Neuroscience Education Institute

COUNT ON IT: OPTIMIZING TREATMENT FOR OCD AND SOCIAL ANXIETY

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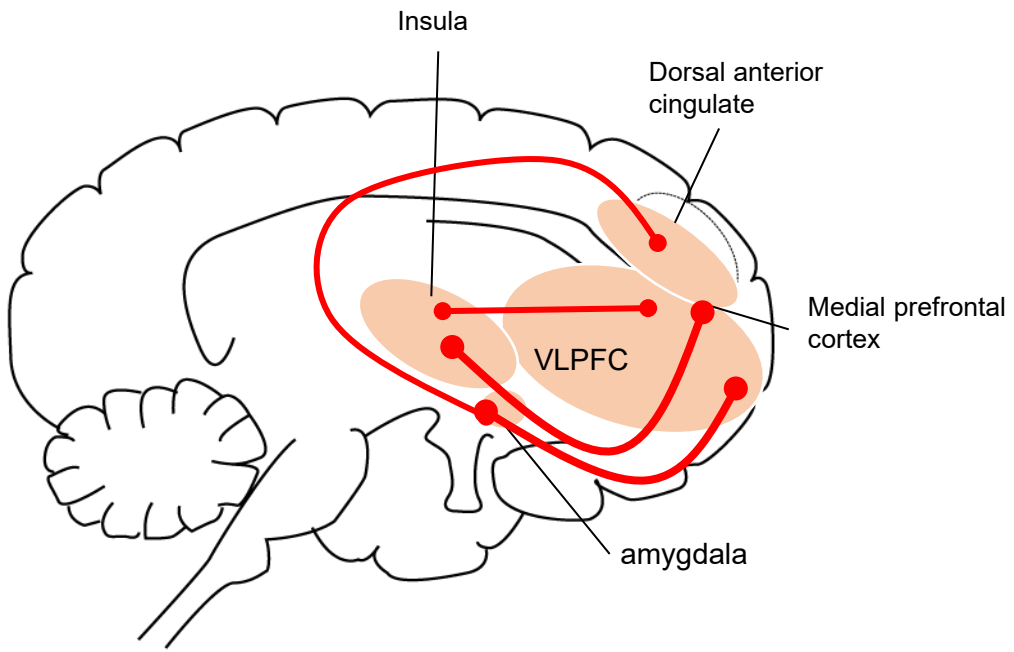
Presented at the 2023 NEI Congress

Learning Objectives

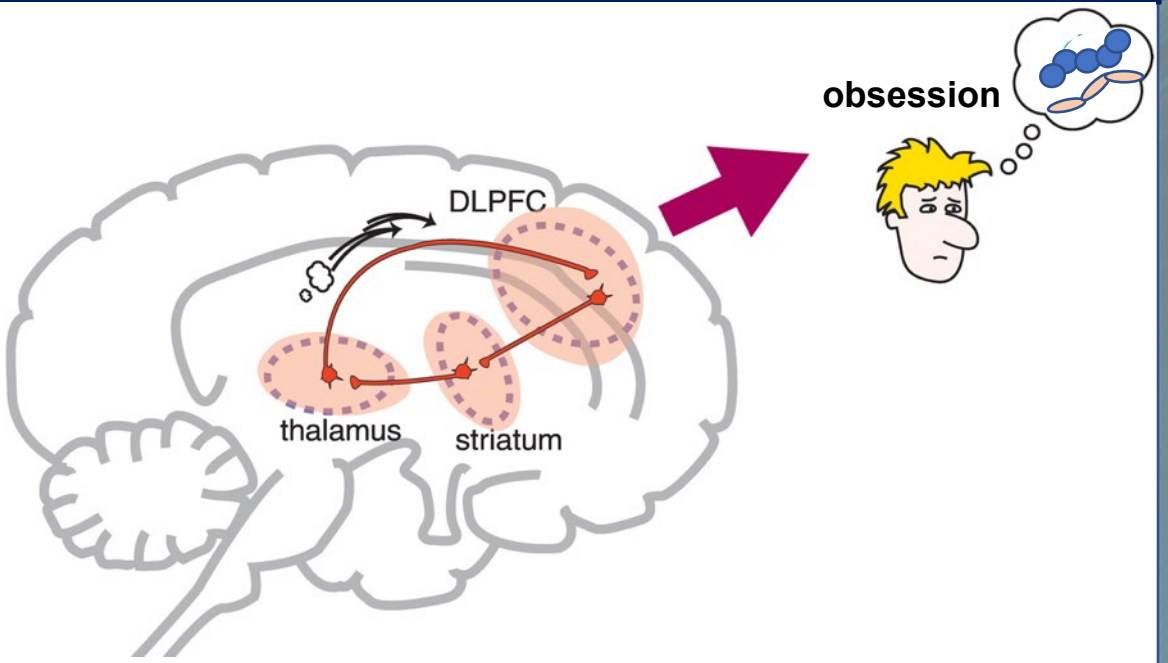
- Identify the clinical, cognitive, and neurobiological similarities between OCD and social anxiety disorders
- Consider the evidence of “next-line” interventions in treatment-resistant OCD and social anxiety disorder
- Describe the use of clomipramine and its monitoring in OCD

Social Anxiety Disorder and OCD

SOCIAL ANXIETY DISORDER



OBSESSIVE-COMPULSIVE DISORDER



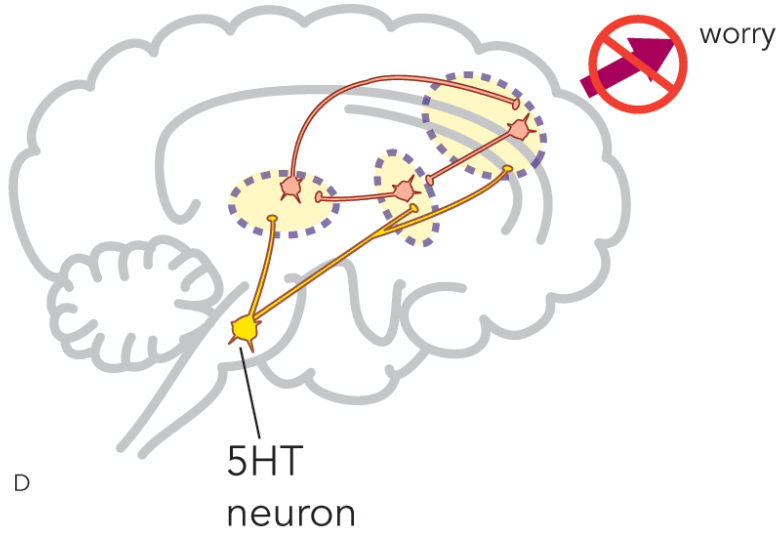
Craske MG et al. Nat Rev Dis Primers 2017;3:17024.
Stahl SM. Stahl's Essential Psychopharmacology; 2021.

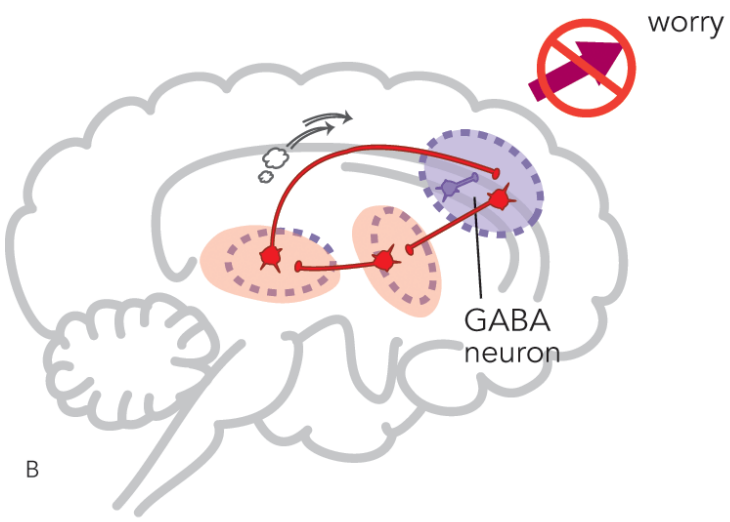
Social Anxiety Disorder and OCD

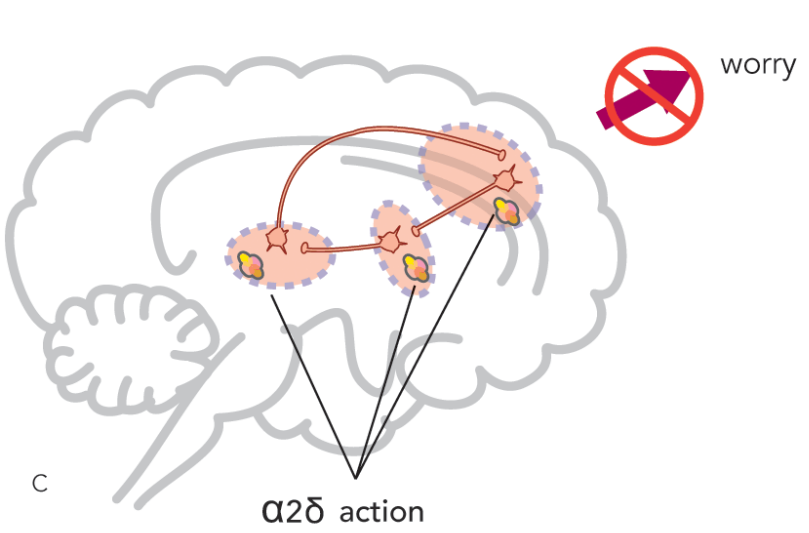
Common Features	
Clinical features	Avoidance and distress with exposure
Cognitive features	Inhibitory learning deficits
Psychotherapy	CBT with emphasis on exposure
First-line pharmacologic treatment	Serotonergic agents (e.g., SSRIs)
Treatment response predictors	Insight

Craske MG et al. Nat Rev Dis Primers 2017;3:17024.
Stahl SM. Stahl's Essential Psychopharmacology; 2021.

Social Anxiety Disorder and OCD: Common Targets

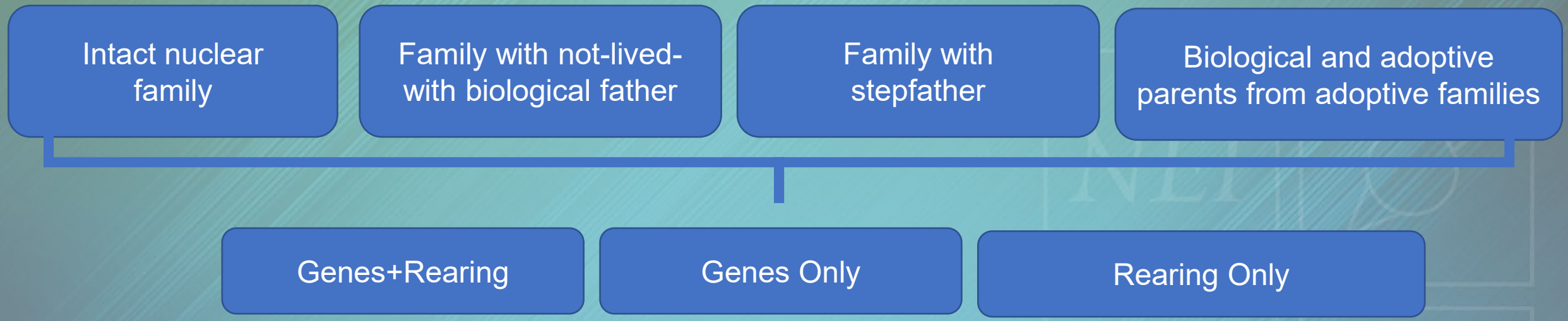






What Is the Relationship Between OCD and Social Anxiety Disorder?

- Swedish population register-based study for offspring born in Sweden from 1960 to 1995
- N=2,413,128 individuals; age 40 + 11 years, 52% male and 48% female

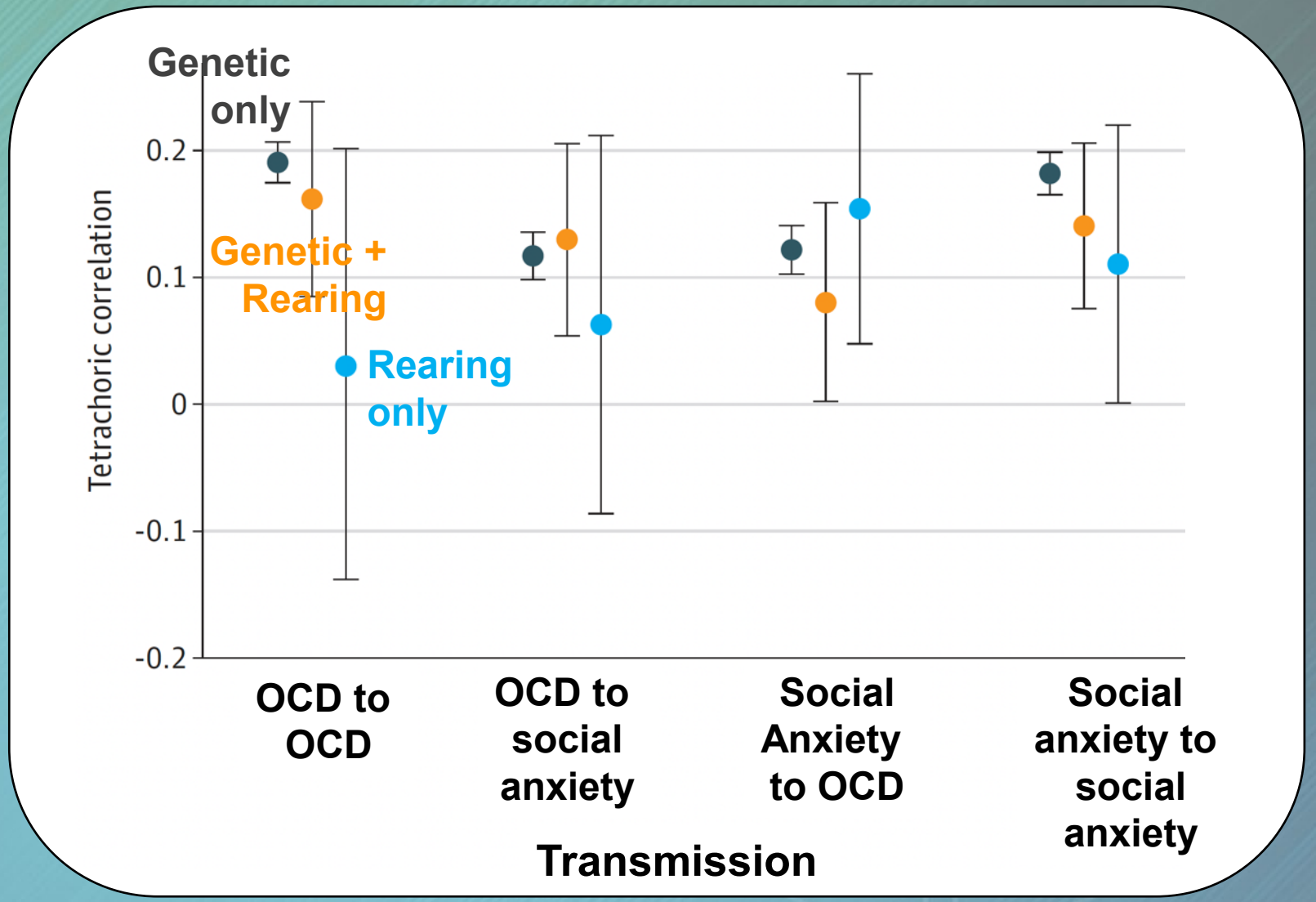


- What is the magnitude of the transmission of OCD from parents to offspring, and to what degree does it result from genetic vs rearing effects?
- What are the sources of the potential familial cross-generational relationship between OCD and all anxiety disorders?
- What are the cross-generational genetic correlations between OCD and anxiety disorders?

Kendler KS et al. Obsessive-compulsive disorder and its cross-generational familial association with anxiety disorders in a national Swedish extended adoption study. JAMA Psychiatry 2023;80(4):314-22.

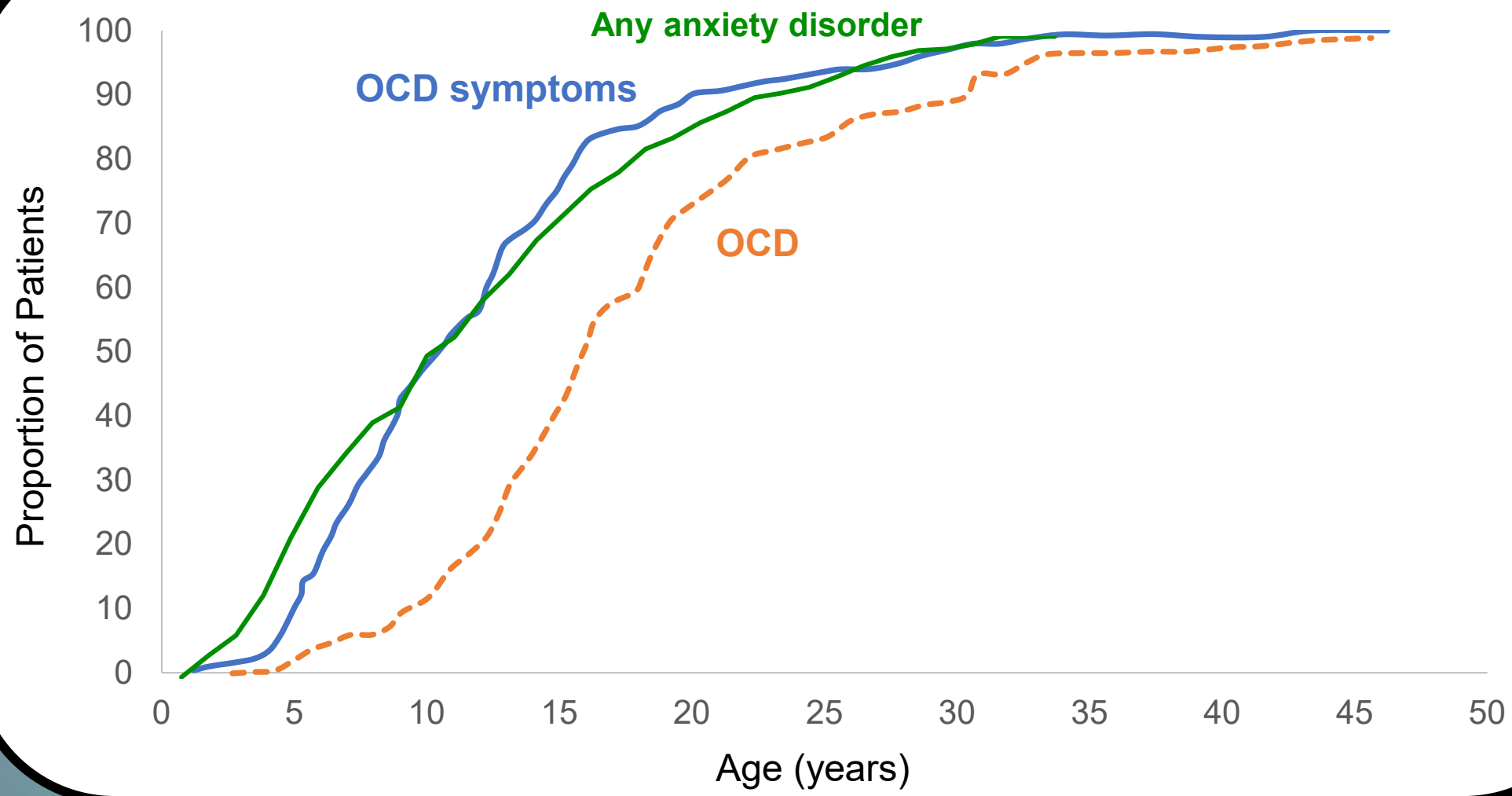
What Is the Relationship Between OCD and Social Anxiety Disorder?

