

Psychopharmacology of OCD

Lisa Zakhary, MD PhD

Division Chief, MGB Outpatient Psychiatry
Medical Director, MGH Center for OCD and Related Disorders
Medical Director, MGH General Adult Psychiatry
Assistant Professor, Harvard Medical School

10/18/2026

Disclosures

Neither I nor my spouse has a relevant financial relationship with
a commercial interest to disclose



Agenda

1	First-Line Treatments
2	Treatment-Resistant OCD
3	Special Populations
4	Emerging Treatments

Commonly Missed OCD

- **Self-harm** OCD, intrusive *egodystonic* thoughts about harming oneself
- **Somatic** OCD, hyperawareness of bodily sensations
- **Existential** OCD, obsession with the meaning of life, reality, existence
- **Relationship** OCD, constant doubt about “rightness” of relationship
- **Sexual orientation** OCD, persistent doubts about sexual orientation
- **Gender identity** OCD, persistent doubts about gender identity
- **False memory** OCD, doubts about ability to accurately recall past events



First-Line Treatments

SSRIs and CBT



- **All SSRIs** and **clomipramine** have demonstrated **efficacy** in OCD
 - Fluvoxamine, 6 RCTs
 - Fluoxetine, 3 RCTs
 - Sertraline, 6 RCTs
 - Escitalopram, 2 RCTs
 - Citalopram, 1 RCT
 - Paroxetine, 4 RCTs
 - Clomipramine (non-selective SRI), 4 RCTs
- **CBT** with exposure and response prevention (**ERP**) has also shown significant benefit and should be a **top priority**
 - Meta-analysis of 16 RCTs of CBT found **large ES** (1.39)
 - Twice weekly **CBT more effective than clomipramine**
 - Reduces SSRI dosing needs and prevents OCD relapses
- **70% will respond** to CBT and/or an SSRI



Choosing an Initial Treatment

CBT alone

- Mild OCD
- Pt refuses medications

CBT + SSRI

- Moderate/severe OCD
- Too distressed to engage in CBT
- Other major comorbidities such as MDD/GAD

SSRI alone

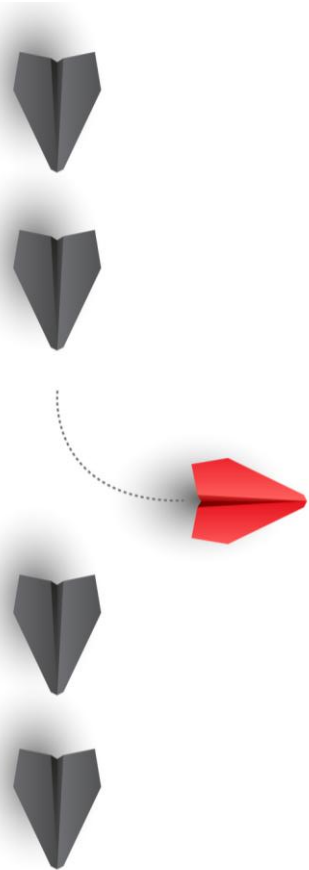
- No access to CBT
- Prior history of failed CBT
- Pt declines CBT

Which SSRI is Best?

SSRIs thought to be equally effective but due to **high dose** requirements in OCD, SSRIs with **lower side effect profiles typically trialed first**

	Drug Name	Target Dose	Advantages	Disadvantages
SSRI	Escitalopram (Lexapro)	20 mg/d	well-tolerated	
	Sertraline (Zoloft)	200 mg/d	well-tolerated	
	Fluoxetine (Prozac)	80 mg/d	well-tolerated, long half-life, activating	drug interactions
	Citalopram (Celexa)	40 mg/d	well-tolerated	potential $\uparrow$ QTc, Reduced max dose may not be sufficient in OCD
	Paroxetine (Paxil)	60 mg/d		sedation, weight gain, short half-life
	Fluvoxamine (Luvox)	300 mg/d		sedation, weight gain
SRI	Clomipramine (Anafranil)	250 mg/d		Sedation, constipation, urinary retention, low BP, $\uparrow$ QTc seizures, drug interactions, weight gain, considered second-line

SSRI Trial in OCD: Many Differences



- **High doses** (max or >max) often required
- **Response delayed** (4-6 wks for initial effect, 10-12 wks for full effect)
- Trial length: **12 wks**
- **Rapid titration** recommended
- Duration of treatment
 - **1-2 years** recommended
 - Consider dose reduction after 1-2 years if mostly asymptomatic
 - **Taper no more than 10%–25% q1–2mo** to prevent relapse



