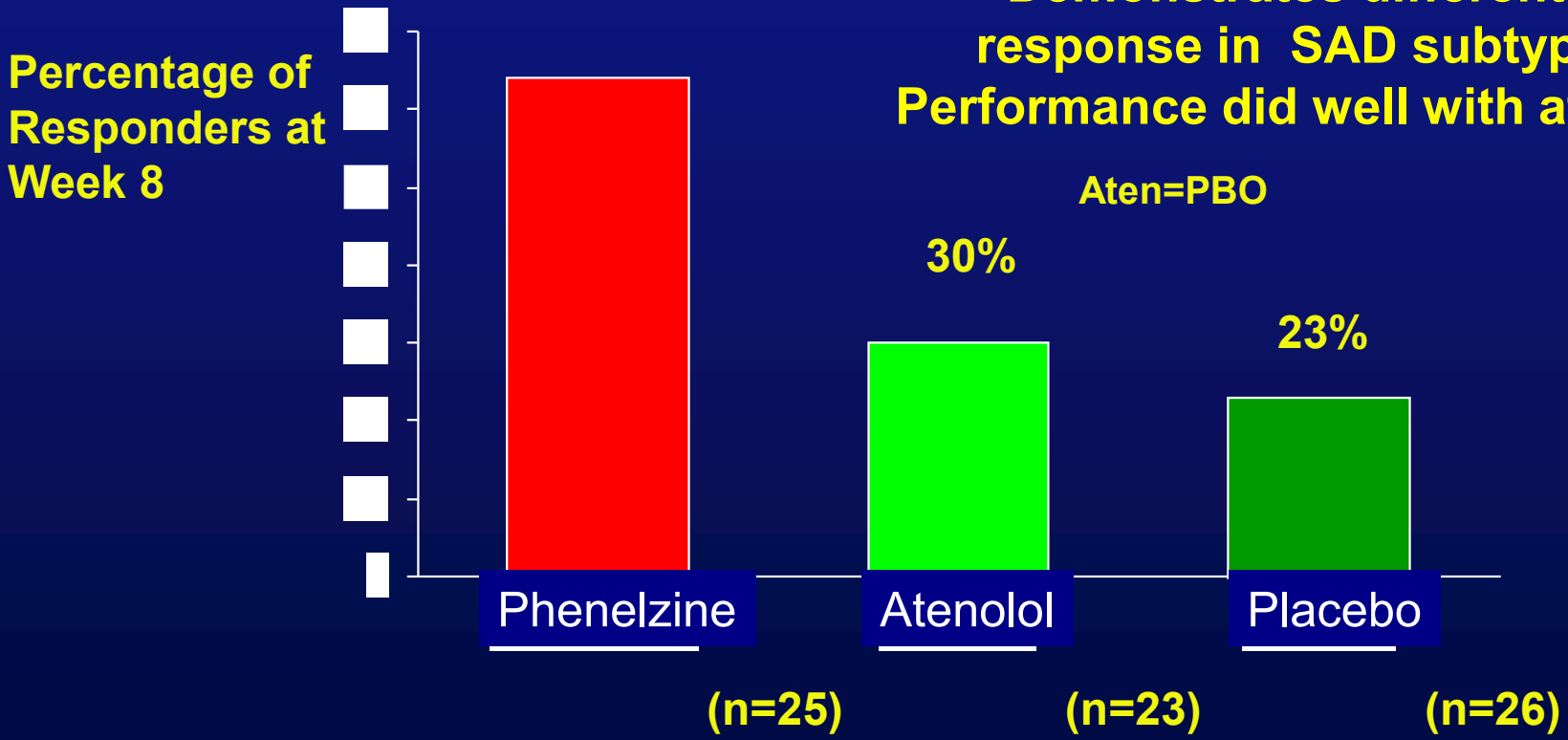
First Pharmacotherapy Study for SAD
2/3 Generalized, 1/3 Non-Generalized [Performance only]

*p<0.05



Demonstrates differential response in SAD subtypes: Performance did well with atenolol