- OCD is transmitted from parents to children largely through a genetic relationship, with rearing playing a minor role
- OCD and anxiety disorders are moderately genetically correlated, with the genetic correlations:
  - strongest between OCD and GAD
  - intermediate for OCD and social phobia
  - weakest between OCD and panic disorder



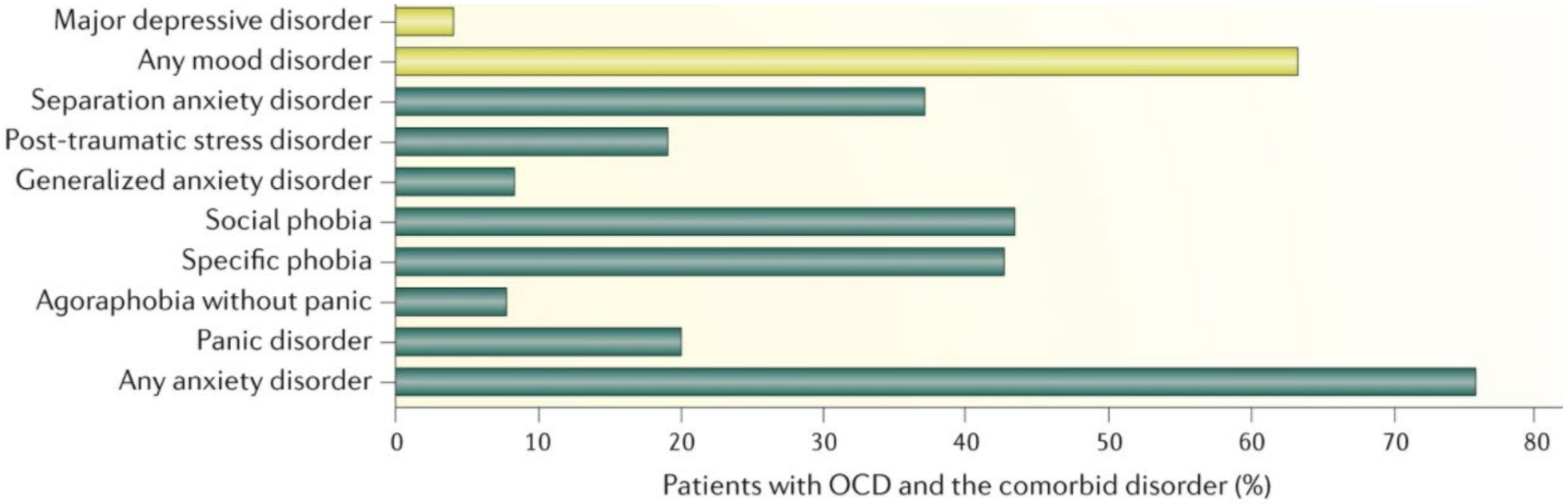
Kendler KS et al. Obsessive-compulsive disorder and its cross-generational familial association with anxiety disorders in a national Swedish extended adoption study. JAMA Psychiatry 2023;80(4):314-22.

Prevalence of OCD and Anxiety: Age of Onset



Coles ME, Johnson EM, Schubert JR. Retrospective reports of the development of obsessive-compulsive disorder: extending knowledge of the protracted symptom phase. Behav Cogn Psychother 2011;39(5):579-89.
Beesdo et al. Arch Gen Psychiatry 2010;67(1):47-57.

Anxiety Comorbidity Is Common in OCD



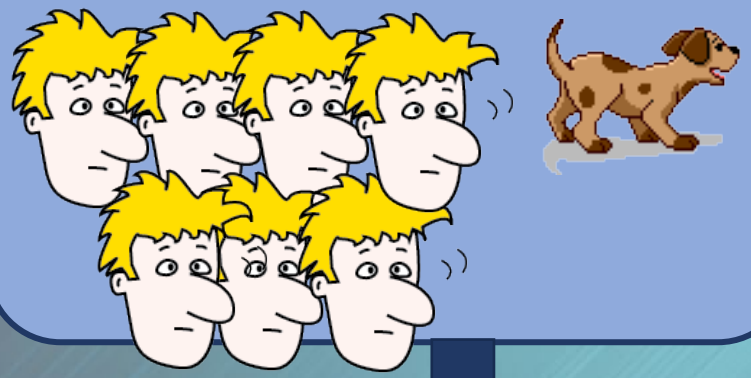
Stein DJ et al. Obsessive-compulsive disorder. Nature Rev Dis Primers 2019;1:5(1):52.

Cognitive Behavioral Therapy in OCD and Social Anxiety

Expectancy violation
Combination
Variability
Removal of safety signals

Inhibitory Learning

Stimulus



Extinction

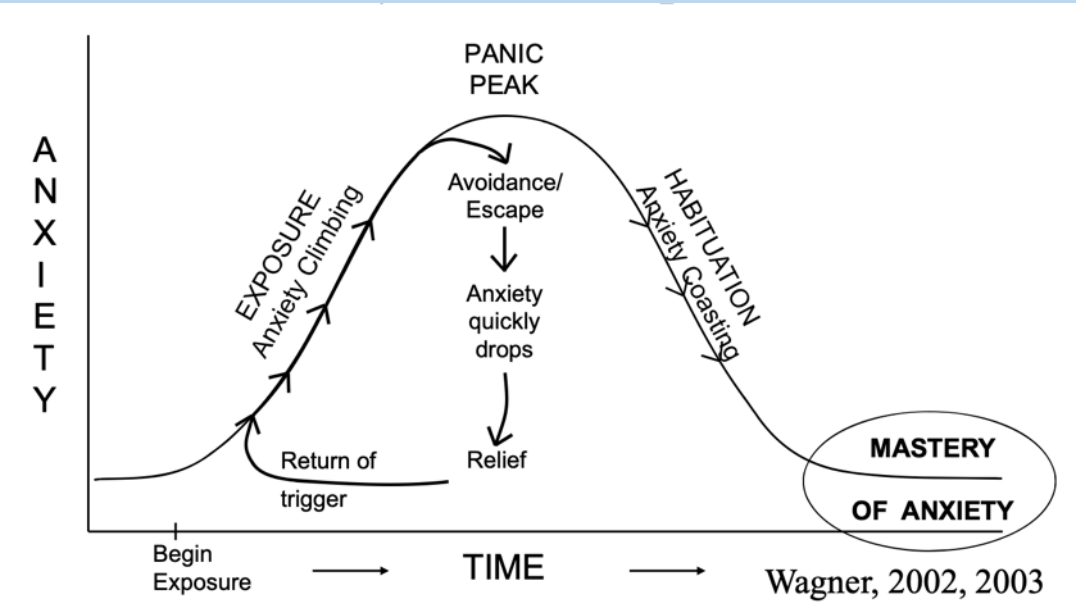
Habituation

Craske MG et al. Maximizing exposure therapy: an inhibitory learning approach. Behav Res Ther 2014;58:10-23; Milad MR et al. Recall of fear extinction in humans activates the ventromedial prefrontal cortex and hippocampus in concert. Biological Psychiatry. 2007;62(5):446-54.

Cognitive Behavioral Therapy in OCD and Social Anxiety

Habituation

- Diminishing of response to repeated stimuli
- Requires fear reduction during exposure to change cognition related to perceived harm
- Fear reduction after exposure does not predict tx response



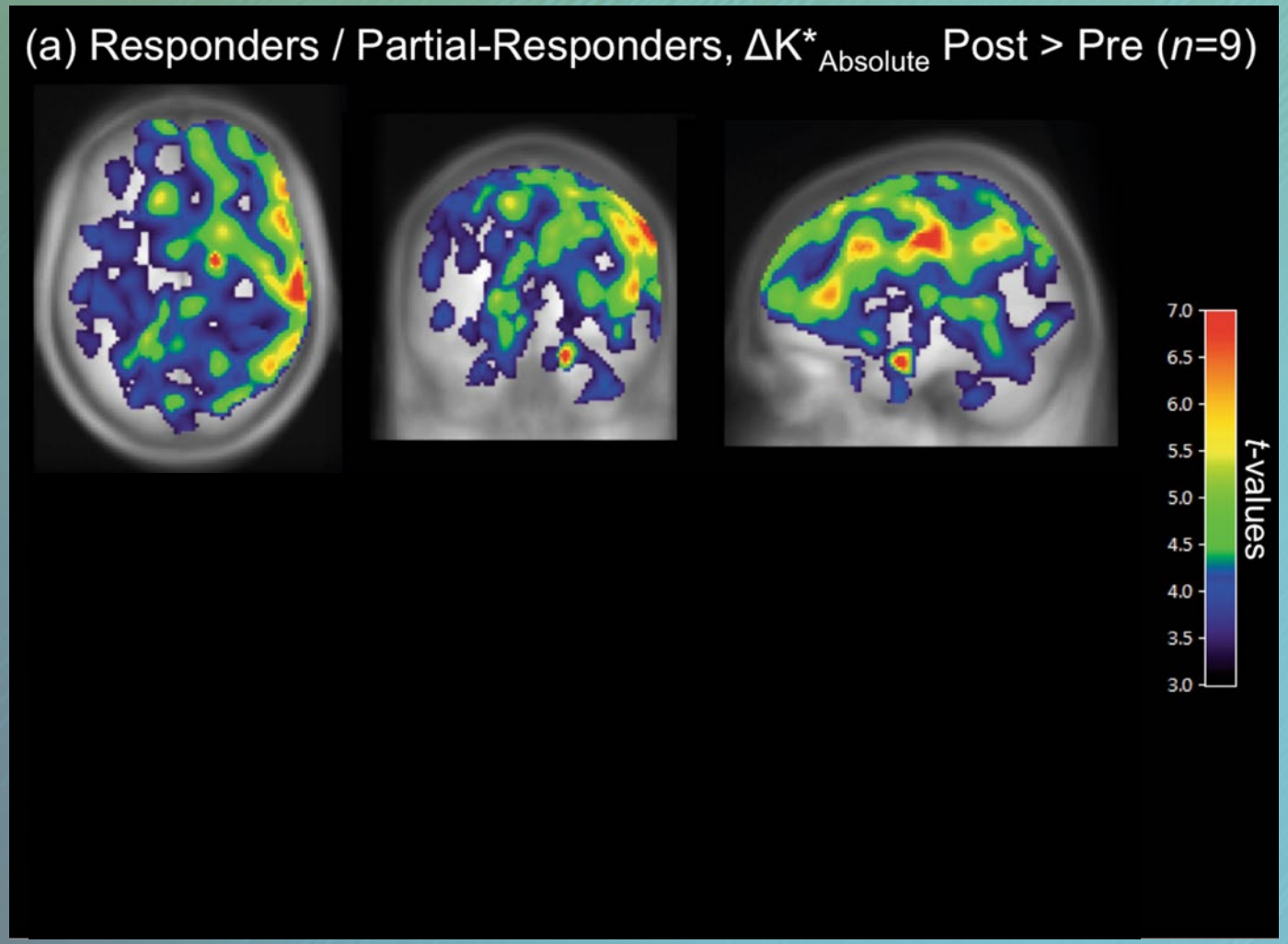
Inhibitory Learning

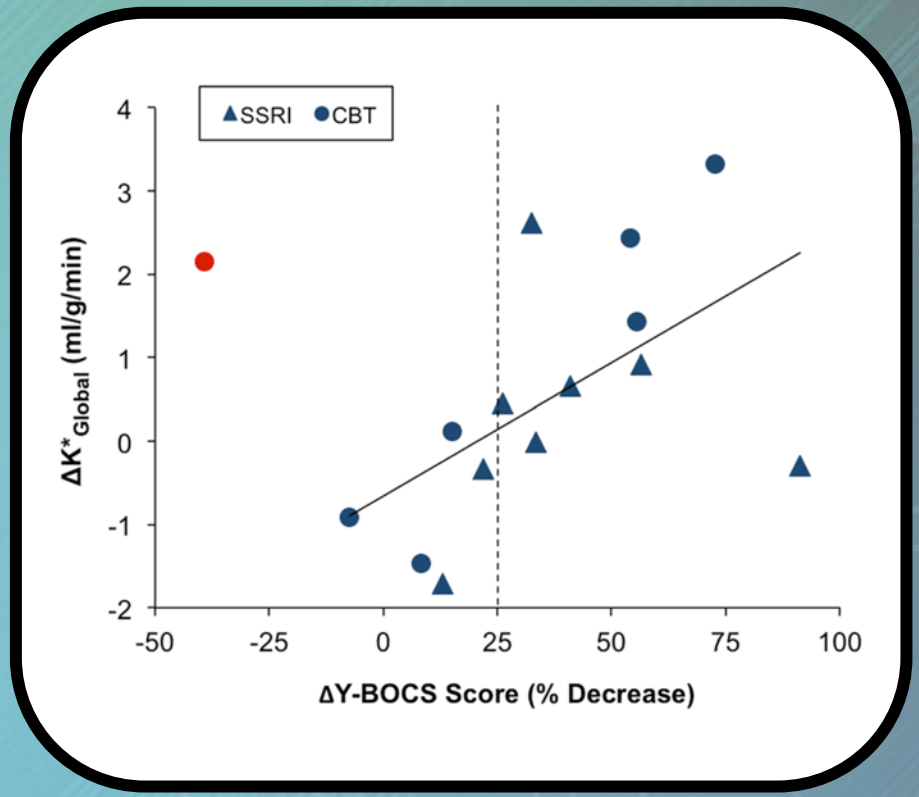
- Learning that the aversive event does not always occur when encountering stimulus
- New learning reduces fear responses to allow for other behavioral responses
- Inhibitory learning models **do not emphasize fear reduction**
  - The amount by which fear has reduced at the completion of extinction does not predict fear at follow-up
    - Fear at follow-up is influenced by passage of time, context shifts, adverse events, or relearning

Craske MG et al. Maximizing exposure therapy: an inhibitory learning approach. Behav Res Ther 2014;58:10-23; Milad MR et al. Recall of fear extinction in humans activates the ventromedial prefrontal cortex and hippocampus in concert. Biological Psychiatry. 2007;62(5):446-54.

Approaching Pharmacologic Treatment of OCD and Social Anxiety Disorder: Commonalities

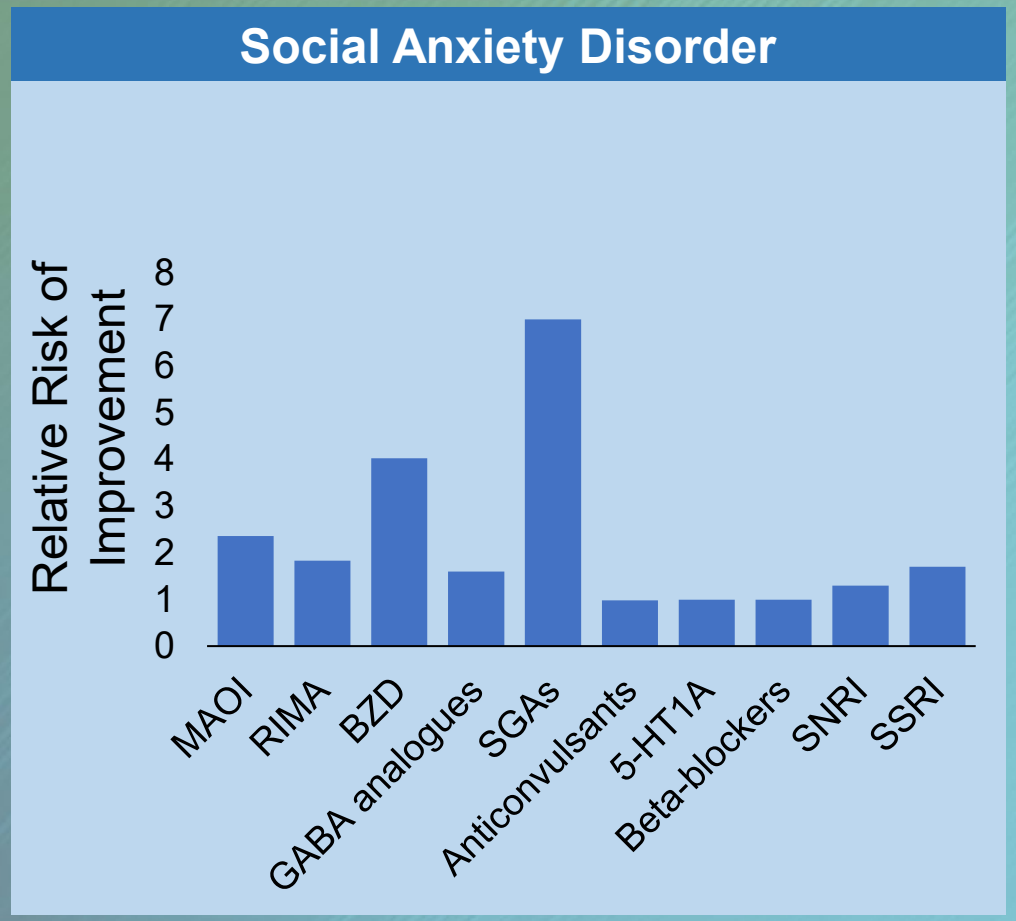
OCD and Serotonin Synthesis

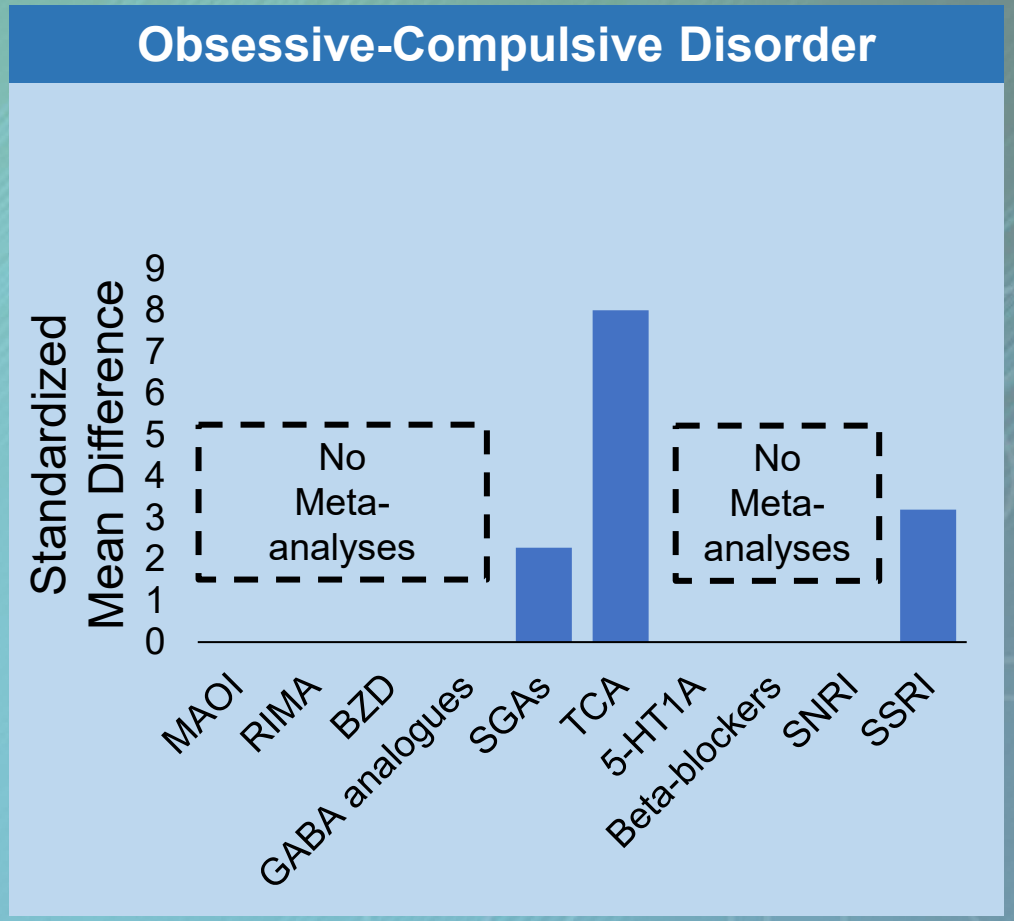




Lissemore JI et al. Transl Psychiatry 2018;8(1):82.

