



MASSACHUSETTS
GENERAL HOSPITAL

PSYCHIATRY ACADEMY

Neurotherapeutics

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Disclosures



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I have received equity and consulting fees from Revival Therapeutics, Inc. and consulting fees from Soleno Therapeutics



Neurotherapeutics: Definition

- No formal definition of what this encompasses
- Operational definition: device-based treatments for psychopathology or pharmaceuticals outside of oral medications



Neurotherapeutics: Modalities

Ketamine
(IV or IN)

Transcranial
Magnetic
Stimulation

Electroconvulsive
Therapy

Vagus Nerve
Stimulation

Deep Brain
Stimulation

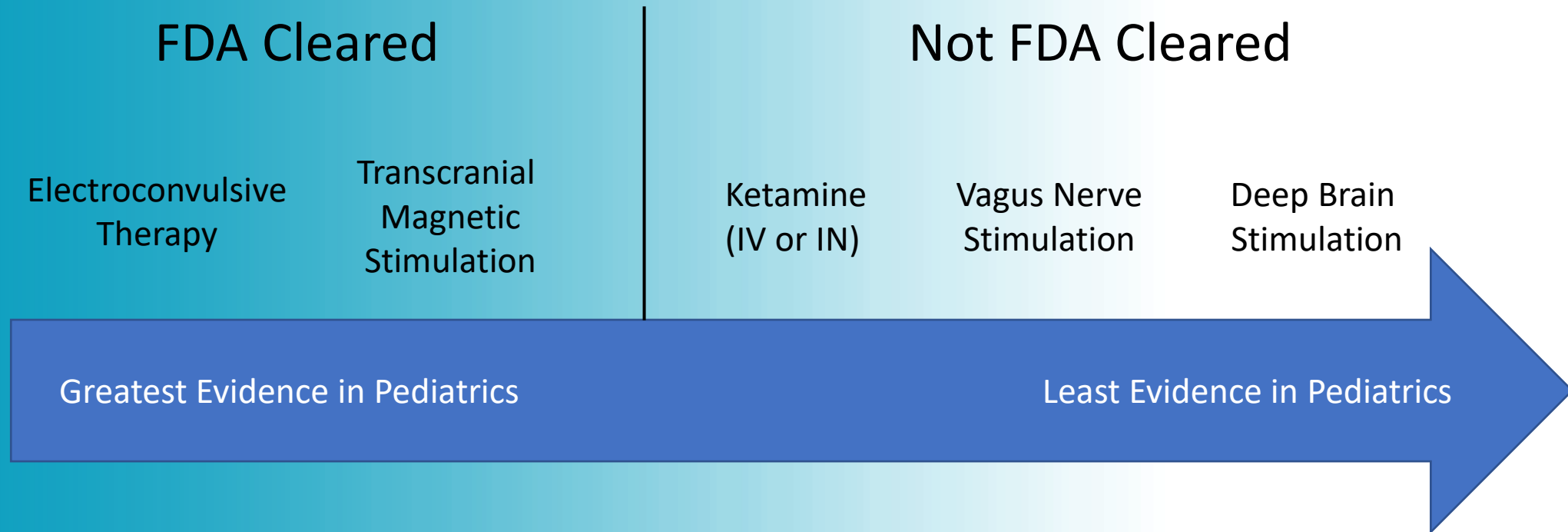
Least Invasive

Most Invasive

Many others in experimental use (photobiomodulation, focused ultrasound, transcranial direct current stimulation, etc)