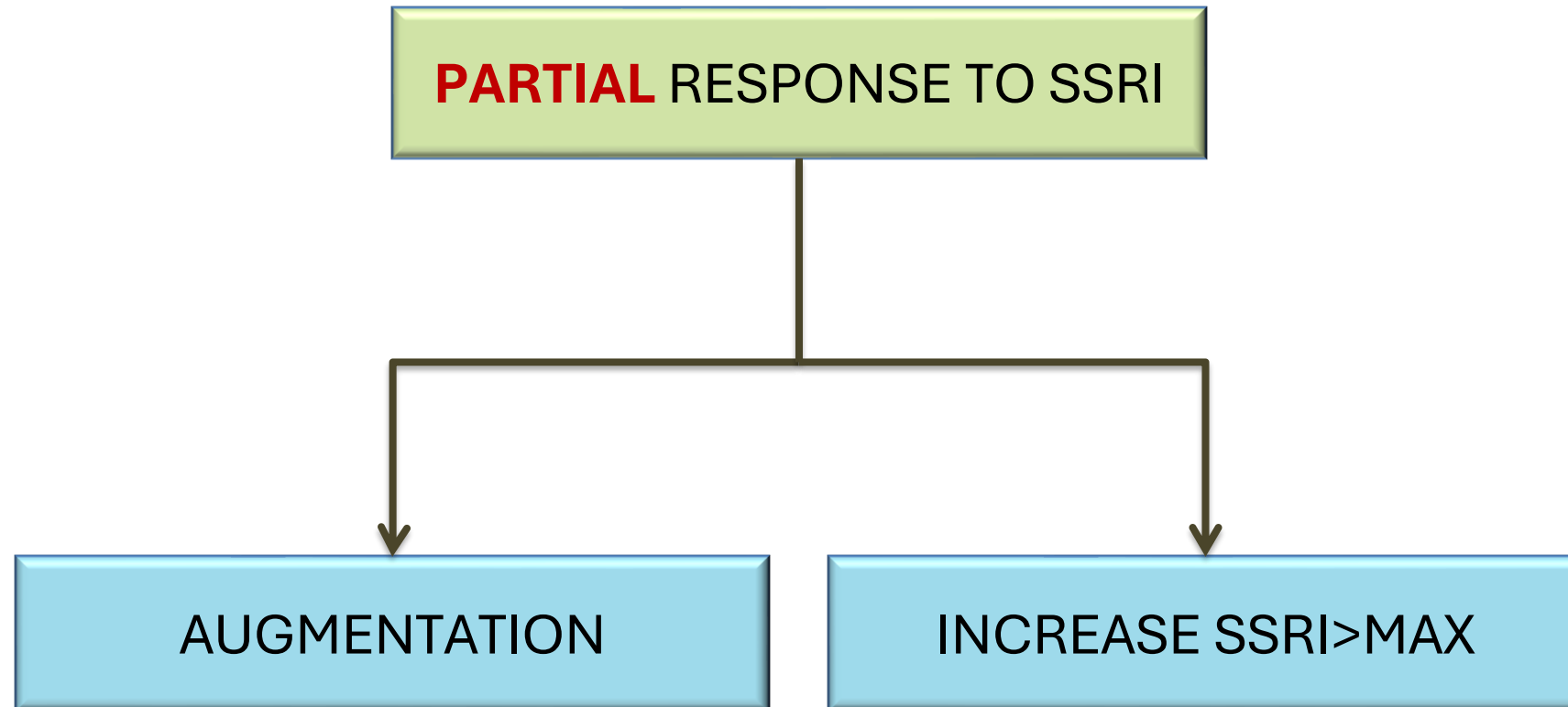
Treatment-Resistant OCD (TR-OCD)

Strategies

- **Intensify CBT**
 - Intensive outpatient programs or residential treatment
 - e.g., McLean OCD Institute, Rogers
- **Medication** options
 - Augmentation (off-label)
 - Higher than max SSRI dosing
 - Clomipramine or another SSRI alternative (off-label)
- **Transcranial magnetic stimulation** (TMS)
- **Psychosurgery** (cingulotomy, capsulotomy, deep brain stimulation)

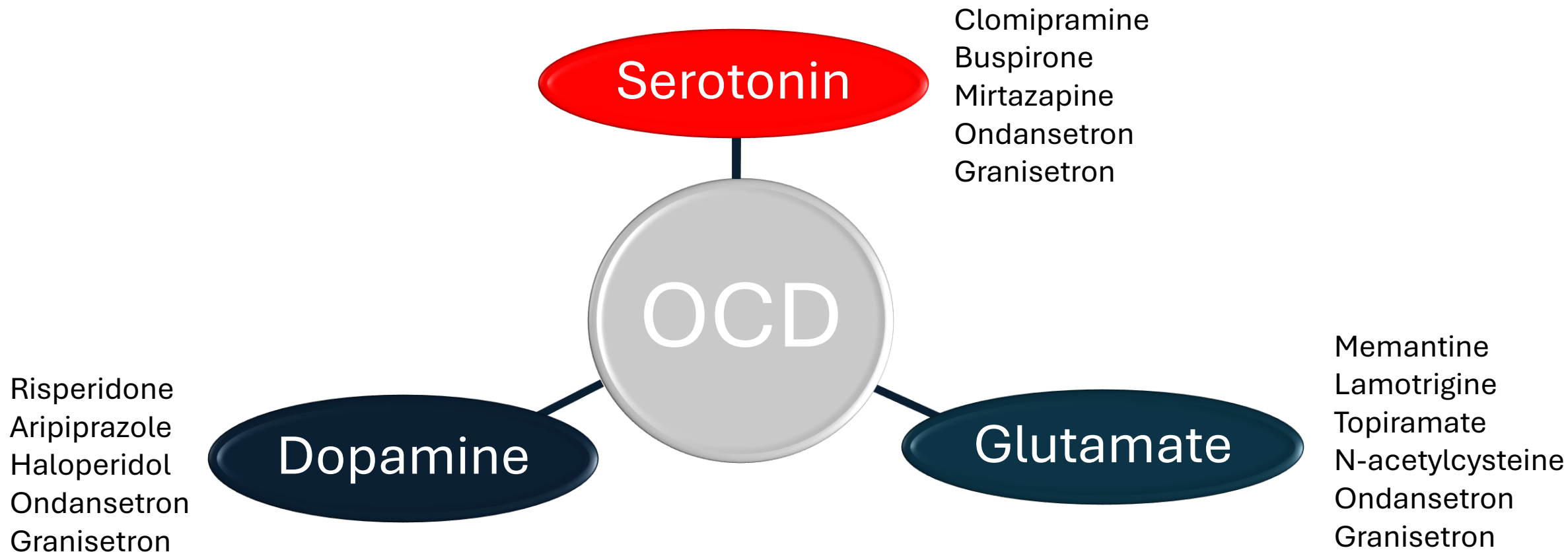


Approach to a Partially Effective SSRI



Augmentation and Relevant Targets

All off-label except clomipramine



First- and Second-Line Add-Ons

2025 CANMAT/ICOCS Clinical Practice Guidelines

First-line

- **Risperidone** (~1-2 mg/d): most used augmenting agent
 - 3 positive RCTs, meta-analysis (multiple): risperidone >>> placebo
 - **Aripiprazole** (~10-15 mg/d): 2 positive RCTs, nice alternative to risperidone given lower metabolic risk
 - **Haloperidol** (~2-6 mg/d): 2 positive RCTs, useful in pts with severe tics
 - Quetiapine and olanzapine have shown mixed results so not as commonly used and not considered first-line