Pharmacotherapy for OCD and Social Anxiety Disorder: The Meta-Analytic Perspective

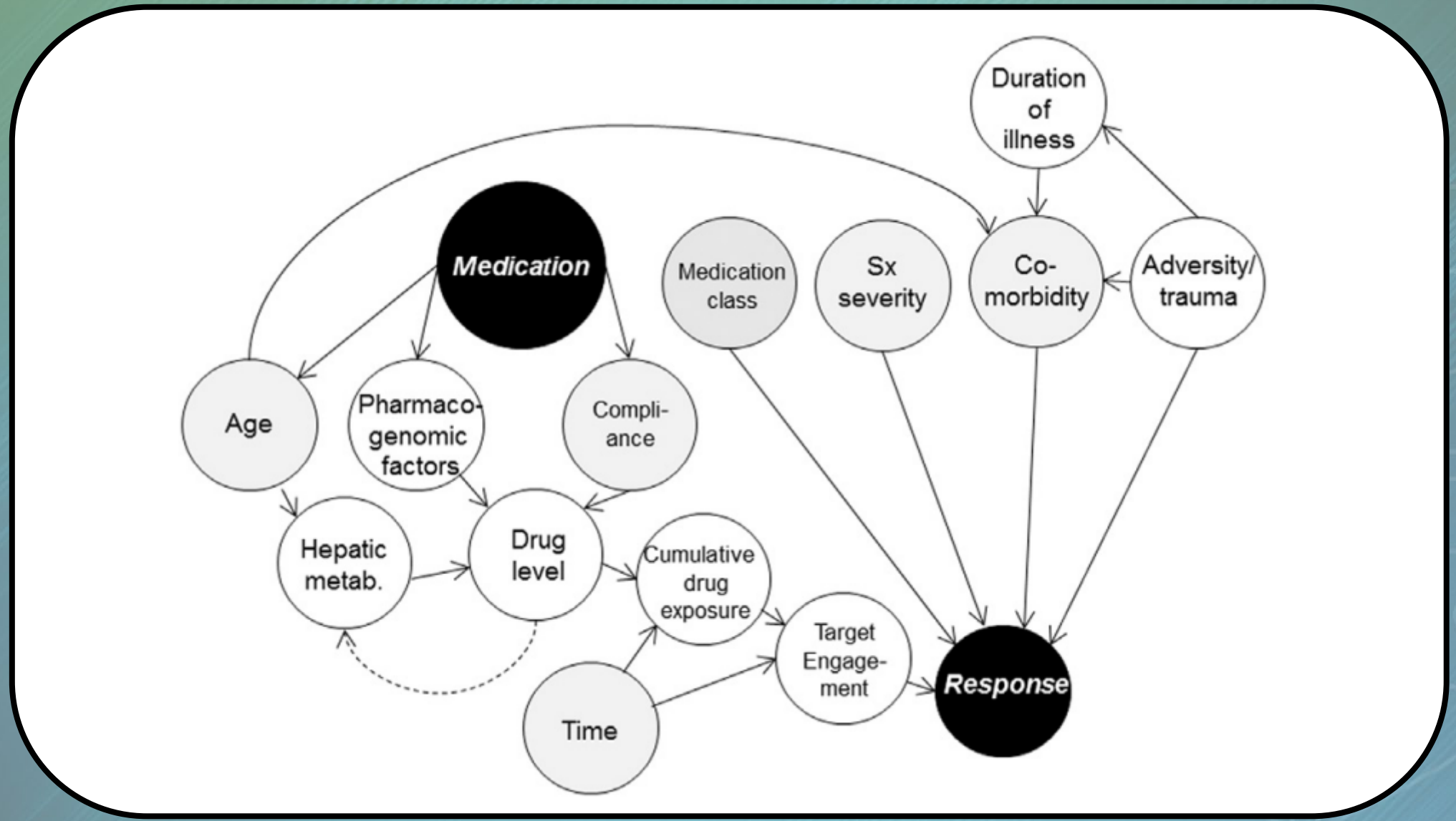




Williams T et al. Pharmacotherapy for social anxiety disorder (SAnD). Cochrane Database Syst Rev 2017;10(10):CD001206; Komossa K et al. Second-generation antipsychotics for obsessive-compulsive disorder. Cochrane Database Syst Rev. 2010;(12):CD008141; Soomro GM et al. Selective serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD). Cochrane Database Syst Rev 2008;2008(1):CD001765; Ackerman DL and Greenland S. Multivariate meta-analysis of controlled drug studies for obsessive-compulsive disorder. J Clin Psychopharmacol 2002;22(3):309-17.

Social Anxiety Disorder and OCD Pharmacotherapy: Common Themes

OCD and Social Anxiety: Considering Dose



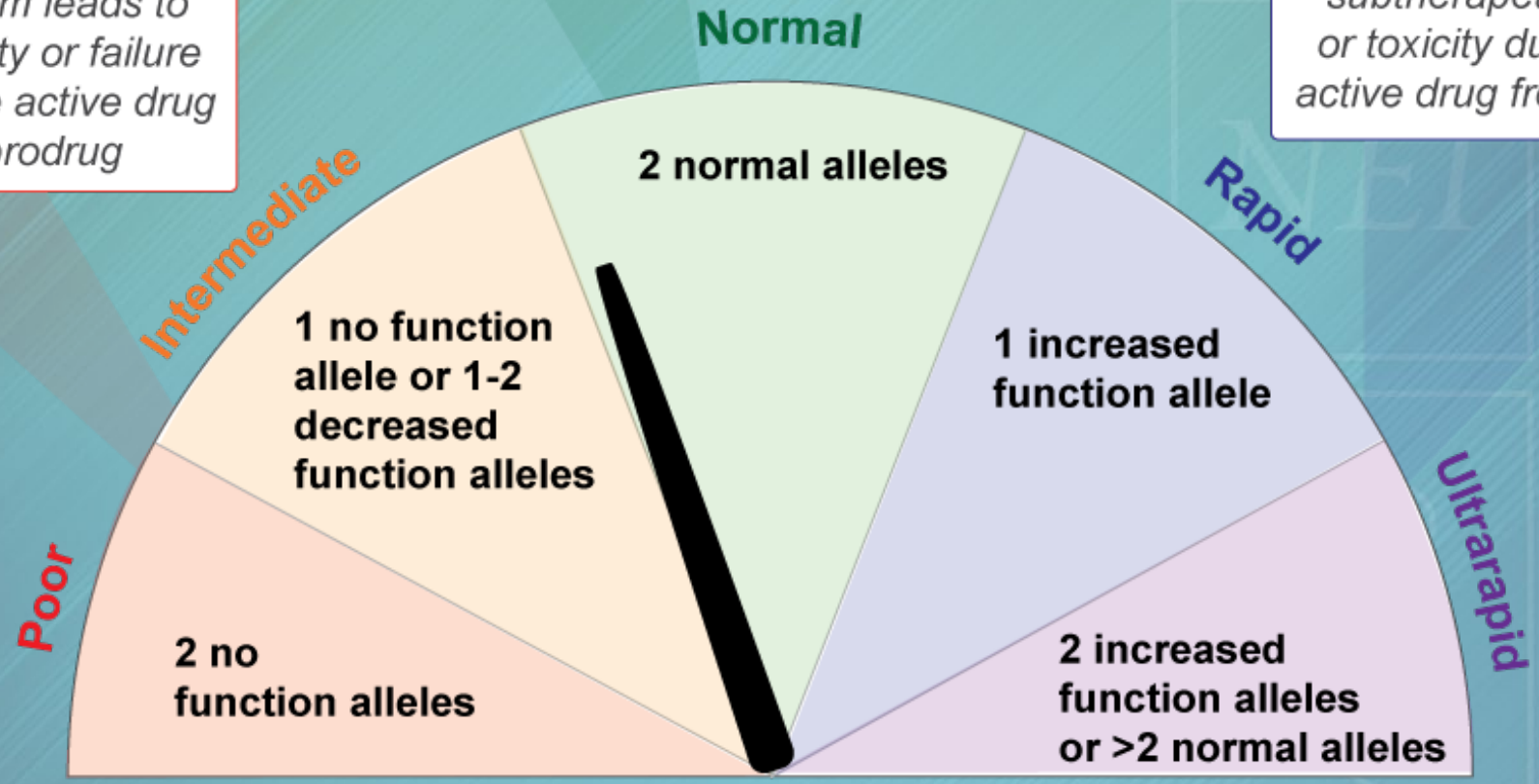
Wehry AM et al. Curr Probl Pediatr Adolesc Health Care 2018;48:40-9.

Pharmacogenetics and SSRIs: Important in OCD & Social Anxiety

Most standard drug dosing is based on population average, representing normal metabolism

Decreased drug metabolism leads to drug toxicity or failure to generate active drug from prodrug

Increased drug metabolism leads to subtherapeutic levels or toxicity due to more active drug from prodrug



Strawn JR & Stahl SM. *Case Studies in Child & Adolescent Psychiatry*; 2023.

Pharmacogenetics: Important in OCD & Social Anxiety

Standard dose = turning water on at same rate in all patients

Metabolizer group = size of drain

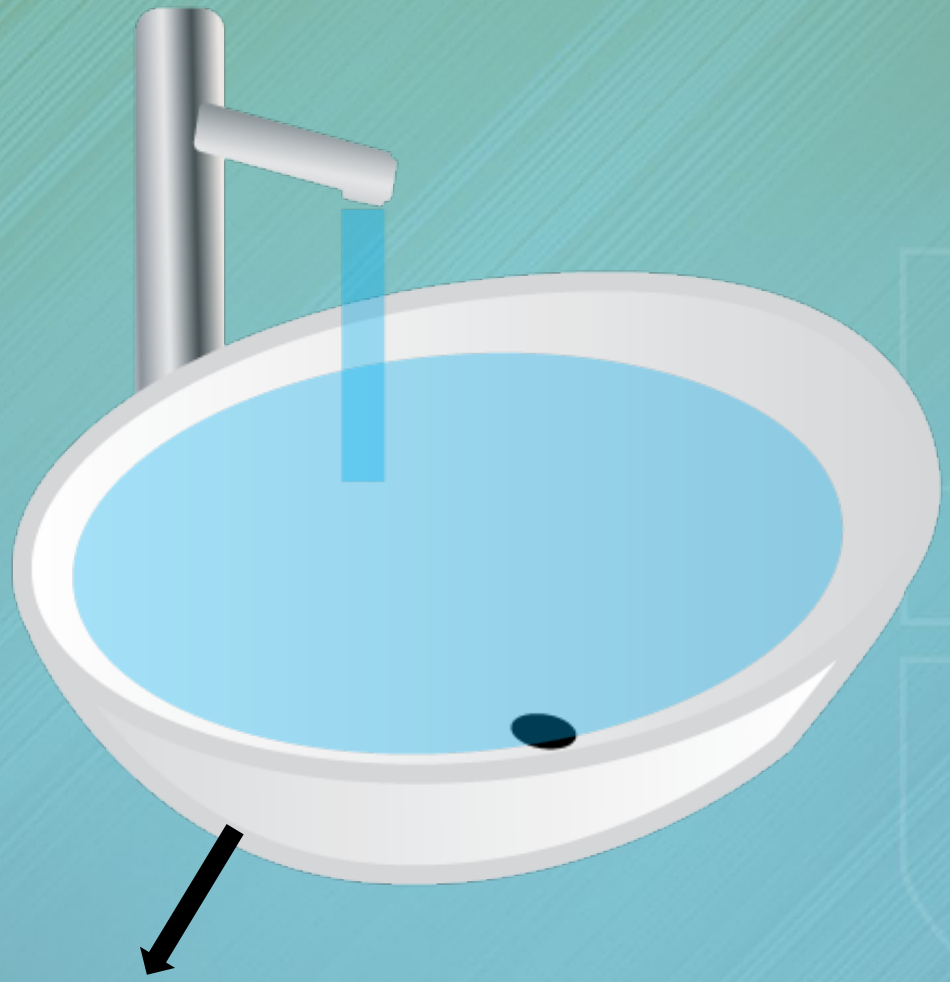
More likely to overflow = high concentrations, high risk of side effects

Poor metabolizer

Pharmacogenetics: Important in OCD & Social Anxiety

Standard dose = turning water on at same rate in all patients

Metabolizer group = size of drain



Intermediate metabolizer

Pharmacogenetics: Important in OCD & Social Anxiety

Standard dose = turning water on at same rate in all patients

Metabolizer group = size of drain

Normal metabolizer

Pharmacogenetics: Important in OCD & Social Anxiety

Standard dose = turning water on at same rate in all patients

Metabolizer group = size of drain

Rapid metabolizer

Pharmacogenetics: Important in OCD & Social Anxiety

Standard dose = turning water on at same rate in all patients

Metabolizer group = size of drain

More likely to have no water = low concentrations, high risk of non-response

Ultrarapid metabolizer

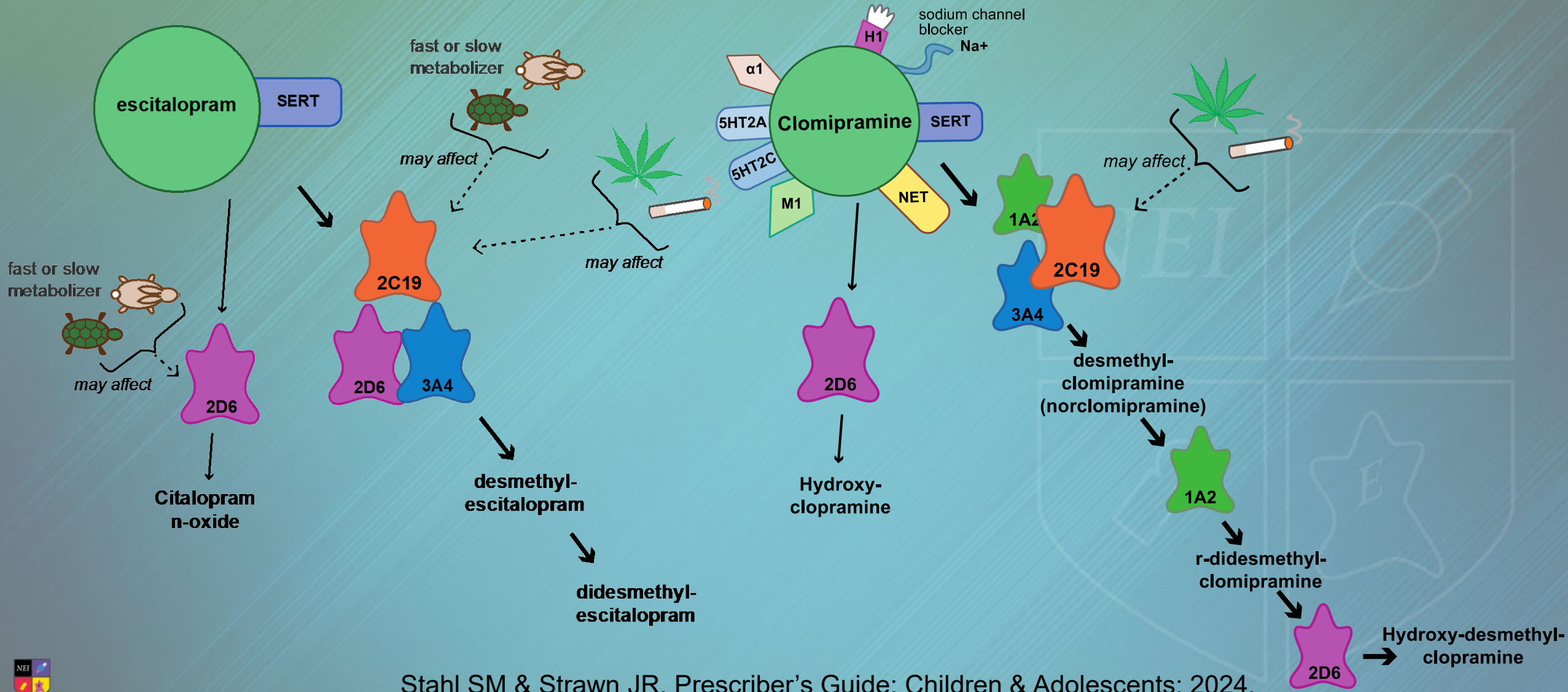
Pharmacogenetics: Important in OCD & Social Anxiety