Liebowitz MR, et al. Arch Gen Psychiatry. 1992;49:290-300

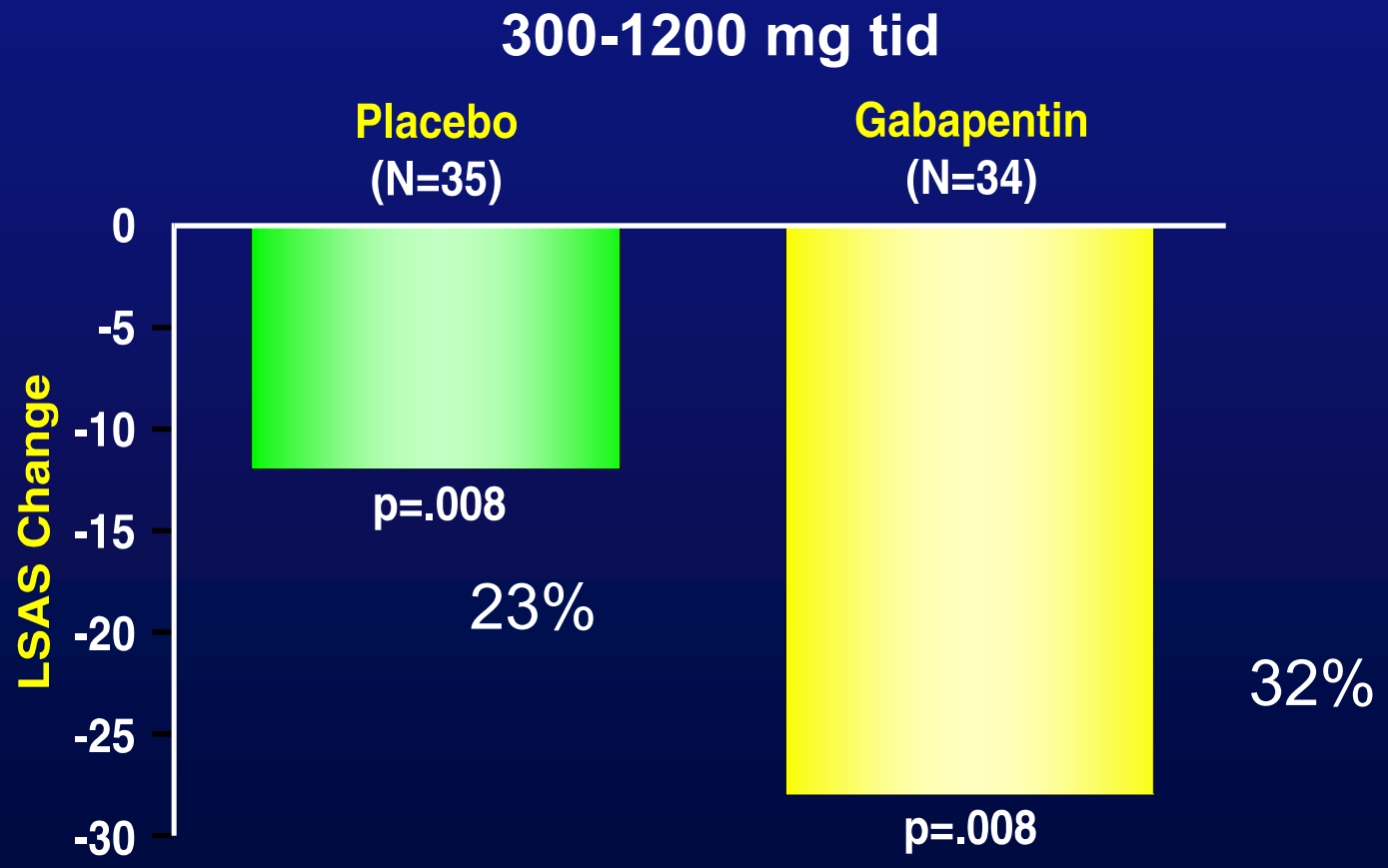
Novel Treatments: Pregabalin for SAD

- Double blind trial, 11-week, N=94 completers (70%)
- Excluded comorbid panic, agoraphobia, OCD
- Pregabalin 600 mg/d > placebo LSAS (p=.02)
  - Responders: CGI-I 43% [p=.03]; LSAS 28% [p=ns]
- Pregabalin 150 mg/d = placebo
- 450 mg/d also effective in a controlled trial*
- Side effects: sedation, dizziness, wt. gain
- Not effective for comorbid major depression

* Kawalec P, et al. Expert Opin Investig Drugs. 2014;Oct 31:1-10
Pande AC, et al. J Clin Psychopharmacol. 2004;24:141-9