Second-line

- **Memantine** (10mg PO BID)
 - 2/3 DBRCTs positive, meta-analysis showing 3.6x greater odds of response
 - Start 5mg PO QHS x7d → 5mg PO BID x7d → 10mg PO BID, 6wk trial
 - Good option for comorbid skin picking and hair pulling
- **Lamotrigine** (~100 mg/d)
 - 2 positive RCTs, useful for comorbid bipolar disorder

Source: Reviewed in Arumugham. *Expert Rev Neurother*. 2013; Veale. *BMC Psychiatry*. 2014; Bloch. *Mol Psychiatry*. 2006; Dold. *Int J Neuropsychopharmacol*. 2013; Stewart. *J Clin Psychopharmacol*. 2010; Ghaleiha. *J Psychiatr Res*. 2013; Haghighi. *Psychopharmacology* 2013; Modarresi A, *Psychiatry Res*. 2019. Bruno. *J Psychopharmacol*. 2012; Khalkhali. *Iran J Psychiatry*. 2016

Third-Line Add-Ons

- **Clomipramine** (~50-75 mg/d): several positive open-label studies and 1 positive RCT
 - SSRIs can unpredictably increase clomipramine levels
 - Check baseline QTc, start low dose (25 mg PO QHS) and then monitor QTc/clomipramine level while titrating
- **Mirtazapine** (15-40 mg/d): 2 positive RCTs
 - beneficial for comorbid depression/GAD
- **Ondansetron** (.5mg PO BID to 4 mg PO BID): 3 positive RCTs
 - Granisetron, 1mg PO BID, positive RCT, well-tolerated
 - monitor QTc for both agents PRN
- **Topiramate** (~180 mg/d): 2 positive RCTs
 - useful for comorbid bipolar disorder, weight gain, HAs, skin picking and hair pulling

Source: Mowla. *CNS Spectr.* 2010; Afshar. *J Clin Psychopharmacol.* 2012; Paydary. *J Clin Pharm Ther.* 2016; Costa. *J Clin Psychiatry.* 2017; Pallanti. *J Clin Psychiatry* 2004; 1992; Heidari. *Int Clin Psychopharmacol.* 2014; Sharafkhah. *Int Clin Psychopharmacol.* 2019; Ghobadian. *BMC Pharmacol Toxicol.* 2022; Soltani. *Hum Psychopharmacol.* 2010; Pallanti *Eur Neuropsychopharmacol.* 2014; Sepehrmanesh. *Archives of Neuroscience.* 2020; Tripathi. *Indian Journal of Health Sciences and Biomedical Research KLEU.* 2021; Pallanti. *Eur Psychiatry* 1999; Ravizza. *Psychopharmacol Bull* 1996; Diniz. *J Clin Psychopharmacol* 2011; Koran. *J Clin Psychiatry.* 2005

Add-ons with Limited Evidence

Drug Name	Mechanism	Dose	Evidence	Notes
Pindolol	Serotonergic	2.5mg PO TID	Mixed: 1/2 RCTs positive	
Buspirone	Serotonergic	30mg PO BID	Mixed: positive OLS but 3 small RCTs negative	Helpful for comorbid depression, anxiety & sexual AEs
N-acetylcysteine (NAC)	Glutamatergic	1200mg PO BID, up to 3000mg TDD	Mixed: 2/4 RCTs positive	Good option for comorbid skin picking/hair pulling , start 600mg PO BID x 2wks → 1200mg PO BID, 6 wk trial, www.swansonvitamins.com/q?kw=NAC
Riluzole	Glutamatergic	50mg PO BID	Mixed: 1/2 RCTs positive	Monitor ALT, riluzole failed phase 3 trial
Pregabalin	Glutamatergic	75-225 mg/d	1 positive RCT	Helpful for comorbid anxiety
Amantadine	Dopaminergic, glutamatergic	100 mg/d	1 positive RCT	More AEs than memantine (insomnia, agitation, psychosis, livedo reticularis) and lowers seizure threshold
Minocycline	Anti-inflammatory, glutamatergic	100mg PO BID	1 positive RCT	Hyperpigmentation
Celecoxib	Anti-inflammatory	200-400 mg PO BID	4 small positive RCTs	Useful with comorbid inflammatory disorders (e.g., arthritis); ↑ GI bleed, CV, and renal risk

Source: Fallon. *Arch Gen Psychiatry*. 1998; Dannon. *Eur Neuropsychopharmacol*. 2000; Emamzadehfard. *Psychiatry Clin Neurosci*. 2016; Pittenger. *J Clin Psychiatry*. 2015; Naderi. *Psychiatry Clin Neurosci*. 2019; Esalatmanesh. *Psychiatry Clin Neurosci*. 2016; Shahini. *Basic Clin Neurosci*. 202; Ahmadpanah. *Psychiatr Res*. 2017; Mowla. *CNS Spectr*. 2019; Sarris. *CNS Drugs*. 2015; Grady. *Am J Psychiatry*. 1993; Markovitz. *Am J Psychiatry*. 1990; Jenike. *J Clin Psychiatry*. 1991; McDougle. *Am J Psychiatry*. 1993; Pigott. *J Clin Psychopharmacol*. 1992