Standard dose = turning water on at same rate in all patients

Metabolizer group = size of drain

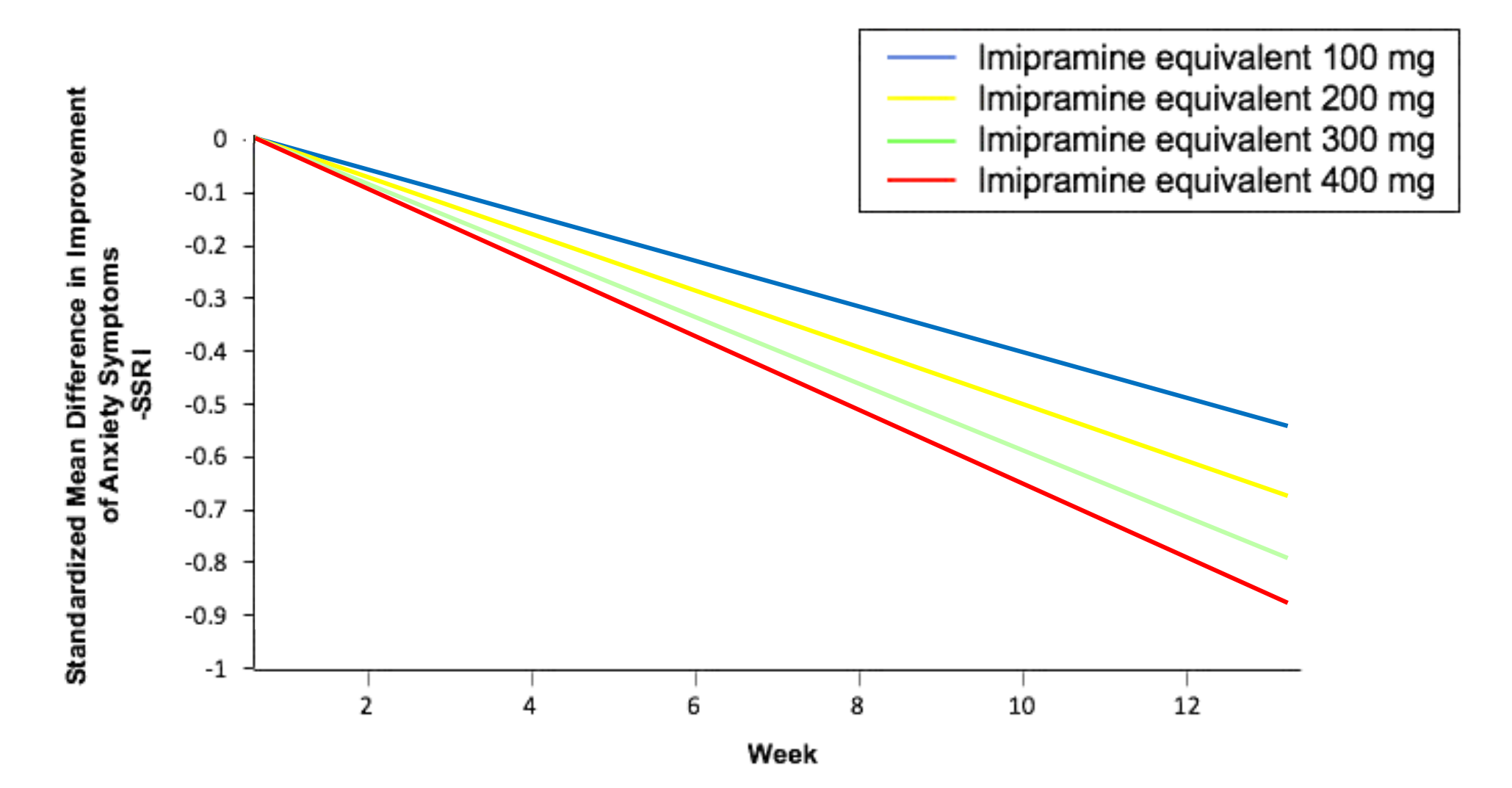
Inhibitor—hair in the drain

Pharmacogenetics: Important in OCD & Social Anxiety



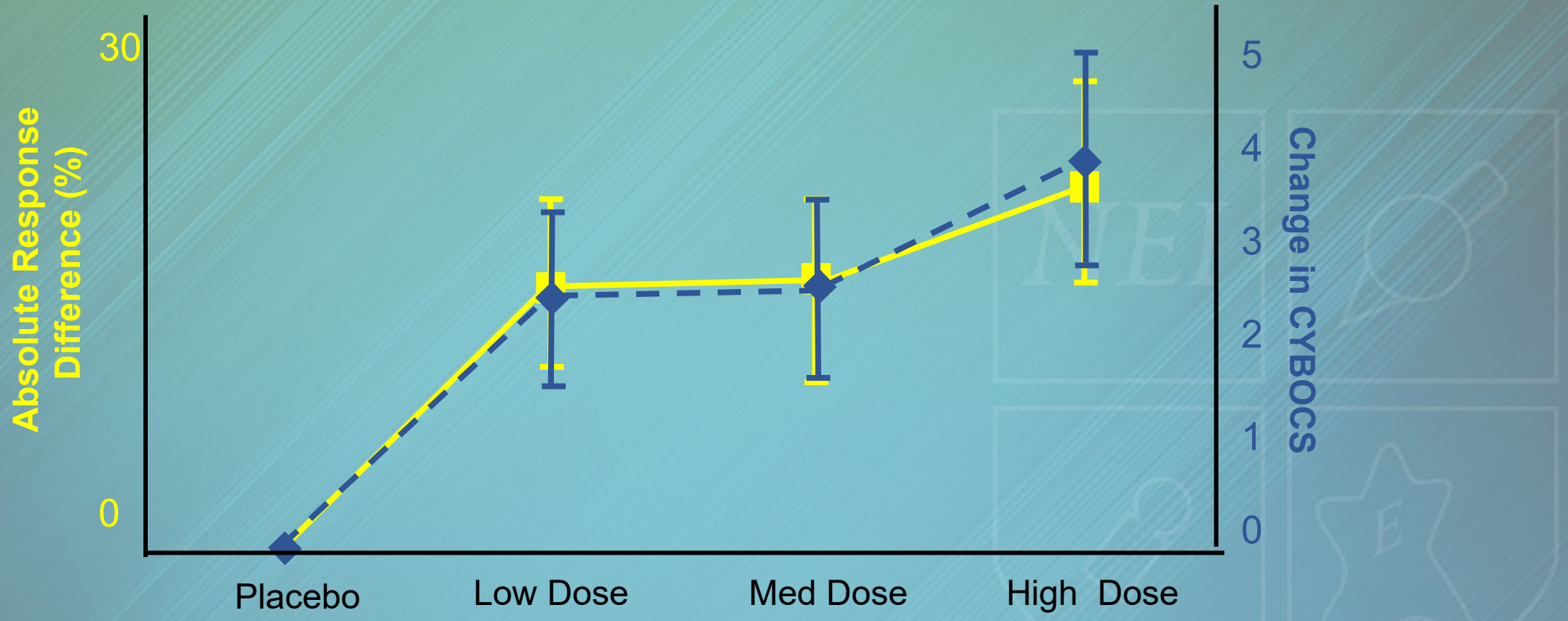
Stahl SM & Strawn JR. Prescriber's Guide: Children & Adolescents; 2024.

SSRI Dosing in Anxiety Disorders



Jakubovski E et al. Systematic review and meta-analysis: Dose–response curve of SSRIs and SNRIs in anxiety disorders. Depress Anxiety 2019;36(3):198-212.

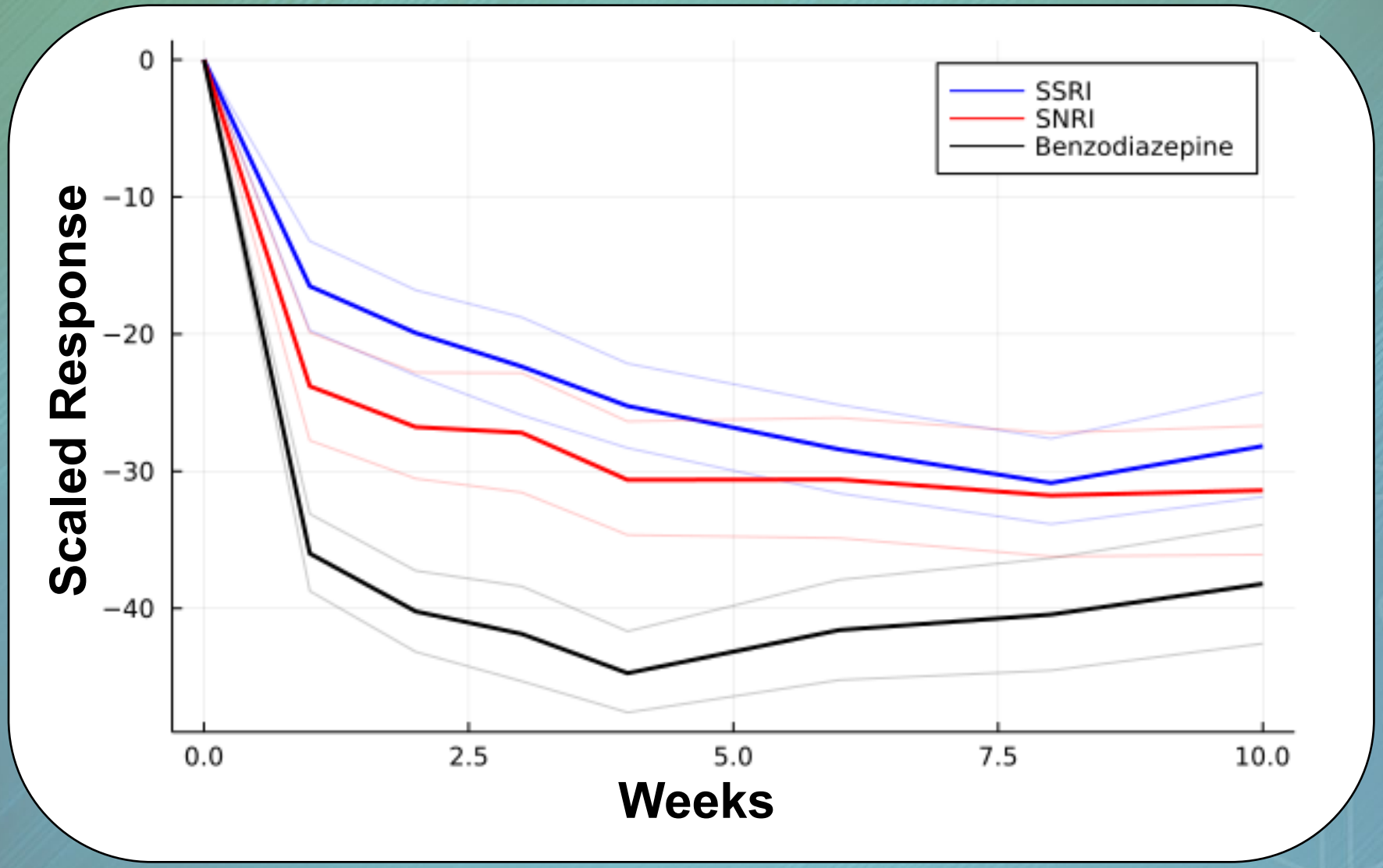
SSRI Dosing in OCD



Jakubovski E et al. Systematic review and meta-analysis: Dose–response curve of SSRIs and SNRIs in anxiety disorders. Depress Anxiety 2019;36(3):198-212; Bloch MH et al. Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. Mol Psychiatry 2010 Aug;15(8):850-5.

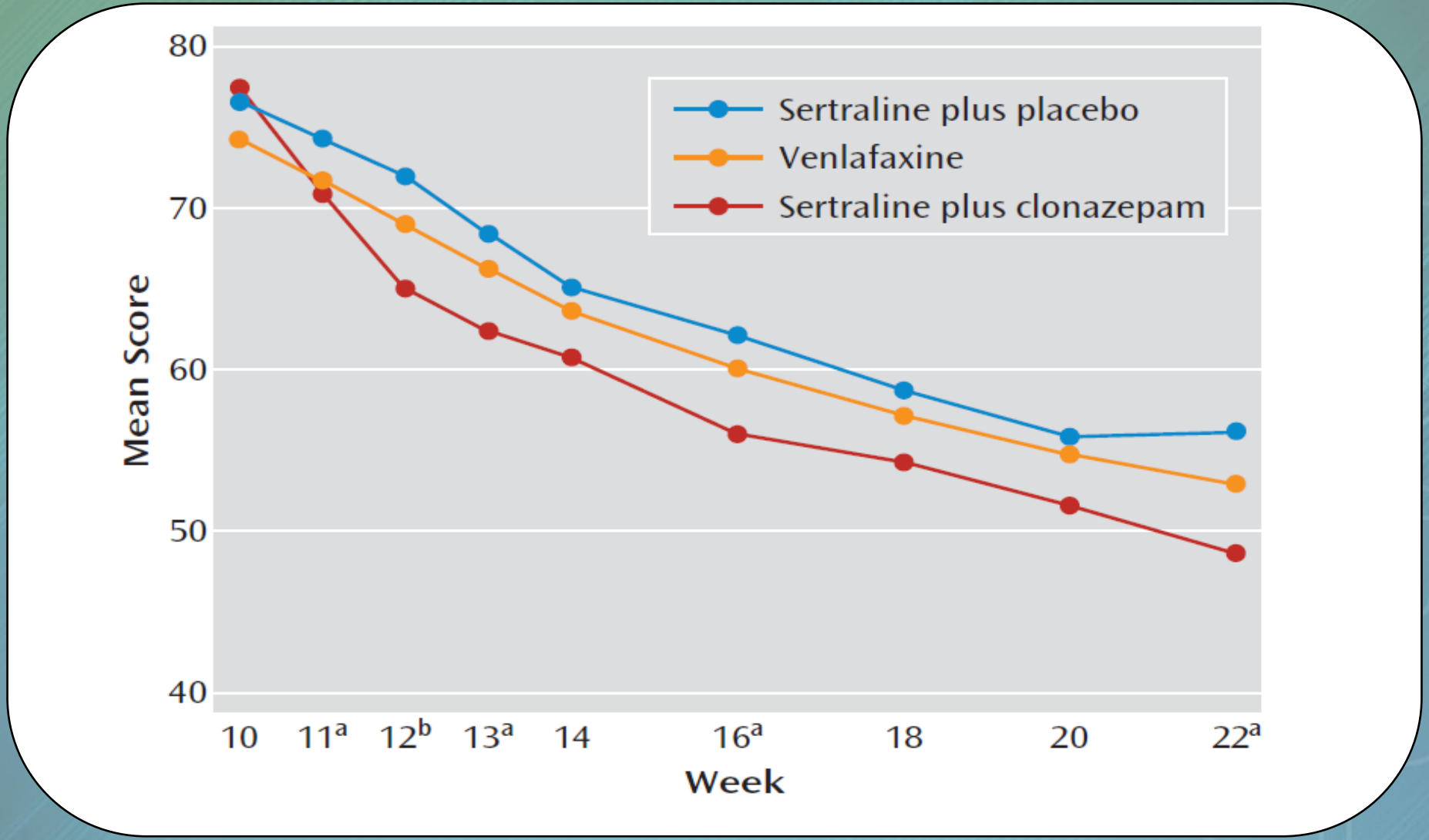
Considering OCD and Social Anxiety Disorder Separately

Efficacy: SSRIs, SNRIs, and Benzodiazepines in Social Anxiety Disorder



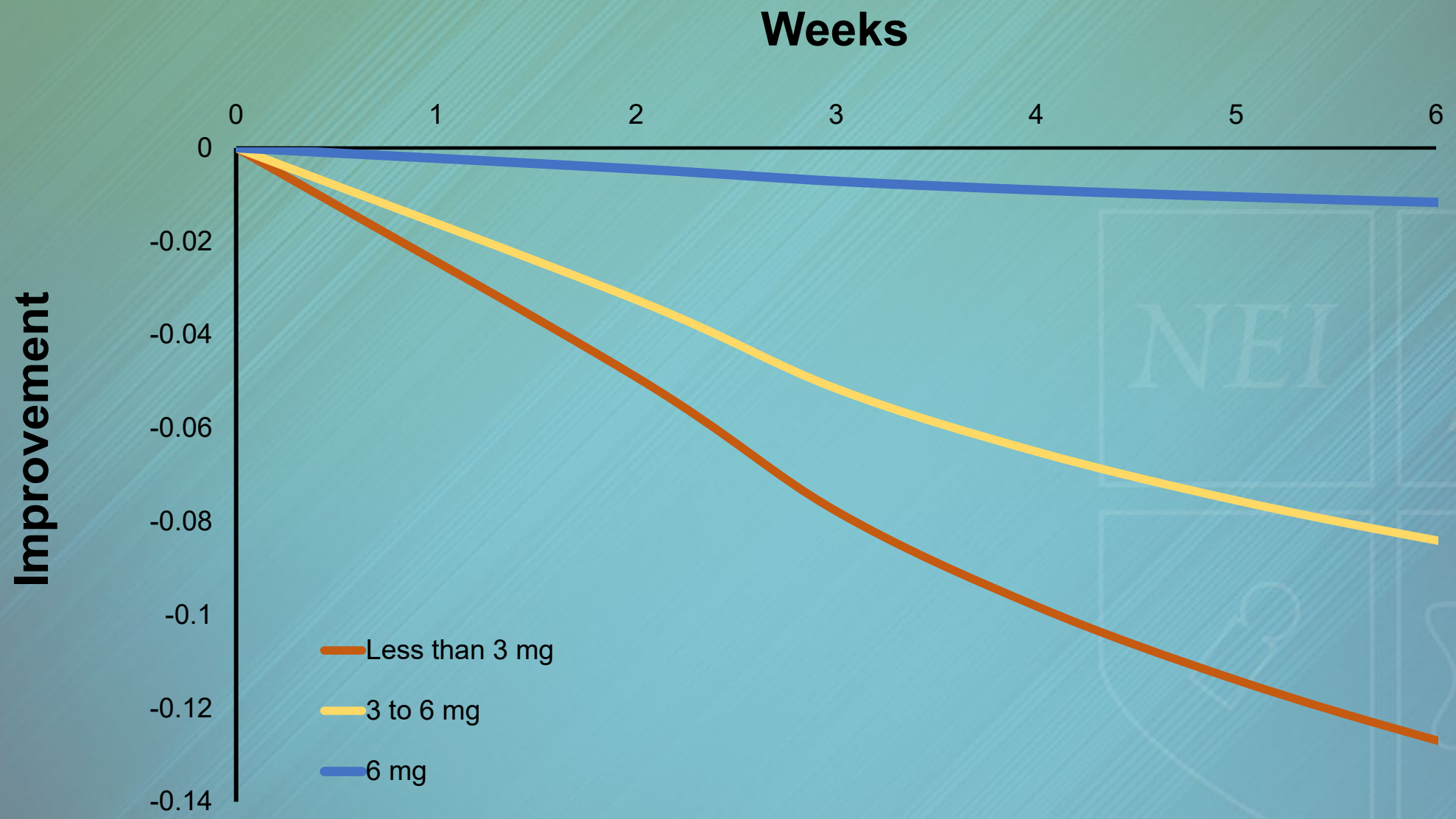
Benzodiazepine data from Stimpfil et al. 2021. SSRI and SRNI data in preparation for publication.