Novel Treatments: Gabapentin in SAD

8-week study ITT Analysis -- Marginal efficacy



* Pande AC, et al. J Clinical Psychopharmacol. 1999; 19:41-8

Atypical Antipsychotics in SAD

Insufficient data to support use

Depping AM, et al. Cochrane Database Syst Rev. 2010 Dec 8;(12):CD008120

- **1 open-label and 1 RCT with quetiapine**
  - Vaishnavi S, et al. Prog Neuropsychopharmacol Biol Psych 2007;31:1464-9
  - Schutters SI, et al. J Clin Psychiatry. 2005;66:540-2
- **1 open-label study with olanzapine**
  - Barnett SD, et al. J Psychopharmacol 2002;16:365-8

CBT in SAD

- **Advantages**
  - It Works: first-line Rx
  - Durable effect
  - Most People Like It
  - Time-Limited
  - Few side-effects
- **Disadvantages**
  - More Time & Work
  - Limited Supply
  - May Not be Covered by Insurance

CBT in SAD: Techniques

- 6-12 sessions. Individual CBT → greater sx decrease than Group CBT
- Cognitive restructuring (dysfunctional thoughts, catastrophizing, failure-focused attention, anxiety will necessarily → failure)
- Exposure (prevent safety behaviors)
- Social skills training (how to say hello/good-bye, maintain eye contact, converse, how close to stand)

Foa EB. J Clin Psychiatry 2006;67(suppl 12):27-30

D-Cycloserine Augmentation of CBT

- Double-blind, 12-week, 50 mg, 1-hour before group CBT, N=144 completers
- D-cycloserine → 24% - 33% faster rate of improvement vs. placebo
- Response and remission rates were not significantly increased

Hofmann SG, et al. Am J Psychiatry. 2013;170:751-8

SAD: Psychosocial Treatments

- Psychoeducation
- Social Skills Training
- Cognitive Behavioral Therapy (CBT)
- Individual or Group Therapy

Heimberg RG. J Clin Psychiatry 2001;62(suppl 1):36-42

Combined CBT and Medication

- Common belief: combination of CBT+ meds is superior to either alone
  - Very limited data - few high quality studies
- Differences getting smaller over time due to more rigorous study design
- CBT + Meds for panic and GAD in short term is superior to CBT + placebo
- At 6 months - not much difference
- Still needs more empirical examination

Hofmann SG, et al. Int. J Cogn Ther. 2009;2: 260-75

Long-Term Treatment Indications

- Persistent, impairing social anxiety symptoms
- History of relapse after stopping prior treatment
- Comorbid conditions requiring prophylaxis

SAD: Conclusions

- SAD is common and disabling
- SAD requires prompt diagnosis to prevent long-term disability
- SAD is:
  - Under-diagnosed
  - Under-treated
- Generalized SAD is responsive to CBT, SSRIs/SNRIs, Benzodiazepines and perhaps to other drug classes
- Long-term treatment (≥ 1 year) is indicated

Additional Resources

Anxiety Disorders Association of America www.adaa.org

National Institute of Mental Health: www.nimh.nih.gov/anxiety/anxietymenu.cfm

Rating scales, neuroscience: www.neurotransmitter.net

Stein DJ, et al. Pharmacotherapy for social phobia. Cochrane Database Syst Rev. 2004;(4):CD001206.

Swinson RP, et al. Clinical practice guidelines: management of anxiety disorders. Can J Psychiatry. 2006;51(suppl 2):1S≲92S.

Saeed SA, et al. Herbal and dietary supplements for treatment of anxiety disorders. Am Fam Physician. 2007 15;76:549-56.

Hofmann SG, et al. Is it beneficial to add pharmacotherapy to CBT? A meta-analysis Int J Cogn Ther 2009 2:160-75

Question #1

The “Performance Only” subtype of Social Anxiety Disorder includes experiencing intense fear in which of the following situations:

a. athletic performance
b. musical performance
c. dancing
d. public speaking
e. urinating in a public bathroom
f. all of the above

Answer: f (Source: DSM-5)

Answers to Questions

- **Q1.** f. All can be associated with Performance Only SAD. (Source: DSM-5)
- **Q2.** True. Male and female prevalence rates are ≈ in clinical samples (Source: DSM-5)
- **Q3.** d is False. About 50% experience remission. (Source: DSM-5)
- **Q4.** b, c, d. 9. Major Depression, Agoraphobia, Alcoholism (**Schneier FR, et al. Arch Gen Psychiatry. 1992;49:282-8)**
- **Q5. a, c, and e. SSRIs, SNRIs, CBT**

Acknowledgements

James Jefferson, MD*

John Greist, MD*

David Katzelnick, MD*

University of Wisconson &

Health Technology Systems. Madison WI

J.R.T. Davidson, MD

Duke University