Benzodiazepines



- **Not recommended** for OCD
 - Clonazepam: 2 RCTs negative
 - Alprazolam: negative OLS
 - May interfere with exposure response prevention therapy
 - May still be appropriate for comorbid GAD or panic disorder
- Other anxiolytics:
 - **Pregabalin:** 1 positive RCT, 75-225 mg/d
 - **Gabapentin:** OLS (600-900 mg/d) hastened SSRI response in OCD but subsequent DBRCT (100-300 mg/d) negative
 - **Hydroxyzine:** no published studies in OCD

Source: Onder. *Eur Arch Psychiatry Clin Neurosci.* 2008; Hollander. *World J Biol Psychiatry.* 2003; Crockett. *Ann Clin Psychiatry.* 2004; Stein. *Hum Psychopharmacol Clin Exp.* 1992; Farnia. *J Psychiatr Res.* 2018

Bupropion



- Does **not improve core OCD**
- **Often used with SSRIs in OCD** to address comorbid depression
- May improve the low energy and poor focus often experienced in OCD
- Can also improve sexual AEs

Above Max SSRI Dosing in OCD

SSRI	Drug	FDA Max Dose	Published above-max dosing	Dosing commonly used in practice	Notes
	Escitalopram	20 mg/d	60 mg/d	30 mg/d	Check EKG
	Sertraline	200 mg/d	400 mg/d	300 mg/d	
	Fluoxetine	80 mg/d	120 mg/d	120 mg/d	
	Paroxetine	60 mg/d	100 mg/d	80 mg/d	
	Fluvoxamine	300 mg/d	400 mg/d	400 mg/d	
	Citalopram	40 mg/d	120 mg/d	60-80 mg/d	High dosing controversial given QTc prolongation risk, consider with EKG, h/o failed medication trials, pt consent
	Clomipramine	250 mg/d	N/A	N/A	Above max dosing not recommended due to seizure risk

Source: Koran. *Am J Psychiatry*. 2007; Ninan. *J Clin Psychiatry*. 2006; Dougherty. *Int Clin Psychopharmacol*. 2009

Managing SSRI Adverse Effects

- **SSRI AEs** are common but **manageable**
- **Hyperhidrosis**
 - Aluminum chloride antiperspirant (e.g., Drysol)
 - Glycopyrrolate: start 1 mg PO BID, usual range 2-8 mg/d (dry mouth)
 - Benztropine: 0.5-1 mg/d (dry mouth)
 - Cyproheptadine: 4 mg PO QHS→ up to 4 mg PO BID (sedation)
 - Terazosin: 1-4 mg PO QHS (start 1mg given risk of HoTN, syncope)
 - Mirtazapine: start 15 mg PO QHS



Sexual AEs

- **Wait**, sexual AEs can take 1-2 mo to improve
- Add **bupropion** (off-label)
 - 2 RCTs positive, dose-dependent, 150 mg/d ineffective but 150 mg BID beneficial
 - Bupropion should not be combined with clomipramine given seizure risk
- Add **maca root** (off-label), OTC
 - 2 RCTs positive (men, women)
 - 500 mg PO BID x7d, then 1000 mg PO BID x7d, then 1500 mg PO BID
 - Consider checking TSH ~1 mo after starting
- Add **buspirone** (off-label)
 - RCT positive (~48 mg TDD)
- For ED, add **sildenafil** or equivalent
- **Reduce SSRI** dose or **switch** antidepressants



Source: DeBattista. *J Clin Psychiatry*. 2005; Masand. *Am J Psychiatry*. 2001; Safarinejad. *J Psychopharmacol*. 2011; Landén. *J Clin Psychopharmacol*. 1999; Dording. *CNS Neurosci Ther*. 2008; Dording. *Based Complement Alternat Med*. 2015