Augmentation in Tx-Resistant Social Anxiety Disorder



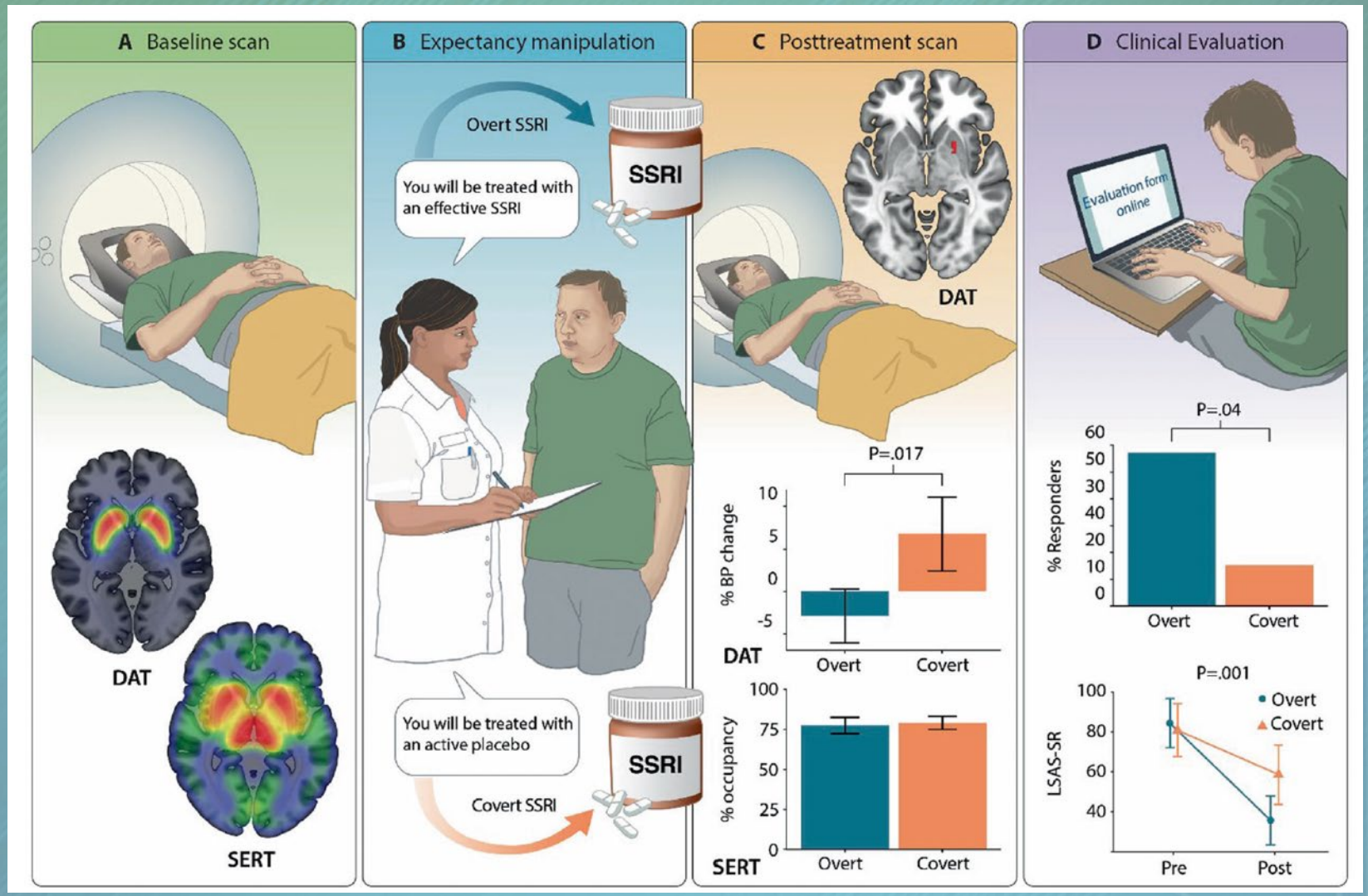
Pollack MH et al. A double-blind randomized controlled trial of augmentation and switch strategies for refractory social anxiety disorder. Am J Psychiatry 2014;171(1):44-53.

Benzodiazepine Dosing and Response in Anxiety Disorders



Strimpfl JN, Mills JA, Strawn JR. CNS Spectr 2023;28(1):53-60.

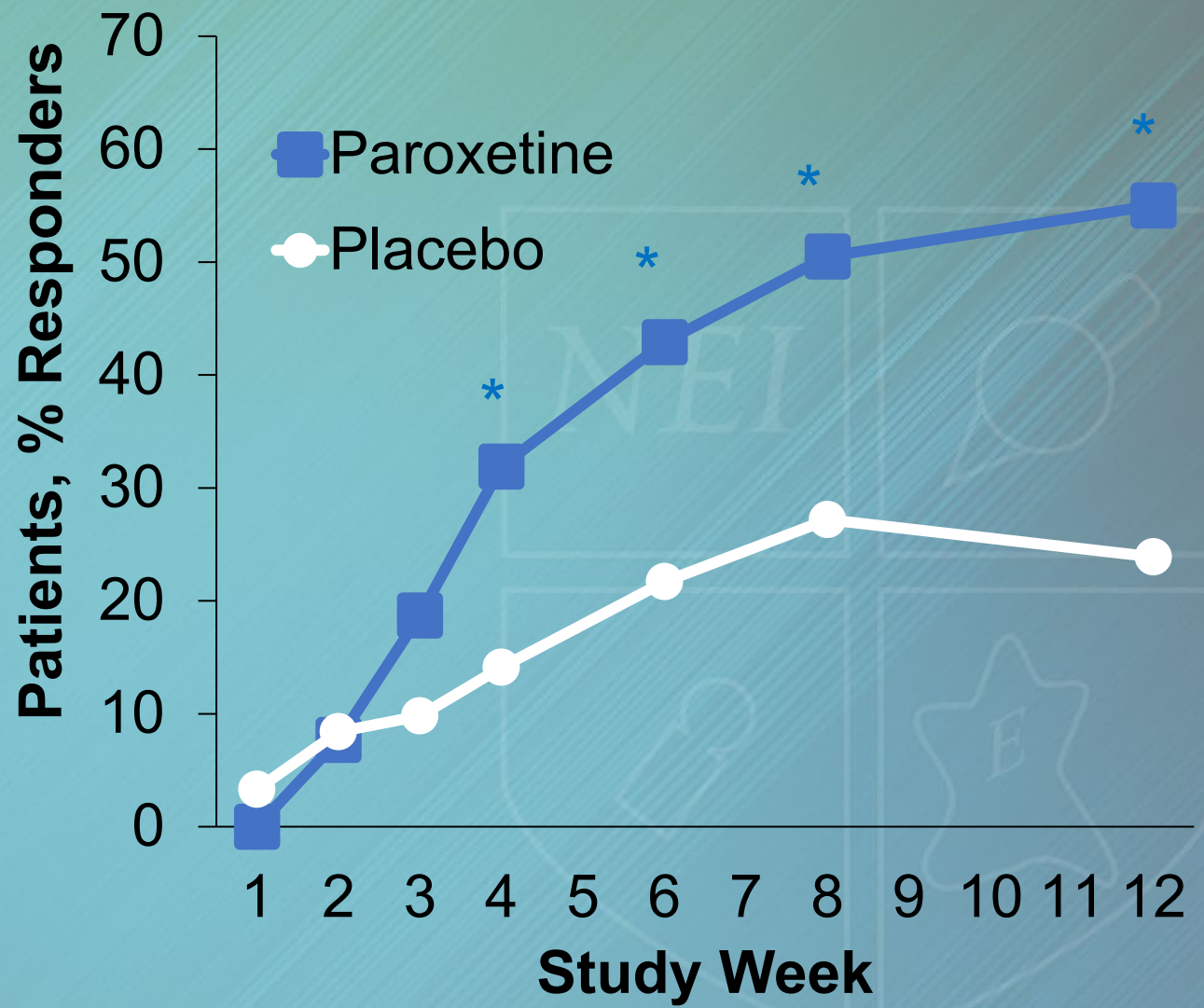
Expectation in Treatment of Social Anxiety Disorder



Hjorth OR et al. Expectancy effects on serotonin and dopamine transporters during SSRI treatment of social anxiety disorder: a randomized clinical trial. Transl Psychiatry 2021;11(1):559.

Paroxetine in Social Anxiety Disorder: The Importance of Time

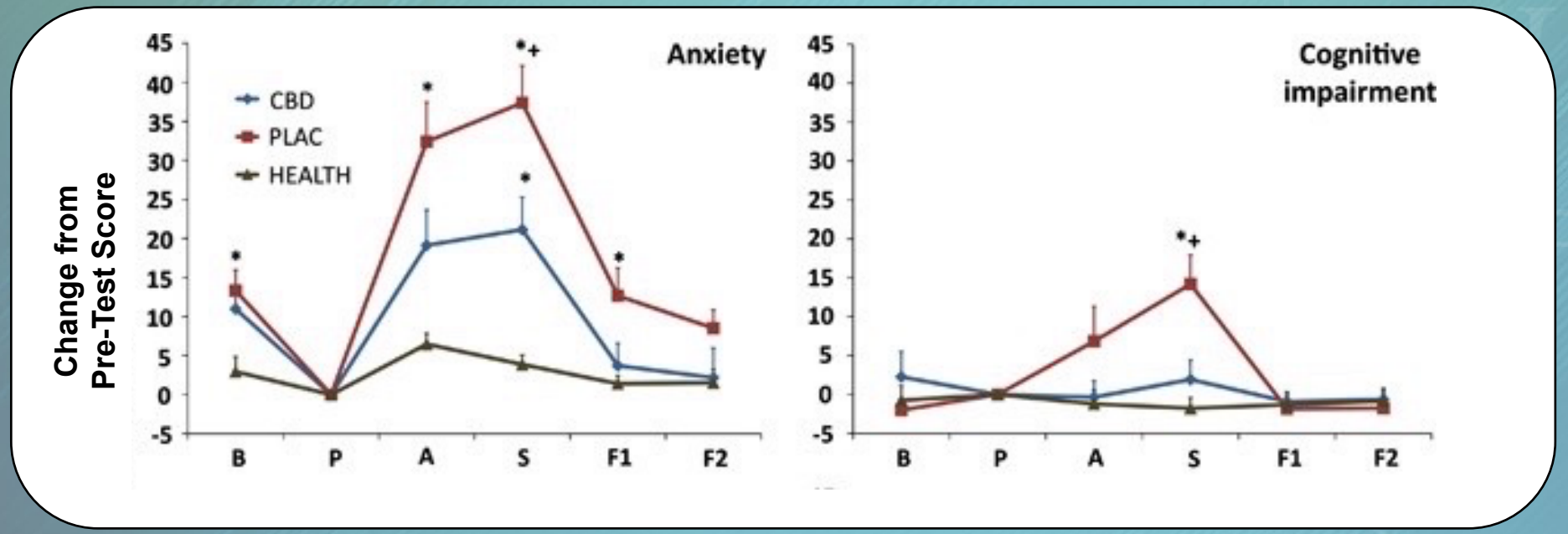
- 12-week, multicenter, randomized, double-blind trial
- 187 persons with social anxiety disorder
- 1-week, single-blind, placebo, run-in period, then double-blind, 11-week course of either paroxetine or placebo
- Initial dosage of paroxetine (or placebo) was 20 mg with increases of 10 mg/d weekly (flexible dosing to a maximum of 50 mg/d) permitted after the second week of treatment
- 55% of persons taking paroxetine and 24% of persons taking placebo were much improved or very much improved at the end of treatment (odds ratio [OR], 3.88; 95% confidence interval, 2.81–5.36)



Stein MB et al. Paroxetine treatment of generalized social phobia (social anxiety disorder): a randomized controlled trial. JAMA 1998;280(8):708-13.

Cannabidiol in Social Anxiety Disorder

- Cannabidiol (CBD)—anxiolytic effects in humans and lower animals
- Patients with social anxiety disorder and healthy controls
- CBD 600 mg (n=12) or placebo (n=12), CBD 90 minutes before the task
- Simulation public speaking test (SPST)
- Placebo group: higher anxiety, cognitive impairment, discomfort, and alertness compared to CBD

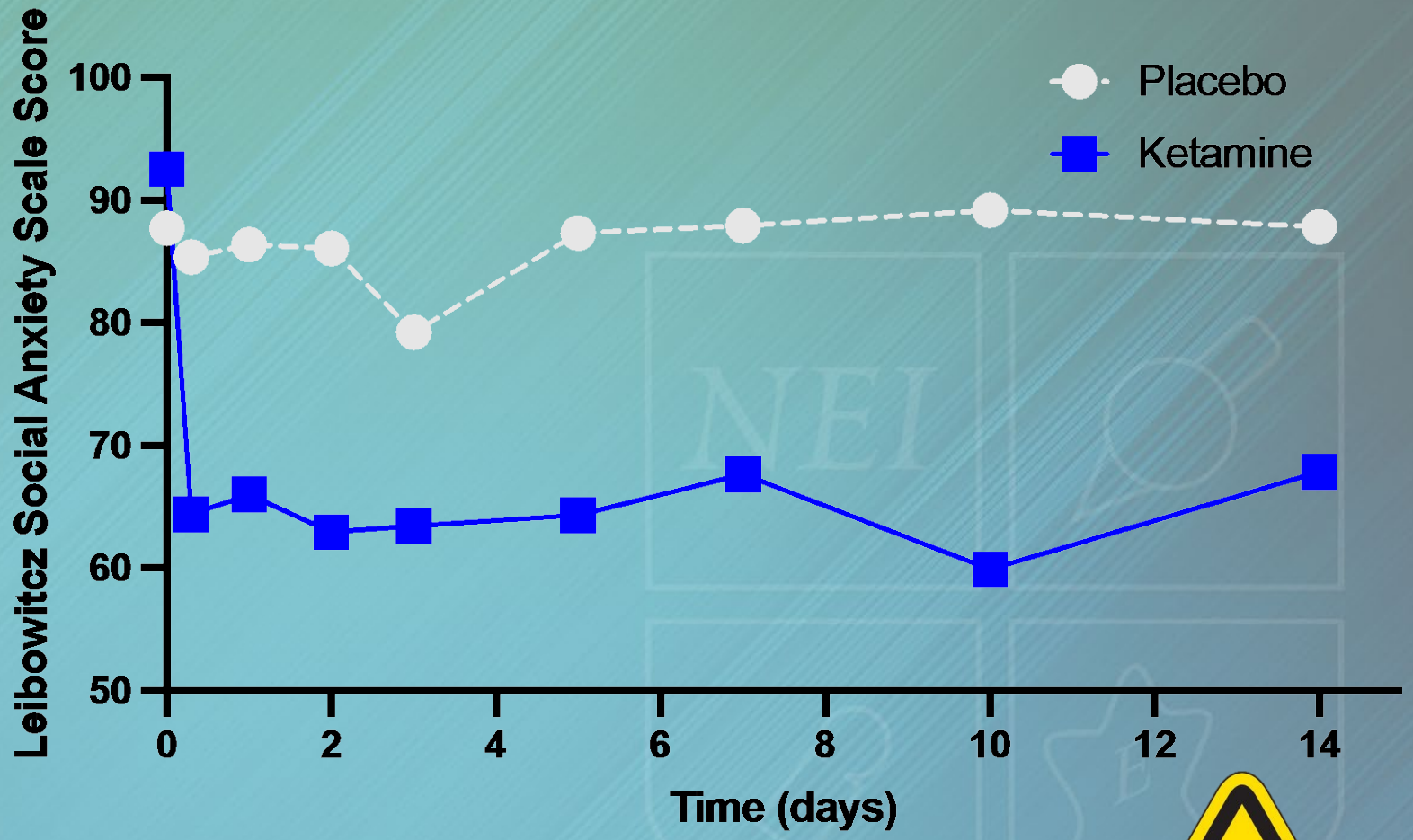


Small N, requires replication

Bergamaschi MM et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. Neuropsychopharmacology 2011;36(6):1219-26; Crippa JA et al. Effects of cannabidiol (CBD) on regional cerebral blood flow. Neuropsychopharmacology 2004;29(2):417-26.

Ketamine in Social Anxiety Disorder

- Adults with SAD (N=18)
- IV ketamine (0.5 mg/kg over 40 min) vs. saline
  - Infusions in a random order with a 28-day washout period between infusions
- Anxiety assessed 3-h post-infusion over 14 d
- Treatment responders (35% LSAS reduction)
  - 33% ketamine
  - 0% placebo



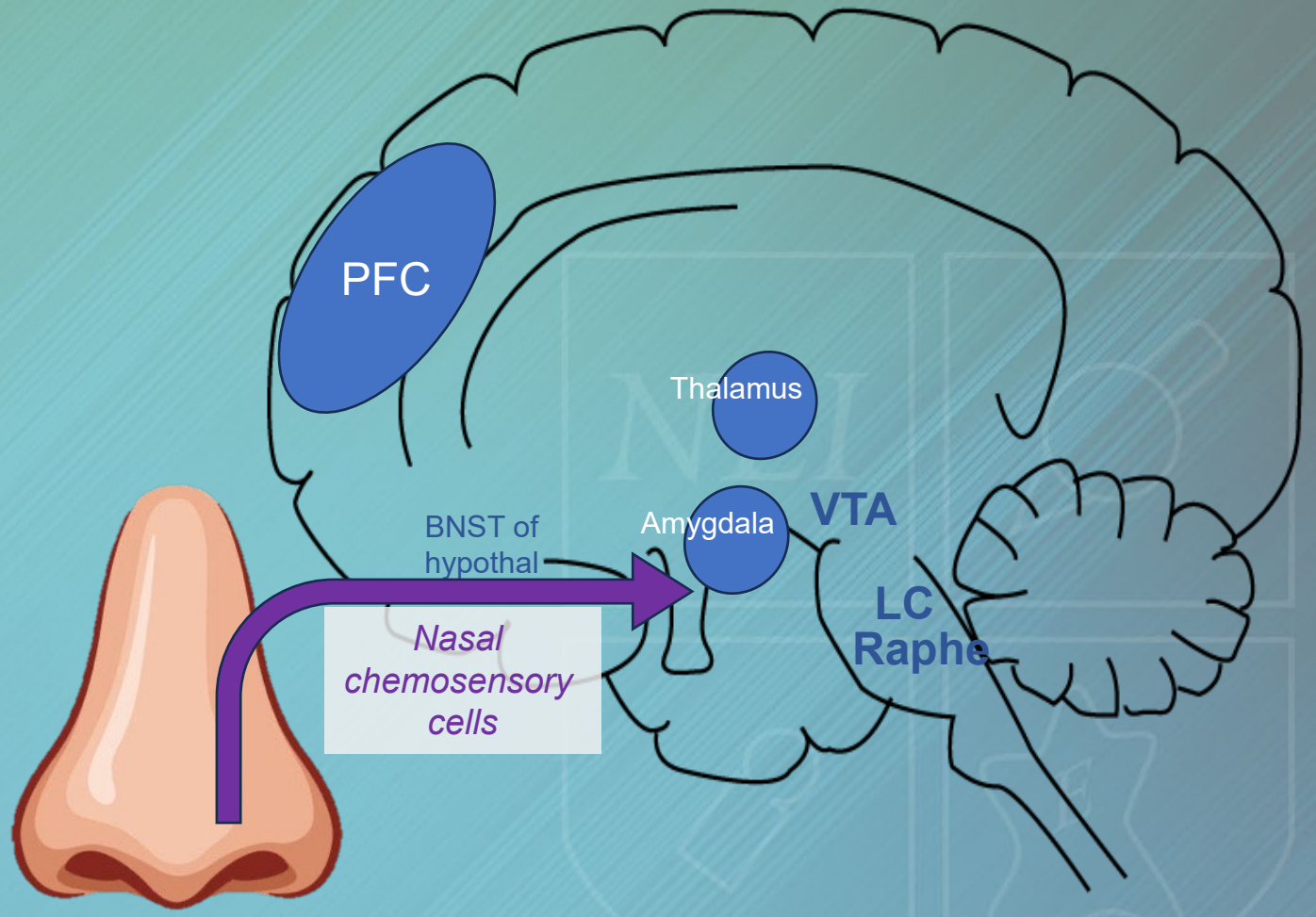
Small N, requires replication

Taylor JH et al. Ketamine for social anxiety disorder: a randomized, placebo-controlled crossover trial. Neuropsychopharmacol 2018;43(2);325-33.

Fasedienol

- Pherines, also known as vomeropherines, are odorless synthetic neuroactive steroids

- May activate nasal chemosensory neurons in the periphery that in turn connect with a subset of olfactory bulb neurons that directly project to GABAergic forward inhibitory neurons in the amygdala regulating fear and anxiety



Liebowitz MR et al. Effect of an acute intranasal aerosol dose of PH94B on social and performance anxiety in women with social anxiety disorder. Am J Psychiatry 2014;171(6):675-82. ClinicalTrials.gov June 2023.