Alternative Monotherapies

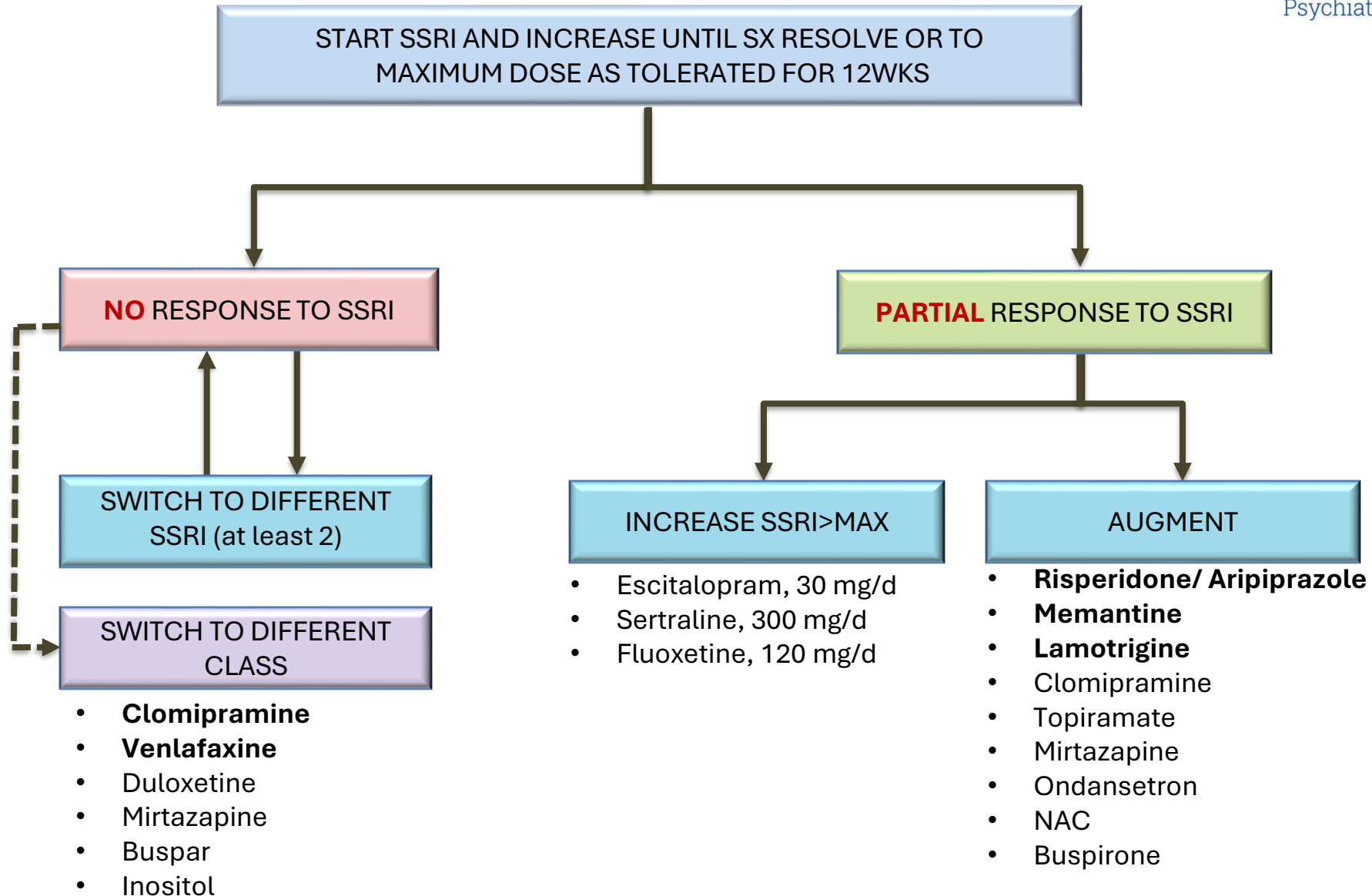
- **Clomipramine**, ~100-250 mg/d, 4 beneficial RCTs, very effective but second-line due to AEs
- **Venlafaxine**, ~225-300mg/d
 - As effective as clomipramine and paroxetine in comparator RCTs
 - No sig effect in 1 small placebo-controlled RCT, but trial too short (8 wks)
 - Larger placebo-controlled RCTs needed but given comparator RCTs, venlafaxine often used
 - **Duloxetine**, not well-studied (beneficial in OLS at ~120 mg/d), but sometimes used given venlafaxine data

Source: Rauch. *J Clin Psychopharmacol.* 1996; Sevincok. *Aust N Z J Psychiatry.* 2002; Hollander. *J Clin Psychiatry.* 2003; Albert. *J Clin Psychiatry.* 2002; Denys. *J Clin Psychopharmacol.* 2003; Yaryura-Tobias. *Arch Gen Psychiatry.* 1996; Dell'osso. *J Psychopharmacol.* 2008; Dougherty. *Int J Neuropsychopharmacol.* 2015; Koran. *J Clin Psychiatry.* 2005; Grady. *Am J Psychiatry.* 1993; Pato. *Am J Psychiatry.* 1991

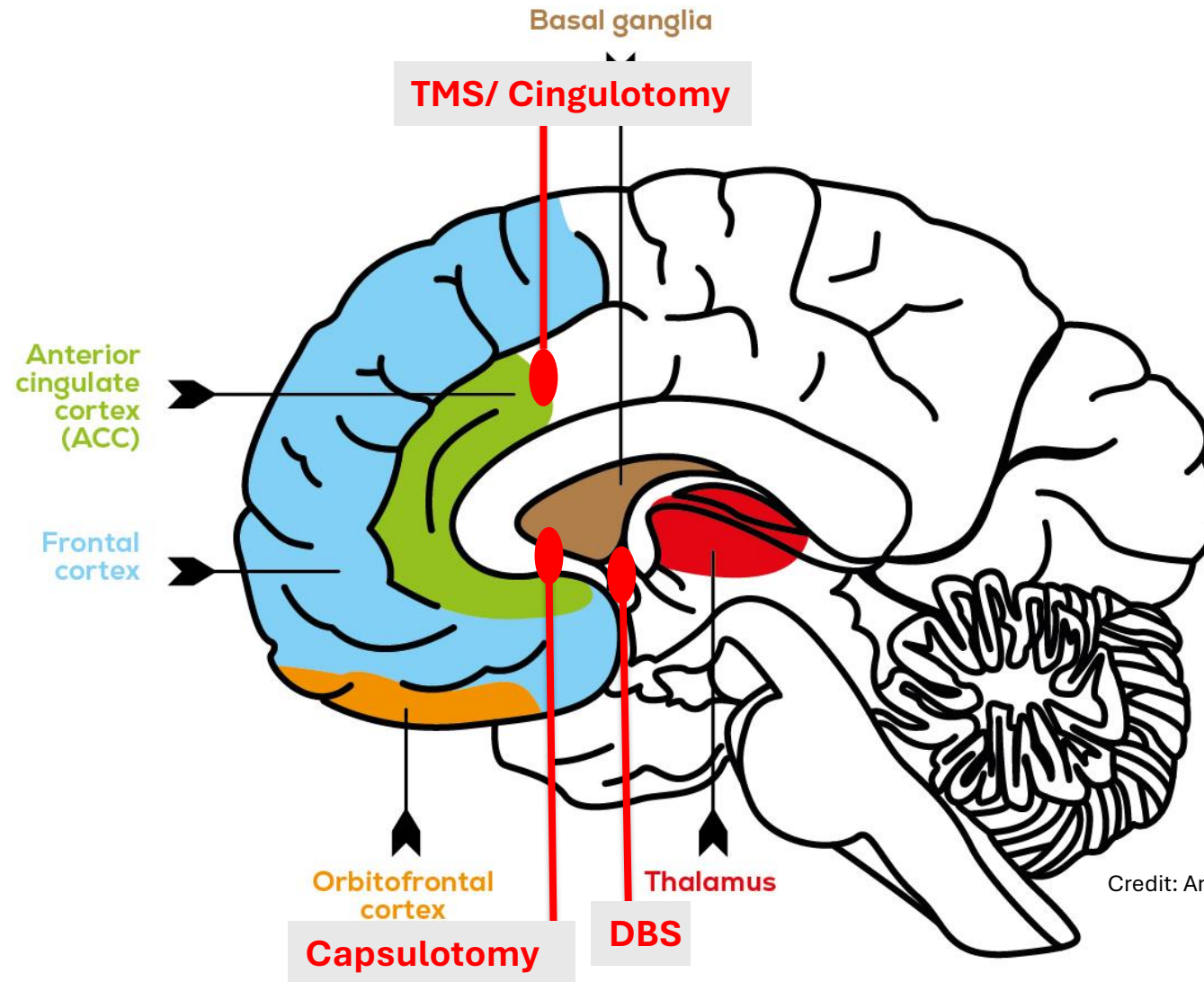
Monotherapies with limited evidence

Drug Name	Dose	Evidence
Inositol	6 g PO TID	Small positive RCT (n=13) as monotherapy; no benefit when combined with SSRI
NAC		Not studied
Mirtazapine	30–60 mg/d	Limited evidence: small OLS and discontinuation study suggest benefit
Buspirone	60 mg/d	Mixed evidence: Comparable to clomipramine in a small DB trial, but subsequent OLS negative, good option for patients reluctant to take an SSRI
MAOIs	Phenelzine 60–90 mg/d	Mixed evidence; case reports positive, but controlled trials largely negative; possible benefit in a small subset

Source: Shapira. *Depress Anxiety*. 1997; Levine. *Eur Neuropsychopharmacol*. 1997; Fux. *Int J Neuropsychopharmacol*. 1999; Jenike *J Clin Psychiatry*. 1983; Insel. *Arch Gen Psychiatry*. 1983; Vallejo. *Br J Psychiatry*. 1992; Jenike. *Am J Psychiatry*. 1997; Koran. *J Clin Psychiatry*. 2005; Pato *Am J Psychiatry*. 1991



Neuroanatomy of OCD



Credit: Andrea Arguindegui

TMS for OCD



- **FDA-approved for OCD** since 2018
- **40% response rate with deep TMS** in RCT of OCD (targets ACC, dmPFC) with symptom provocation
- Treatments daily for **4-6 weeks**, minimal AEs
- Contraindications: seizures, metal devices, implants, DBS
- Caution: **bipolar disorder**
- Under investigation
 - Accelerated protocols (e.g., 5-10 session pers day, 1-2 wks)
 - Theta burst stimulation (3-6 min sessions vs standard 18-20min)
 - Need for symptom provocation

Source: Carmi. *Am J Psychiatry*. 2019; Reviewed in Kammen. *Front Neurol*. 2022 and <https://iocdf.org/about-ocd/ocd-treatment/tms/>; Bello. *JAMA Psychiatry*. 2025; photo from <https://iocdf.org/about-ocd/ocd-treatment/tms/>

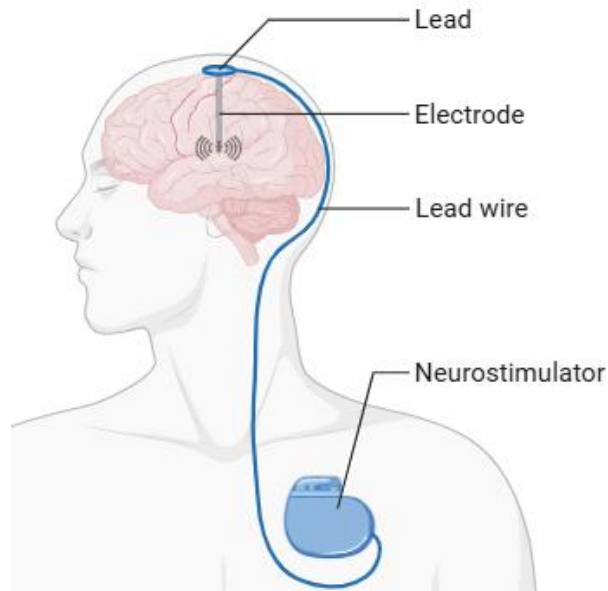
Cingulotomy/capsulotomy

- Considered last resort, eligibility is determined by psychosurgical committee and limited to **treatment-refractory** cases
- Response rates **~35-47% with cingulotomy** and **~50% with capsulotomy**
- AEs:
 - transient post-op headaches/nausea/urinary retention
 - intracerebral hemorrhage (rare)
 - infection (rare)
 - seizure (rare)
- Non-invasive options:
 - **Gamma knife radiosurgery**, minimal AEs, availability limited
 - Under investigation: **MRI-guided focused ultrasound**



Source: Ballantine. *Biol Psychiatry*. 1987; Sheth. *J Neurosurg*. 2013; reviewed in Rasmussen. *Neuropsychopharmacology*. 2022; Jung. *Mol Psychiatry*. 2015; Chang *Mol Psychiatry*. 2025
Hamani. *Biol Psychiatry*. 2025; Copyright © 2023, iStock.com/FangXiaNuo

Deep brain stimulation (DBS)



- Much less well studied than ablative surgery but **reversible, adjustable and has FDA-approval**
- Also requires approval by psychosurgical committee
- **60% response rate seen with ventral capsule/ventral striatum** placement
- AEs: Intracerebral hemorrhage, infection, transient agitation, sadness, anxiety, and cognitive AEs, **mania**
- Caution: **bipolar disorder**
- Personalized approaches under investigation
 - **Stereo-EEG (SEEG)**: temporary recording electrodes are placed in several brain regions to map OCD circuit first and identify optimal DBS target
 - **Adaptive DBS**: uses electrodes to monitor neural activity and automatically adjusts stimulation when detecting brain signals associated with OCD sx

Source: *Mol Psychiatry*. 2010; Haber. *Biol Psychiatry*. 2020; Reviewed in Bais. *Psychiatr Clin North Am*. 2014; image prepared with BioRender: Provenza. *Nat Med*. 2024; Lee. *Transl Psychiatry*. 2025; Saal. *Neuromodulation*. 2026

The background of the slide is a complex, abstract pattern. It consists of numerous thin, dark blue lines that are wavy and curved, creating a sense of movement and depth. These lines are set against a solid black background, which makes the blue lines stand out. The overall effect is a textured, almost organic-looking pattern that fills the entire frame.