Liebowitz MR et al. Effect of as-needed use of intranasal PH94B on social and performance anxiety in individuals with social anxiety disorder. Depress Anxiety 2016;33(12):1081-9.

Monti L, Liebowitz MR. Neural circuits of anxiolytic and antidepressant phermine molecules. CNS Spectr 2022;27(1):66-72.

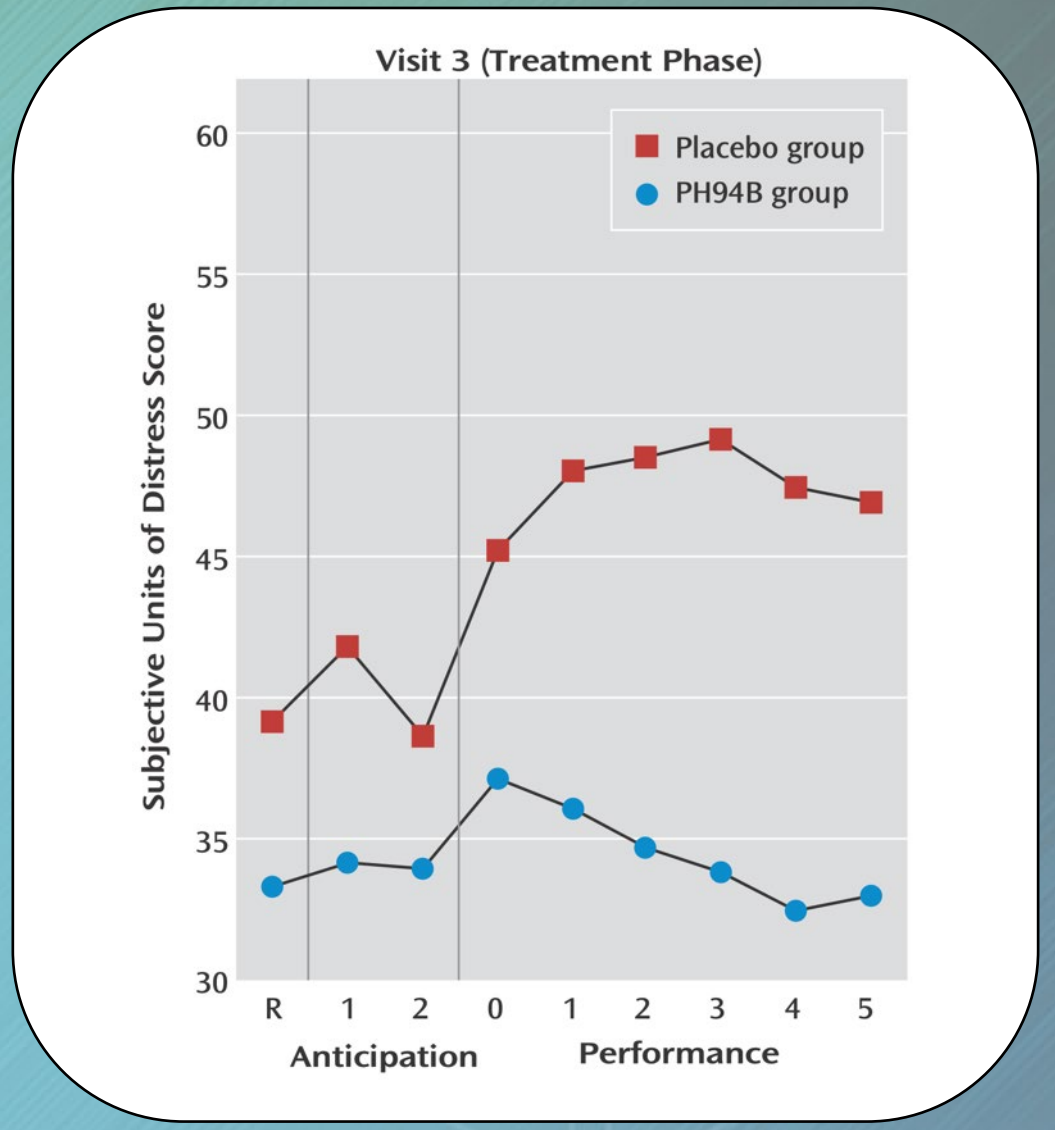
Fasedienol in Social Anxiety Disorder

Trial 1

- Randomized, double-blind, placebo-controlled study
- 91 women (age: 19–60) with social anxiety disorder
- Laboratory-simulated public speaking and social interaction challenges
- Intranasal fasedienol or placebo
- Greater proportion of the fasedienol group was much or very much improved from the first to the second sets of challenges compared with the placebo group (75% and 37%)

Trial 2

- Patients aged 18 to 65 years with social anxiety disorder (N=481)
- Fasedienol IEN up to QID for acute anxiety x 12 mos
- At 1, 2, and 3 months, 36%, 44%, and 55%, of patients experienced a 20-point or greater reduction on the LSAS, respectively
- 57% had ≥1 treatment-related adverse event



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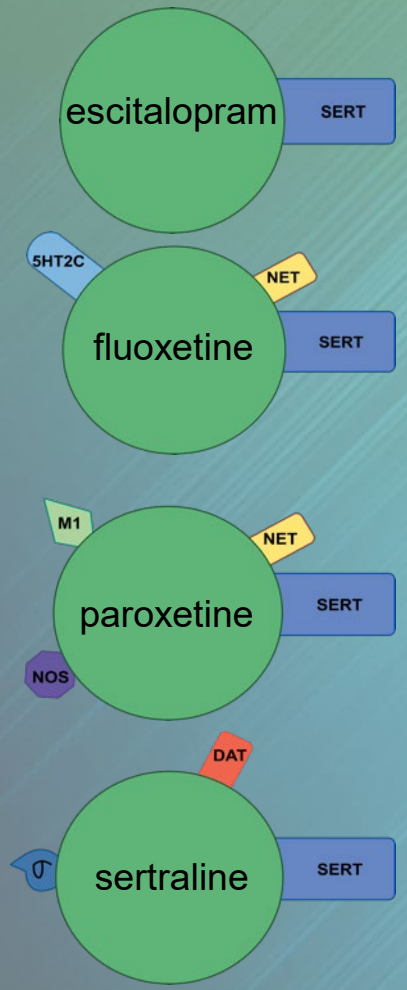
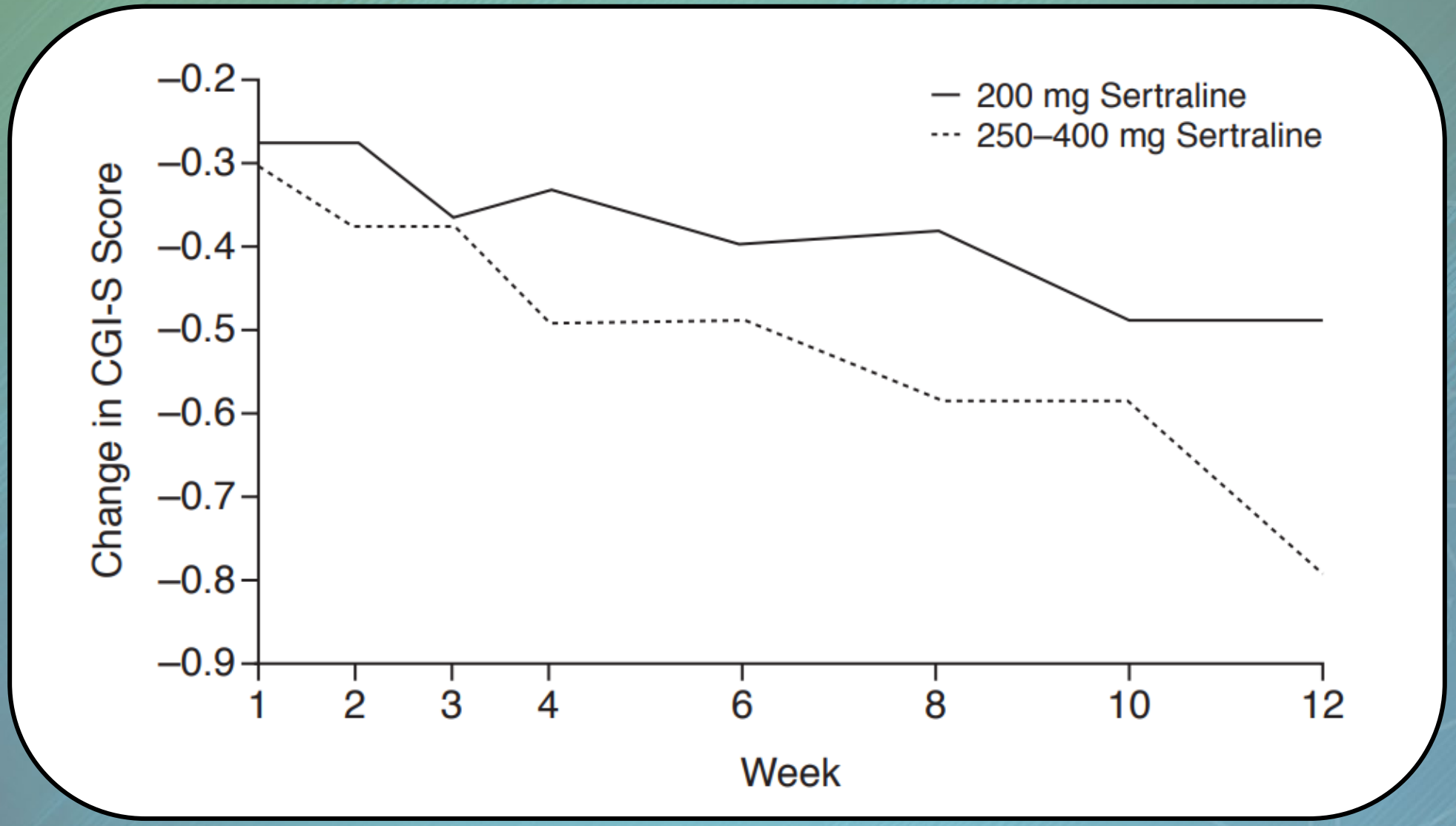
Considering OCD and Social Anxiety Disorder Separately

Double-Blind, Placebo-Controlled Studies of Relapse Prevention in Adult OCD



Escitalopram, N=158 16 wks (24 double blind) (Fineberg et al. 2007)	• Faster relapse on placebo compared to escitalopram • Greater relapse rate with placebo
Fluoxetine, N=52 20 wks (52 double blind) (Romano et al. 2001)	• Relapse rate on placebo and fluoxetine similar, but placebo relapse rate > fluoxetine rate at 60 mg dose
Paroxetine, N=105 12 wks (24 double blind) (Hollander et al. 2003)	• Relapse rate > in patients who received placebo compared to those who received paroxetine
Sertraline, N=223 52 wks (28 double blind) (Koran et al. 2002)	• Acute OCD exacerbation more common with placebo • Drop out more common with placebo

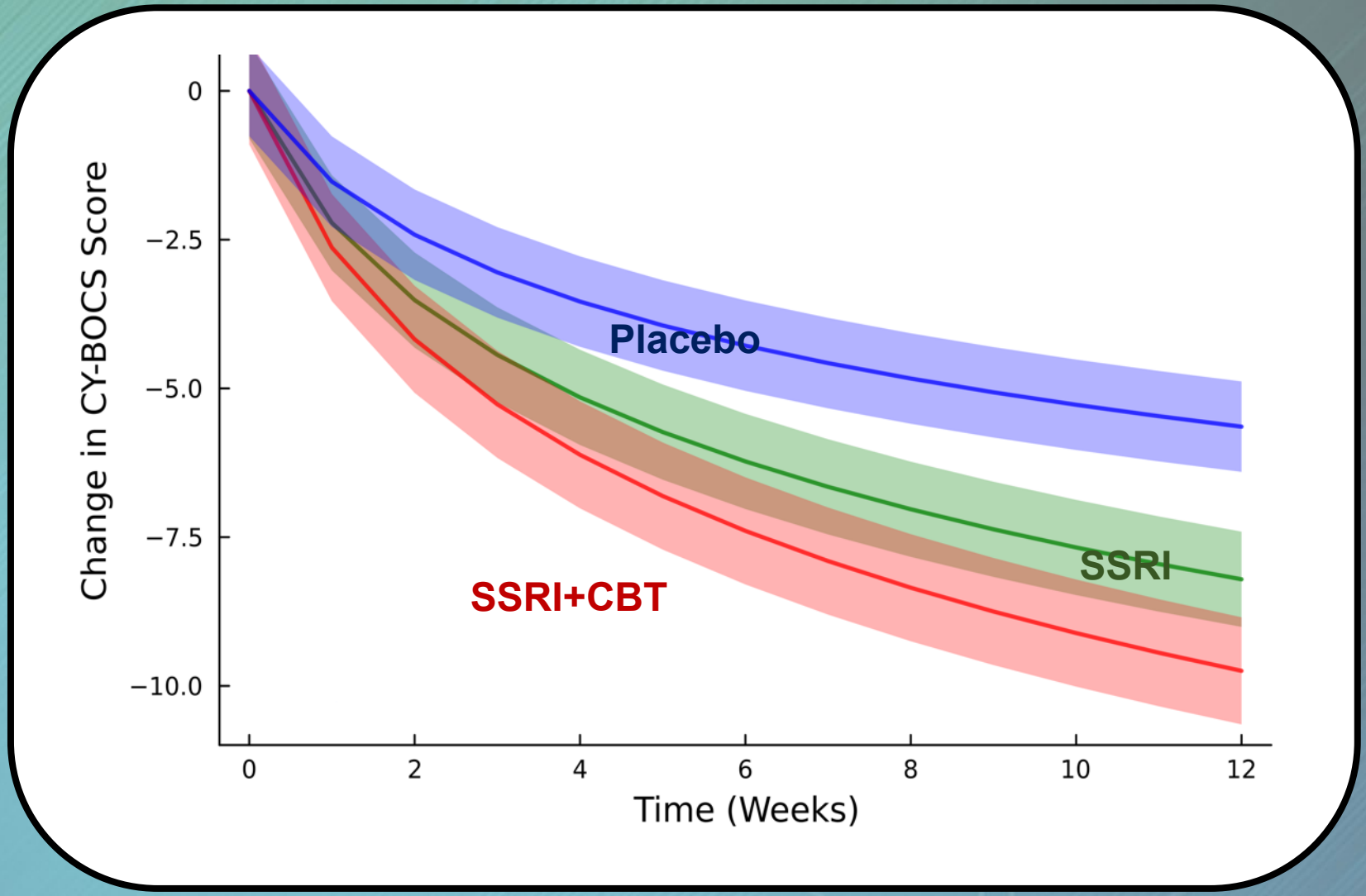
Supra-Maximal SSRI Dosing in Treatment-Resistant OCD



Ninan PT et al. High-dose sertraline strategy for nonresponders to acute treatment for obsessive-compulsive disorder: a multicenter double-blind trial. J Clin Psychiatry 2006;67(1):15-22.

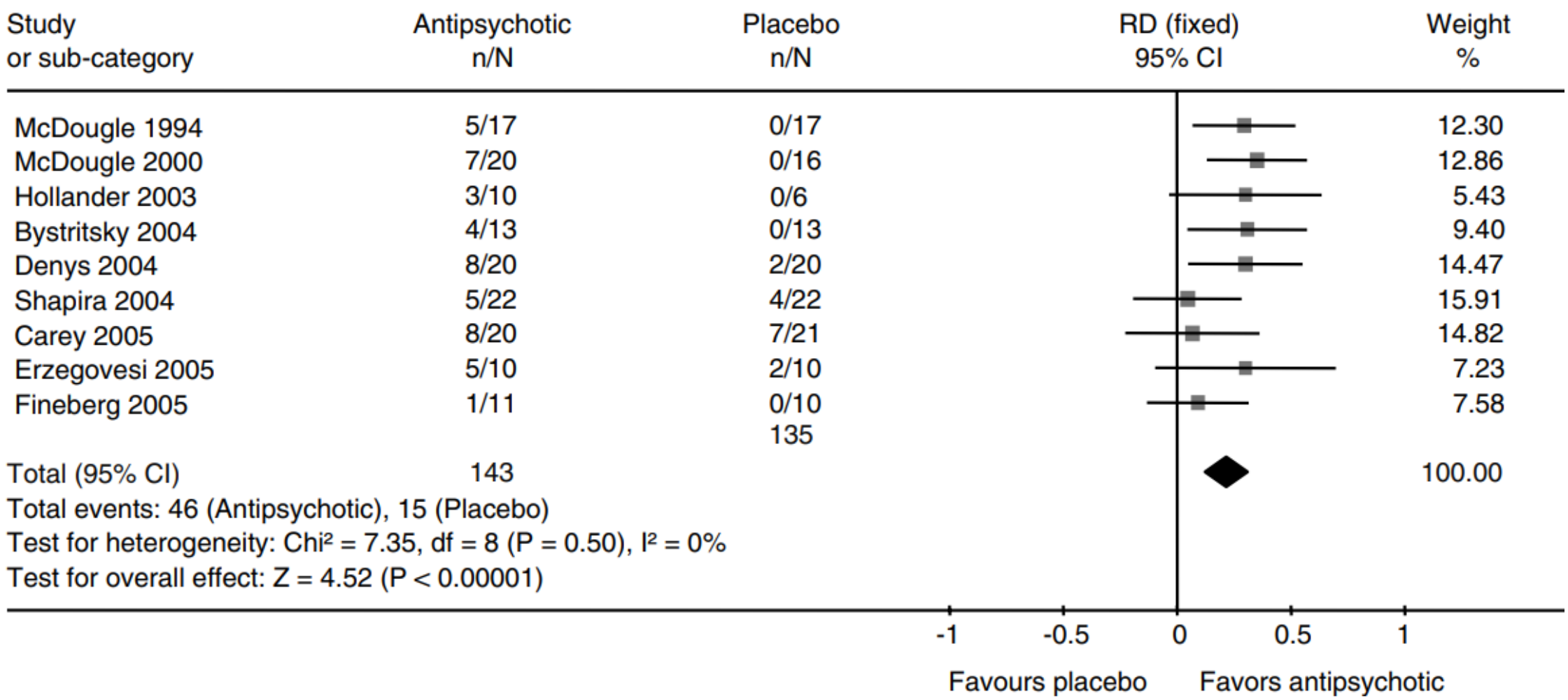
CBT+SSRIs in OCD: Lessons From Child Psychiatry

- Meta-analysis of 1146 patients (12.7±1.3 yrs, 42% female)
- Adding CBT to an SSRI produced numerically (but not statistically significantly) greater improvement over 12 weeks
- Greater improvement was observed in studies with more boys ($p<0.001$), younger patients ($p<0.001$), and in studies with greater baseline symptom severity ($p<0.001$)



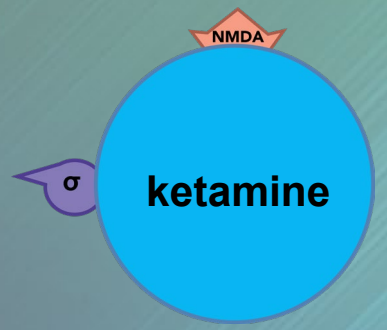
Mendez EM et al. What is the added benefit of combining cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) in youth with obsessive-compulsive disorder? A bayesian hierarchical modeling meta-analysis. J Child Adolesc Psychopharmacol 2023;doi:10.1089. Online ahead of print.