Special Populations

Comorbid Bipolar Disorder

- **11-25% pts** with BD have OCD
- SSRIs can induce mania
- Limited studies, although several principles have emerged
 - OCD sx often occur with depression or mania, prioritize **mood stabilization**
 - If OCD persists after mood stabilization (e.g., lithium, valproate), consider adding an evidence-based OCD treatment with low risk of inducing mania
 - **Risperidone, aripiprazole, lamotrigine**
 - **Topirimate, memantine, NAC**
 - **CBT** should also be prioritized
 - Reserve **SSRIs for refractory cases**; use with a mood stabilizer, and titrate cautiously
 - **Psychosurgery**

Source: Reviewed in Kazhungil. *Indian J Psychiatry*. 2016; Perugi. *J Clin Psychiatry*. 2002; **Amerio. *J Affect Disord*. 2014 and 2019**; Sahraian. *J Affect Disord*. 2014; Koukopoulos. *J Affect Disord*. 2012; Koukopoulos. *Bipolar Disord*. 2010; Berk. *Biol Psychiatry*. 2008; Magalhães. *Aust NZ J Psychiatry*. 2013; Afshar. *J Clin Psychopharm*. 2012

Perinatal OCD

- **One in three** women experience **worsening OCD** during pregnancy
- In a prospective study of 763 pregnant women:
 - **17%** experienced OCD **postpartum**
 - **9%** developed OCD **de novo** postpartum, most within **10 weeks**
- Postpartum OCD is often **underreported** because pts fear of disclosing taboo OCD
- Women with OCD are more likely to consider **discontinuing meds in pregnancy**
- Approach
 - Weigh the risks of untreated OCD (**lower birth weight/gestational age, postpartum depression/OCD**) vs potential risks of SSRI exposure
 - Consider **likelihood of relapse if SSRI is stopped**: prior suicide attempts, hospitalizations, prior treatment failures
 - Prioritize **CBT**



Source: Nakić. *BMC Pregnancy Childbirth*. 2025; Holingue. *J Obsessive Compuls Relat Disord*. 2021; Fairbrother. *J Clin Psychiatry*. 2021; Fang. *Harv Rev Psychiatry*. 2018; Uguz. *Psychiatry Res*. 2015; Uguz F. *Braz J Psychiatry*. 2015; Copyright © 2021, iStock.com/globalmoments

Schizophrenia and OCD

- **25%** of pts with SCZ have OC sx, **12%** meet criteria for **OCD**
- **Schizo-Obsessive Disorder** (proposed in the 1990s, not recognized in DSM-5):
 - OCD criteria met during the course SCZ; causes additional distress/impairment separate from that expected with SCZ
 - Obsessions/compulsions should be distinct from psychotic symptoms
 - If tied to psychotic symptoms (hand-washing 2/2 to CAH), other clear OCD must be present
 - Exclude symptoms due to medication (e.g., clozapine), substances, or medical conditions
 - Treatment (limited evidence):
 - Treat SCZ first with antipsychotic, avoid clozapine if feasible
 - Then treat OCD: CBT + SSRIs
- **OCD with absent insight/delusional beliefs** (DSM-5):
 - Individual is convinced that OCD beliefs are true but do not have other psychotic sx, “I will develop HIV from touching this doorknob,”
 - Treat as OCD: CBT + SSRIs, antipsychotic augmentation may be considered

Source: Scotti-Muzzi. *CNS Spectr.* 2017; Poyurovsky. *Schizo-obsessive Disorder*. 2013. *J Psychiatry Neurosci.* 2005; <https://iocdf.org/expert-opinions/schizophrenia-and-ocd-a-consideration-of-schizo-obsessive-disorder/>

Autoimmune OCD

- Rare form of **OCD triggered by autoimmune/inflammatory processes**
- Acute (days to wks) onset OCD with new neuropsychiatric symptoms
- Most often described in children as PANDAS/PANS, but adult cases occur
 - **PANDAS**, acute-onset OCD and/or tics following **Group A strep**
 - **PANS** (Pediatric Acute-onset Neuropsychiatric Syndrome)
 - Broader category of acute onset OCD
 - Triggered by infx (e.g., mycoplasma, Lyme), metabolic disturbance, or inflammation
 - Dx requires ≥ 2 neuropsychiatric sx
- **Diagnosis is clinical** (no definitive test); labwork can help to identify an underlying cause
- Treatment
 - Standard OCD treatment (**CBT + SSRIs**)
 - Treat the underlying condition when identified
 - **NSAIDs, steroids, IVIG**, plasmapheresis (extreme cases)

Source: Frankovich. *J Child Adolesc Psychopharmacol*. 2017; more on labwork at www.pandasnetwork.org/understanding-pandas/diagnosis/; treatment guidelines at www.liebertpub.com/doi/10.1089/cap.2016.0148#T3

The background of the slide is a complex, abstract pattern. It consists of numerous thin, dark blue lines that are wavy and curved, creating a sense of movement and depth. These lines are set against a solid black background, which makes the blue lines stand out. The overall effect is a textured, almost organic-looking pattern that fills the entire frame.