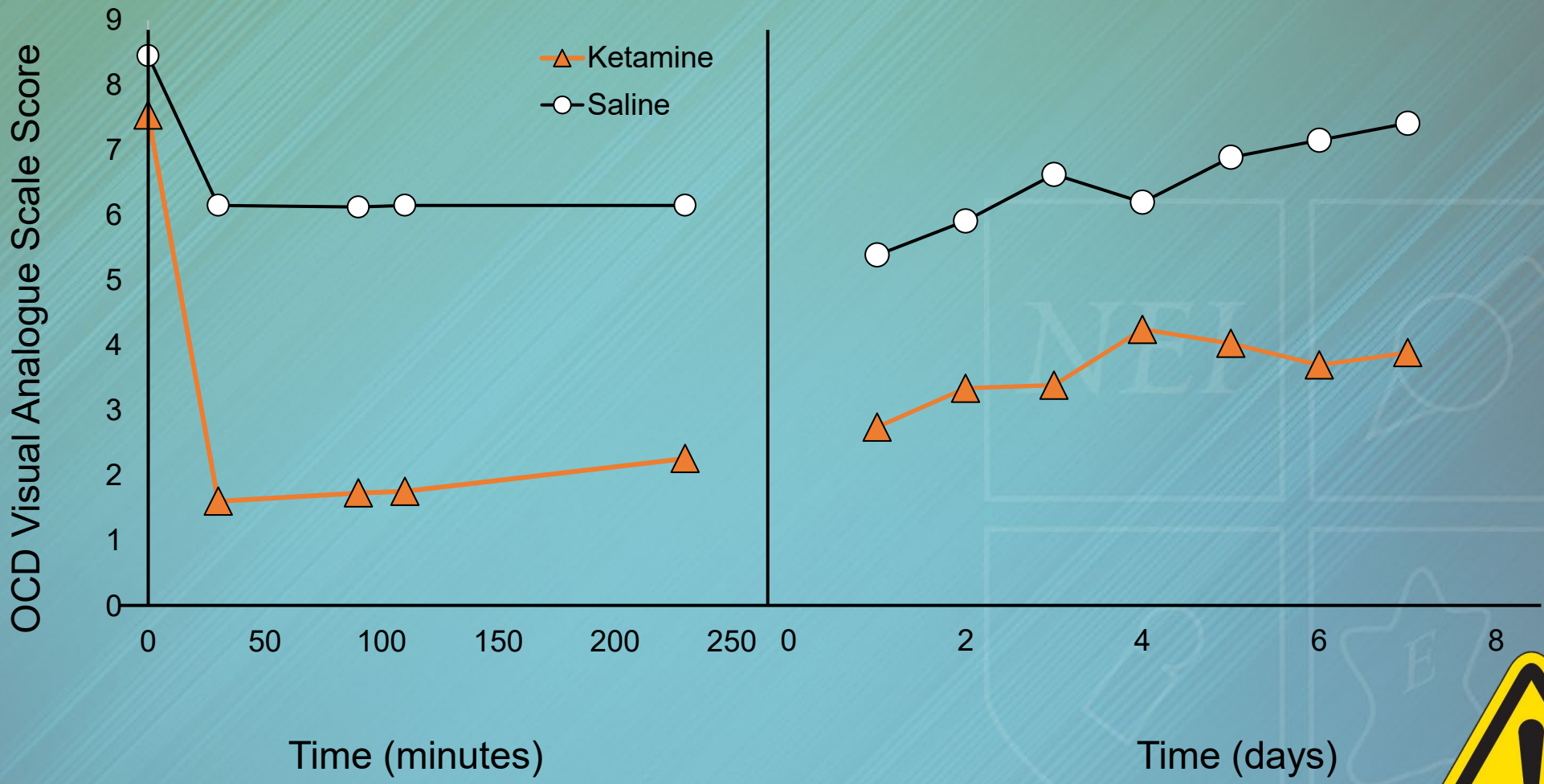
Second-Generation Antipsychotic Augmentation in Treatment-Resistant OCD



Veale D et al. Atypical antipsychotic augmentation in SSRI treatment refractory obsessive-compulsive disorder: a systematic review and meta-analysis. BMC Psychiatry 2014;14:317; Bloch MH et al. Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. Mol Psychiatry 2010;15:850–5.

Ketamine in Adults With OCD



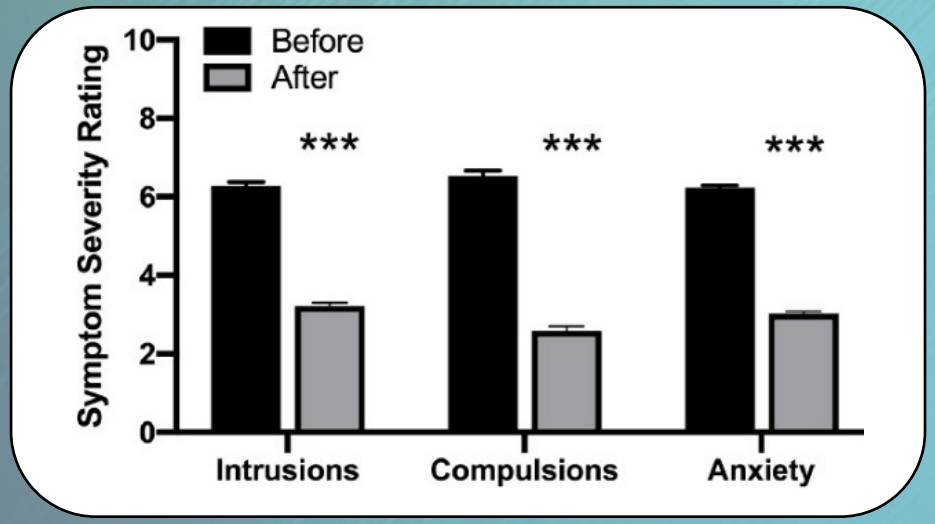


Small N, requires replication

Rodriguez CI et al. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. Neuropsychopharmacology 2013;38(12):2475-83.

Cannabis Effects on OCD Symptoms

- **Acute cannabis use** (Mauzay et al, 2021)
  - ↓ compulsions (60%) and intrusions (49%)
  - ↑ CBD and ↑ dose → more reduction in compulsions
  - Tolerance OCD effect develops over time
  - No long-term benefit
  - Examined inhaled cannabis vs other types of administration

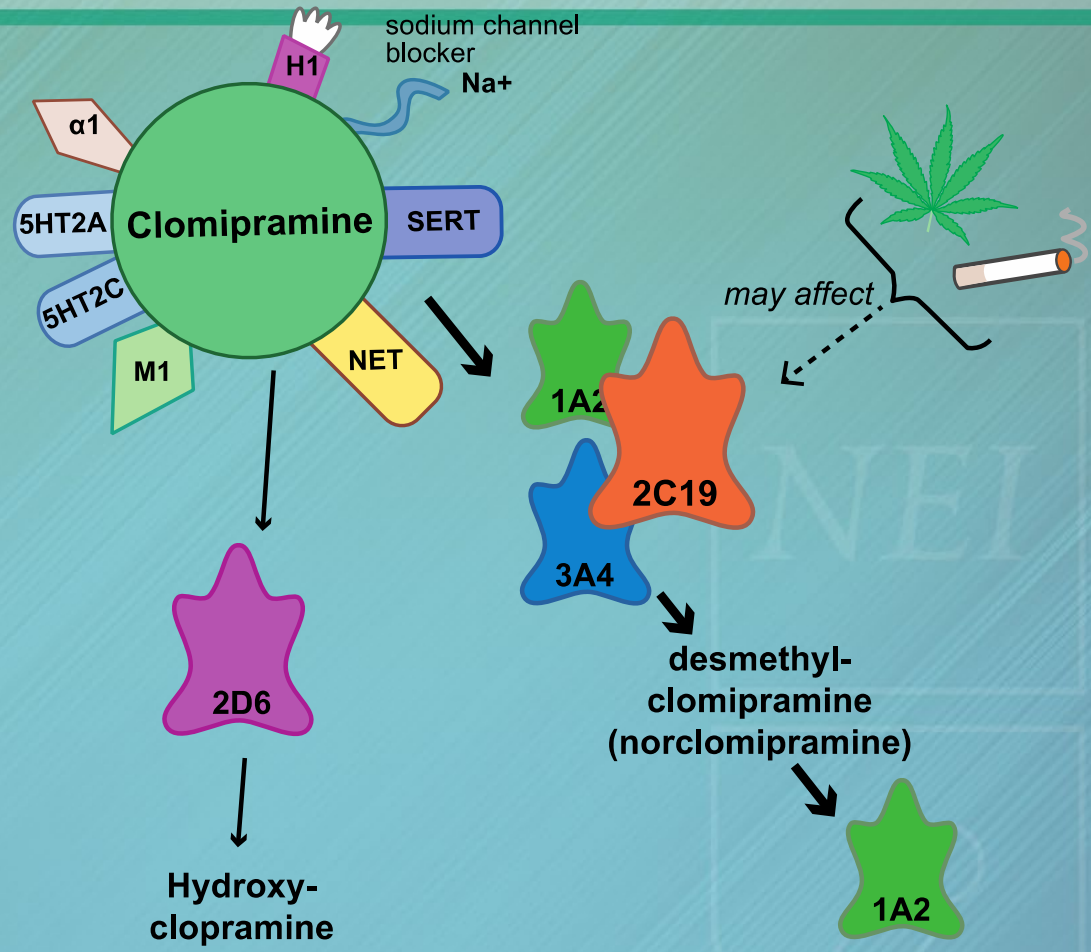


- **Acute CBD/THC use** (Kayser et al, 2020)
  - Smoked cannabis, whether primarily THC or CBD, has little acute impact on OCD sx
- **18-month longitudinal study** (Daumann et al, 2004)
  - ↑ OCD sx in users
  - ↓ in sx in abstinence → "cannabis use may aggravate OCD sx"

Kayser RR et al. The endocannabinoid system: a new treatment target for obsessive compulsive disorder? Cannabis Cannabinoid Res 2019;4(2):77-87; Kayser RR et al. Acute effects of cannabinoids on symptoms of obsessive-compulsive disorder: A human laboratory study. Depress Anxiety 2020;37(8):801-11; Mauzay D, LaFrance EM, Cuttler C. Acute effects of cannabis on symptoms of obsessive-compulsive disorder. J Affect Disord 2021;279:158-63; Daumann J et al. Self-reported psychopathological symptoms in recreational ecstasy (MDMA) users are mainly associated with regular cannabis use: further evidence from a combined cross-sectional/longitudinal investigation. Psychopharmacology (Berl) 2004;173:398-404.

Clomipramine in OCD

- **Potent inhibitor of serotonin reuptake**
  - Active N-demethylated metabolite, norclomipramine, inhibits 5HT and NE reuptake
- Well absorbed
- 1st pass metabolism to norclomipramine → active metabolite
- High protein binding
- Elimination half-lives
  - Clomipramine is 24 h
  - Demethyl-clomipramine (norclomipramine) is 96 h
- Time to steady-state for active moieties ≈ 3 weeks



Ackerman DL, Greenland S. J Clin Psychopharmacol 2002;22(3):309-17;
Stahl SM. Stahl's Prescriber's Guide. 7th ed; 2020.
Strawn JR & Stahl SM. Case Studies in Psychopharmacology: Children and Adolescents; 2023.

Clomipramine Therapeutic Drug Monitoring in OCD

Therapeutic Drug Monitoring

- Peak 1–3 hrs post-dose, >12-h trough level
- Include active metabolite
- Side effects do not correlate with plasma levels and are generally anticholinergic (not serotonergic)

Clomipramine + norclomipramine

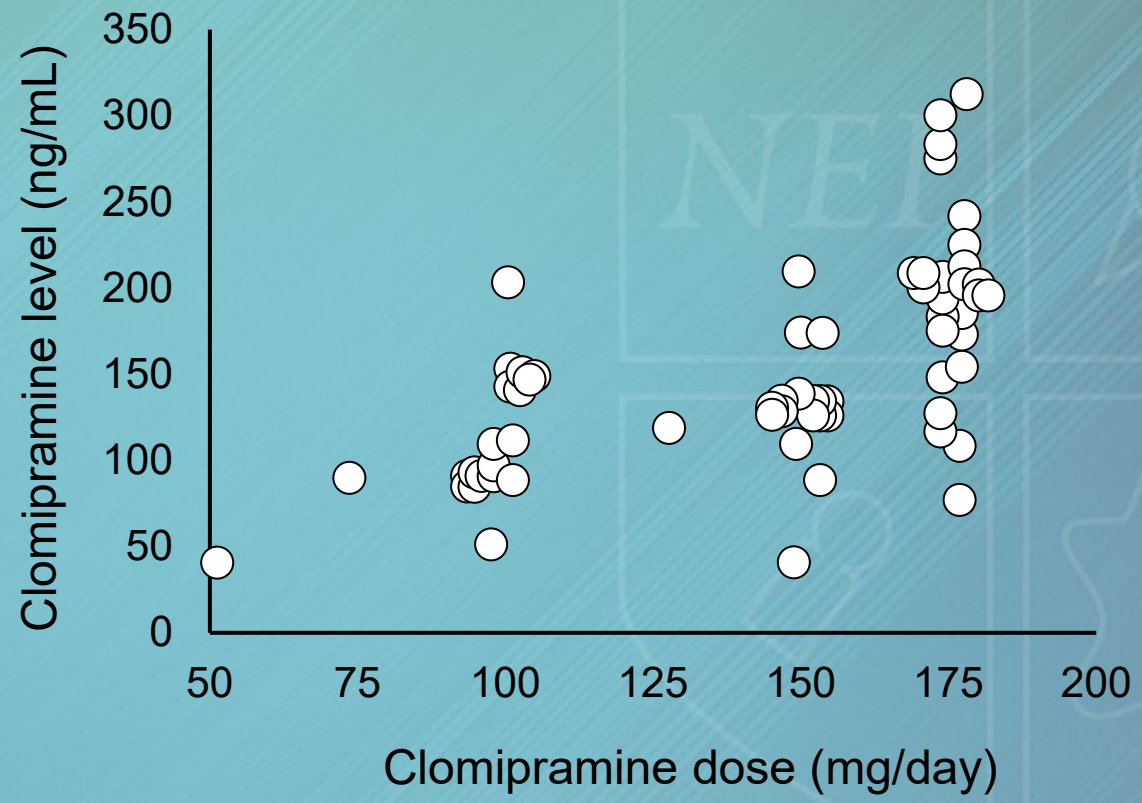
- Toxicity >900 ng/mL
- Clomipramine/metabolite ratio may help to evaluate metabolic state or adherence
  - Higher CMP/norclomipramine ratio → better OCD response
  - Ratio affected by smoking and EtOH consumption

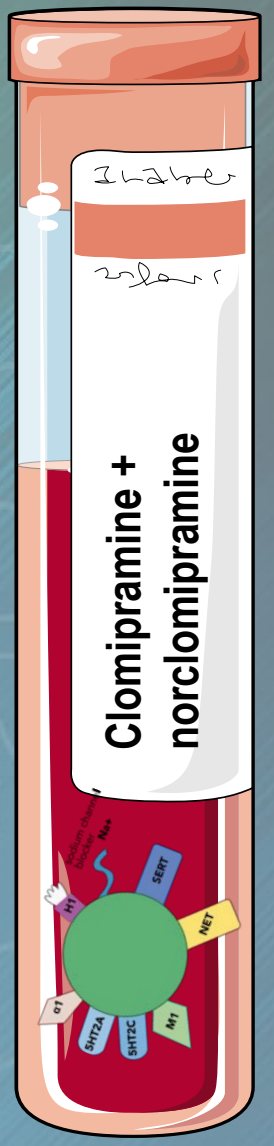
Ordering pearls

- 1.5 mL whole blood, red top
- Order name: “Clomipramine and metabolite levels”

General Monitoring

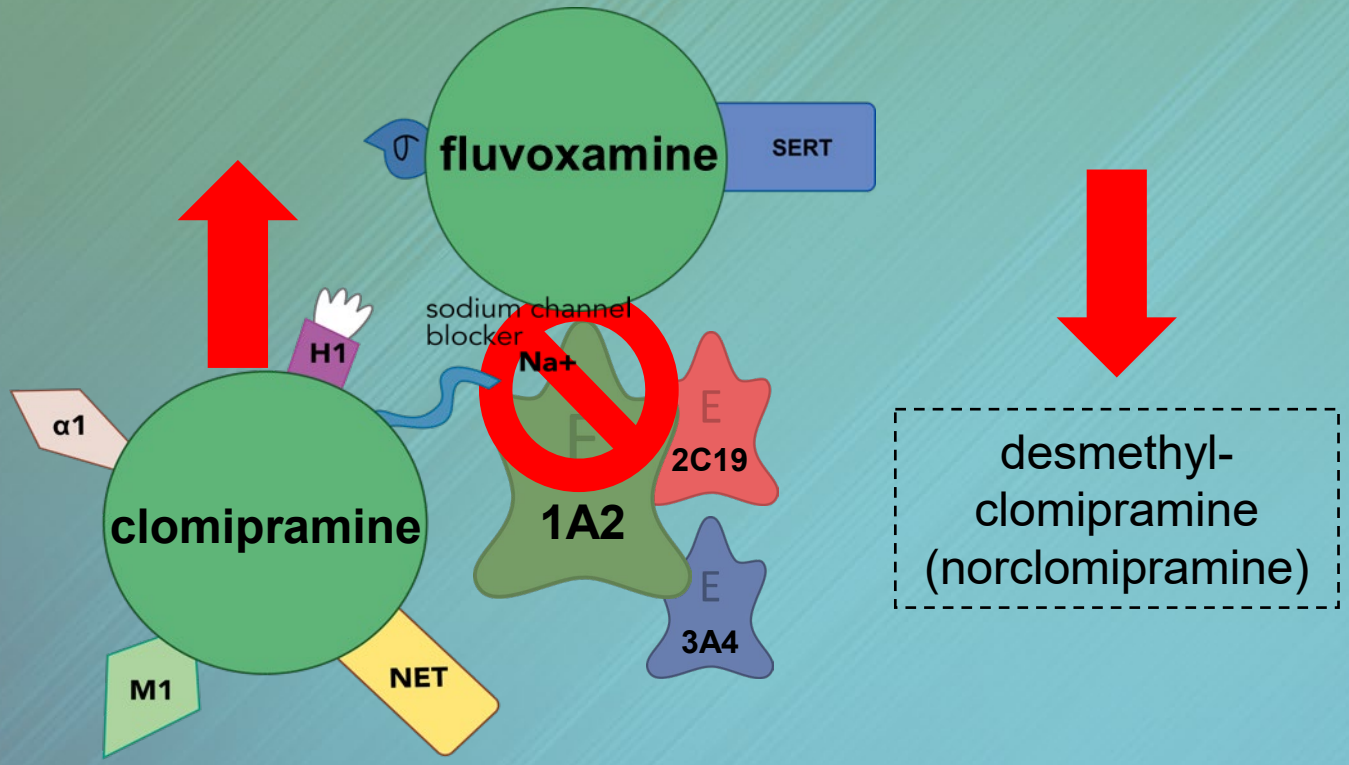
- EKG at baseline and after dose adjustment in youth and patients >50 years of age and in patients with a cardiac history





Vandel B et al. Eur J Clin Pharmacol 1982;22(1):15-20; Burch JE et al. Psychopharmacology (Berl) 1982;77(4):344-7; Mavissakalian MR et al. J Clin Psychopharmacol 1990;10(4):261-8; Dencker SJ, Nagy A. Acta Psychiatr Scand 1979;59(3):326-34; Stern RS et al. Br J Psychiatry 1980;136:161-6.