Emerging Treatments

Cannabinoids

- One **negative RCT** (n=14)
 - **No significant change** in OCD with THC/CBD
 - NIDA cigarettes had substantially lower % THC (7% vs 20%)
- Naturalistic app-based study (87 individuals on medicinal cannabis with self-reported OCD, 31mo)
 - **50-60%** reported **acute symptom reduction** but **baseline OCD severity** was **unchanged**
 - Higher doses better, **tolerance** reported
 - Higher CBD associated with fewer compulsions
- Internet survey (n=601 with diagnosed or probable OCD)
 - **70%** reported subjective **improvement** in OCD symptoms
 - **42%** met criteria for **cannabis use disorder**
- Bottom line
 - Evidence does not currently support cannabis as an evidence-based treatment for OCD
 - May provide **benefit for some in the short term**, but increases risk of **cannabis use disorder**
 - Review risks: drug interactions, impaired driving, hyperemesis, depression, anxiety, psychosis...



Source: Kayser. *J Obsessive Compuls Rel Disord*. 2021; Kayser. *Depress Anxiety*. 2020; Kayser. *Cannabis Cannabinoid Res*. 2019; Mauzay. *J Affect Disord*. 2021

Ketamine



- Need for rapid-acting treatments
- **Single** ketamine (.5 mg/kg)
 - 2013 RCT (n=15, severe OCD, not on SSRI), **↓↓ OCD x 7d**
 - 2016 OLS (n=10, severe OCD, not on SSRI), **+ 10 CBT, ↓↓ OCD x 14d**
 - 2025 RCT (n=12, IM, severe OCD, on SSRI), **↓↓ OCD x 7d**
- **Repeated** ketamine
 - Chart review (n=14 adult inpts with TR-OCD, 2-3x/wk for 3 wks), **3/14 pts robust responders**, 11/14 no response
 - Case series (n=8 with TRD and OCD, standard antidepressant protocol x12 wks)
 - 4/8 OCD response
 - Depression improved by 4 wks, OCD by 8-12 wks
- **Bottom line:** may **benefit a subset of pts** but optimal **protocols** for OCD **not yet established**, not FDA-approved for OCD

Source: photo from <https://www.neuromendcenter.com/spravato-vs.-ketamine>; Bloch. *Biol Psychiatry*. 2012; Rodriguez. *Neuropsychopharmacology* 2013; Rodriguez. *J Clin Psychiatry*. 2016; Sharma. *Asian J Psychiatry*. 2020; reviewed in Bandeira *Harvard Review of Psychiatry*. 2022; Beaglehole. *J Psychopharmacol* 2025; López-Rodríguez. *BMC Psychiatry*. 2026

Psilocybin



Study	Design	Findings
2006 Repeated-Dose OLS	n=9 4 escalating doses, 0.1→0.3 mg/kg	• Rapid onset (hours), lasting up to 6mo • 70% achieved ≥50% reduction in sx
2026 Repeated- Dose DBRCT	n=15 Phase 1: 0.1 vs 0.3 mg/kg vs lorazepam weekly x 4 Phase 2: All received 0.3 mg/kg weekly x 4	• Rapid onset, lasting up to 6mo • At 8 wks, 73% response; 40% remission
2026 Single-Dose DBRCT	n=28 0.25mg/kg x1	• Rapid onset, lasting for 12 wks (study duration) • 70% response • 2022 CR, YBOCS 24→0, sustained for over 1y

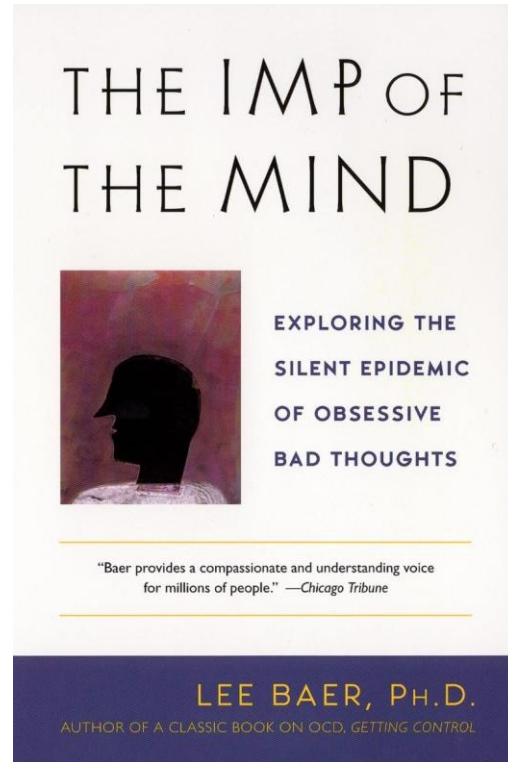
Source: Moreno. *J Clin Psychiatry*. 2006; Leonard. *Am J Psychiatry*. 1987; Moreno. *Am J Psychiatry*. 1997; Hanes. *J Clin Psychopharmacol*. 1996; Kelemendi. *Heliyon*. 2022; Copyright © 2021, iStock.com/Yarygin; Pellegrini. *Compr Psychiatry*. 2025., Moreno *J Psychopharmacol*. 2026

GLP-1 receptor agonists

- May reduce **reward-driven and compulsive behaviors** by modulating mesolimbic and cortico-striatal circuits
 - Substance use disorders (alcohol, nicotine, cocaine)
 - Binge eating disorder
 - Gambling disorder
- OCD and OCRDs
 - Anecdotal reports on social media of improvement in OCD and nail biting
 - **No published OCD studies**
 - **Phase 2 OLS** of semaglutide in trichotillomania underway (PI: Dr. Jon Grant)



Resources



Questions? LZAKHARY@MGB.ORG