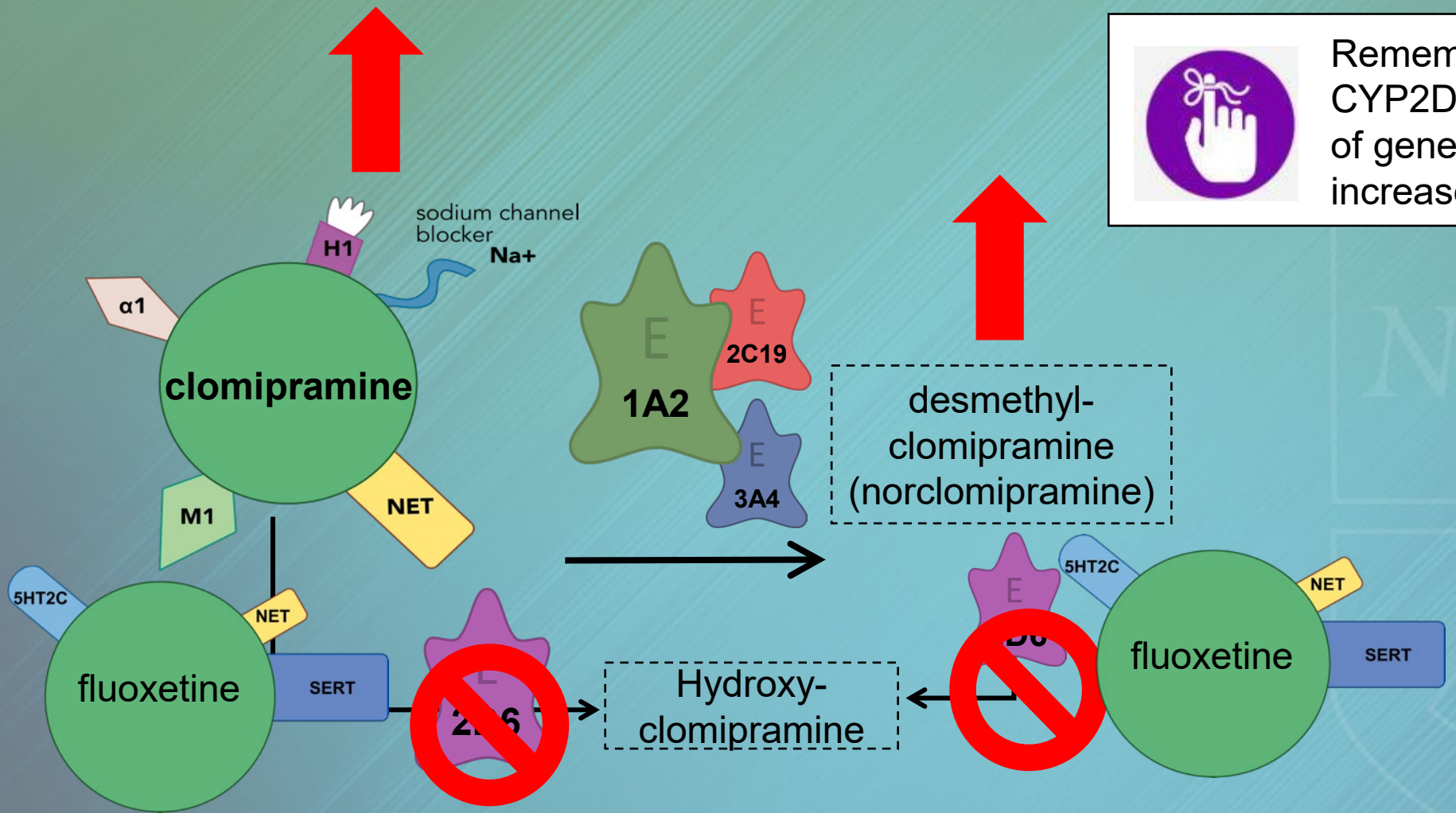
Clomipramine and Fluvoxamine for Refractory OCD



Fluvoxamine is a potent inhibitor of CYP1A2, CYP2C19, and CYP3A4 and a weak 2D6 inhibitor. Thus, the combination of CMI + fluvoxamine improves the ratio of CMI > desmethylclomipramine but increases overall blood levels of CMI + desmethylclomipramine.

Balant-Gorgia AE et al. Clin Pharmacokinet 1991;20(6):447-62;
Whirl-Carrillo M et al. Clin Pharmacol Ther 2012;92(4):414-7;
de Vos A et al. Pharmacogenomics J 2011;11(5):359-67.

Clomipramine and CYP2D6 Inhibitor

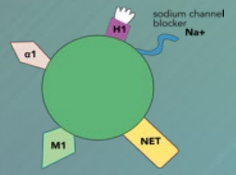


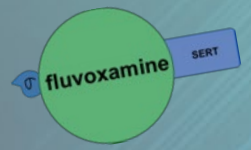
Remember: Patients who have CYP2D6 hypometabolism because of genetic variation may be at increased risk of build-up of DCMI

Balant-Gorgia AE et al. Clin Pharmacokinet 1991;20(6):447-62;
Whirl-Carrillo M et al. Clin Pharmacol Ther 2012;92(4):414-7;
de Vos A et al. Pharmacogenomics J 2011;11(5):359-67.

Clomipramine + Fluvoxamine

1:3



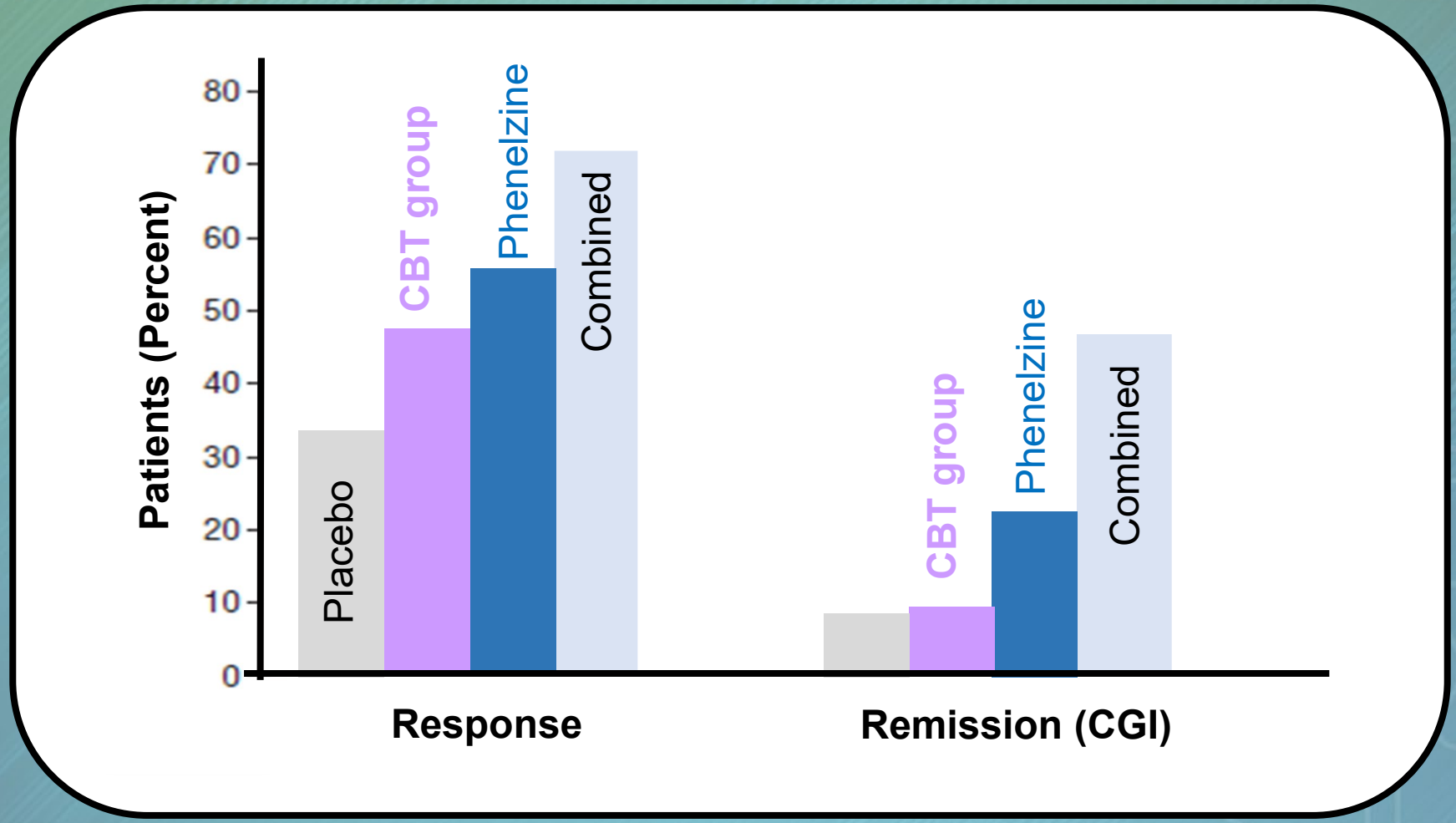


- At steady state, clomipramine to norclomipramine (desmethylclomipramine) is 1:2–3
- Caution with clomipramine + SSRIs other than fluvoxamine, particularly CYP2D6 inhibitors (e.g., fluoxetine and paroxetine)
  - DCMI is metabolized by CYP2D6
  - Clomipramine in combination with fluoxetine or other 2D6 inhibitors leads to increased serum concentration of desmethylclomipramine, an even greater desmethylclomipramine >> CMI ratio, and increased risk for undesirable adrenergic effects
- Fluvoxamine is a potent inhibitor of CYP1A2, CYP2C19, and CYP3A4 and a weak 2D6 inhibitor
  - Clomipramine +fluvoxamine ↑ CMI > desmethylclomipramine, and ↑ total clomipramine + desmethylclomipramine
- Recommend an adequate trial of fluvoxamine; if fluvoxamine is ineffective, may consider slowly adding clomipramine until the clomipramine:desmethylclomipramine ratio is >3 and still within the therapeutic range of clomipramine + desmethylclomipramine ≤ 450 ng/mL

Fung R et al. J Can Acad Child Adolesc Psychiatry 2022;30(3):150-5;
Figueroa Y et al. J Child Adolesc Psychopharmacol 1998;8(1):61-7.

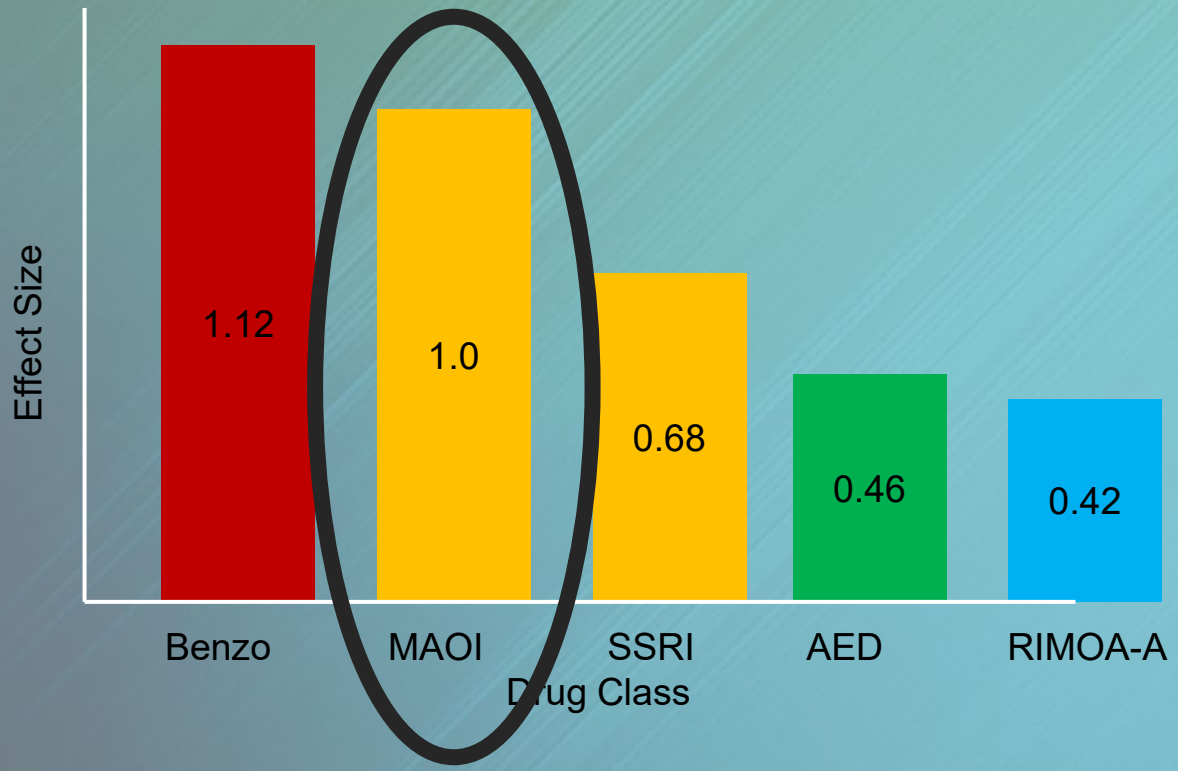
MAO Inhibitors

Phenelzine, CBT, or Combination Therapy in Social Anxiety Disorder



Blanco C et al. A placebo-controlled trial of phenelzine, cognitive behavioral group therapy, and their combination for social anxiety disorder. Arch Gen Psychiatry 2010;67(3):286-95.

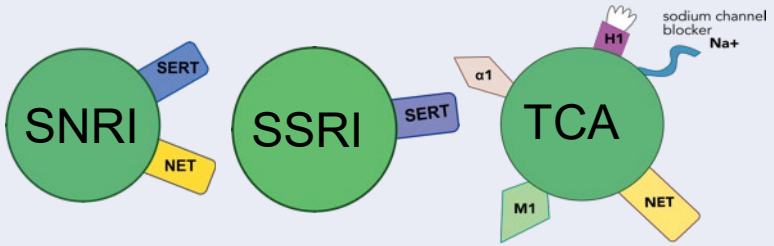
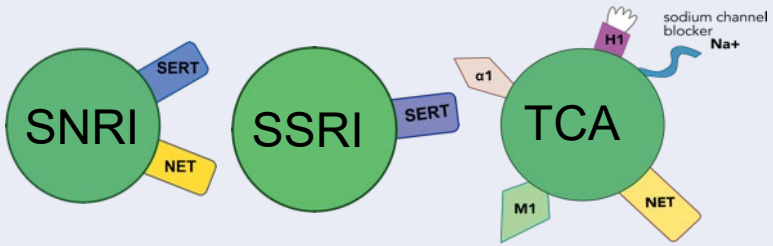
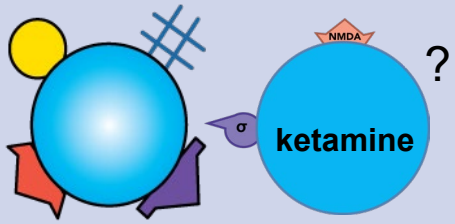
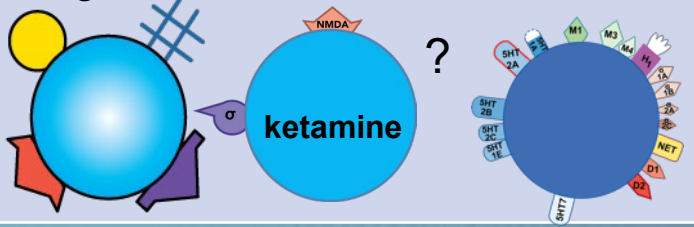
How Do MAOIs Stack Up?



	Initial Dose (mg/d)	Titration (mg/d)	Initial Target Dose (mg/d)	Maximum Daily Dose (mg/d)
Isocarboxazid	10–20	None	30–60	30–60
Moclobemide	150	None	300	600
Phenelzine	15–45	15 every 2–3 weeks	15–60	90
Selegiline transdermal	6	3 no less than every 2 weeks	6	6–12
Tranylcypromine	10–30	10 every 2–3 weeks	30–40	60

Thase ME. J Clin Psychiatry 2012;73(suppl 1):10-6.

Summary: Treatment of OCD and Social Anxiety Disorder

	Social Anxiety Disorder	OCD
Evaluating non-response	Consider unrecognized substance use, OTC medications, context-related anxiety, comorbidity (e.g., personality disorders, ADHD, trauma)	Consider unrecognized substance use, OTC medications, context-related anxiety, comorbidity (e.g., personality disorders, ADHD, trauma)
Most evidence-based psychotherapy		
Role of benzodiazepines		
Evidence-based psychotherapy	Yes, generally incorporates exposure	Yes, and…must incorporate exposure
Additional interventions (not discussed)	Pregabalin, quetiapine, and gabapentin 	Pregabalin, quetiapine, and gabapentin lamotrigine, other mood stabilizers 

Not discussed, generally small N, require replication

Conclusions

- OCD and social anxiety disorder have overlapping risk factors and neurobiology

Common Features	
Clinical features	Avoidance and distress with exposure
Cognitive features	Inhibitory learning deficits
Psychotherapy	CBT with emphasis on exposure

- Serotonergic agents are first-line psychopharmacologic interventions for both social anxiety disorder and OCD
  - OCD: SSRIs, SNRIs, TCAs
  - Social anxiety disorder: SSRIs, SNRIs, TCAs, and MAOIs
  - Dose/exposure is important—consider sources of variation (e.g., pharmacogenetics)
- Benzodiazepines
  - OCD: generally, no
  - Social anxiety disorder: may have role
- Clomipramine
  - Peak 1–3 hrs post-dose—need >12-h trough level
  - Include active metabolite in testing
  - Side effects do not correlate well with plasma levels and are generally anticholinergic (not serotonergic)

Posttest 1

Augmentation of clomipramine with fluvoxamine, a potent inhibitor of CYP1A2, will:

1. Increase the ratio of clomipramine to norclomipramine
2. Decrease the ratio of clomipramine to norclomipramine
3. Decrease total clomipramine and norclomipramine concentrations
4. Have no effect on clomipramine or norclomipramine concentrations

Posttest 2

A 50-year-old preschool teacher with social anxiety disorder begins treatment with a benzodiazepine for her severe anxiety. Which of the following is associated with the fastest response?

1. A dose >12 mg/day in lorazepam equivalents
2. A dose >6 mg/day in lorazepam equivalents
3. A dose between 3 and 6 mg/day in lorazepam equivalents
4. A dose <3 mg/day in lorazepam equivalents

Posttest 3

In both anxiety disorders and OCD, treatment response:

1. Is better with higher doses
2. Is unrelated to dose
3. Is better with lower doses