Neurotherapeutics: Evidence Base





ECT: Background

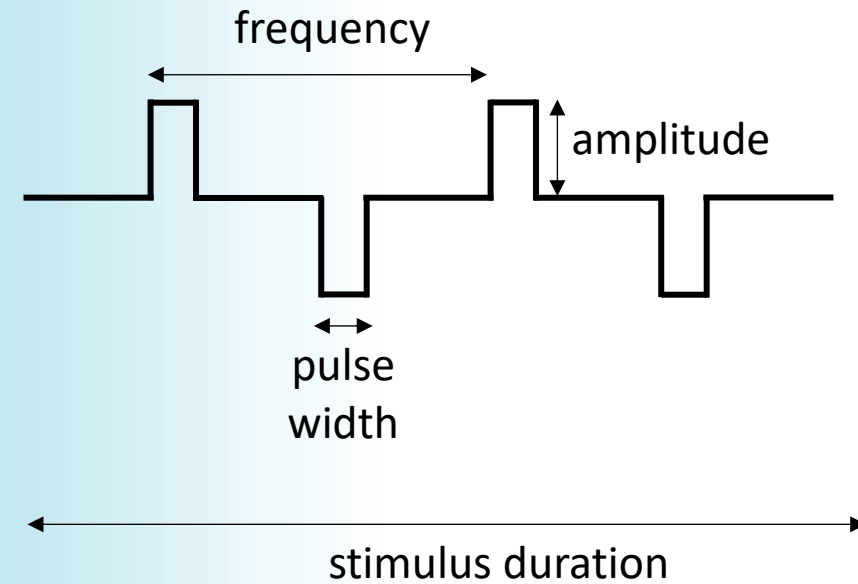
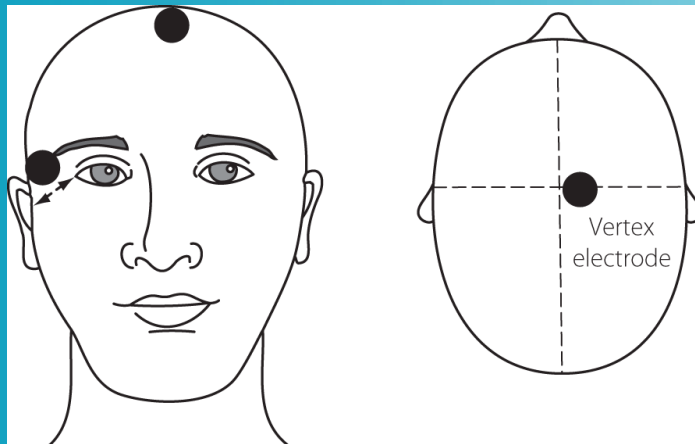
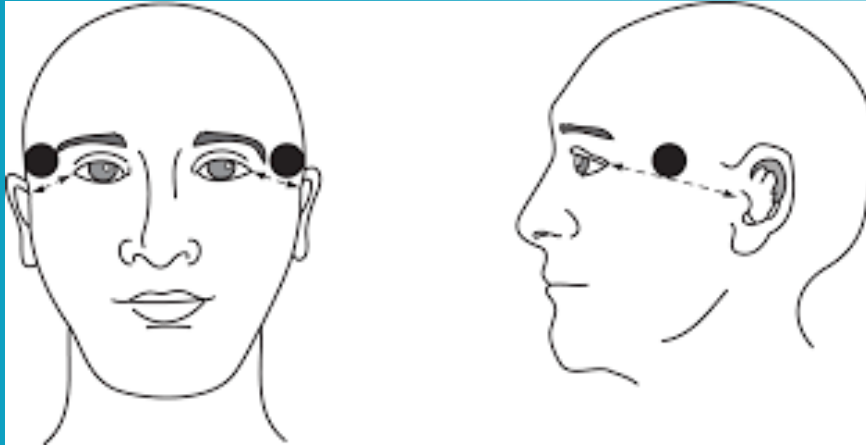
- First Use: 1938 (Rome; Cerletti)
- Use in Children: 1941 (Hemphill and Walter)
- Case series n=98 in 1947 (Bender)

- Devices FDA Cleared (Class II) in 2018
 - Depression (unipolar or bipolar)
 - Catatonia
 - Ages 13+
 - Treatment-resistant or requiring rapid response
- Performed under general anesthesia, with muscle relaxation
- Covered by insurance

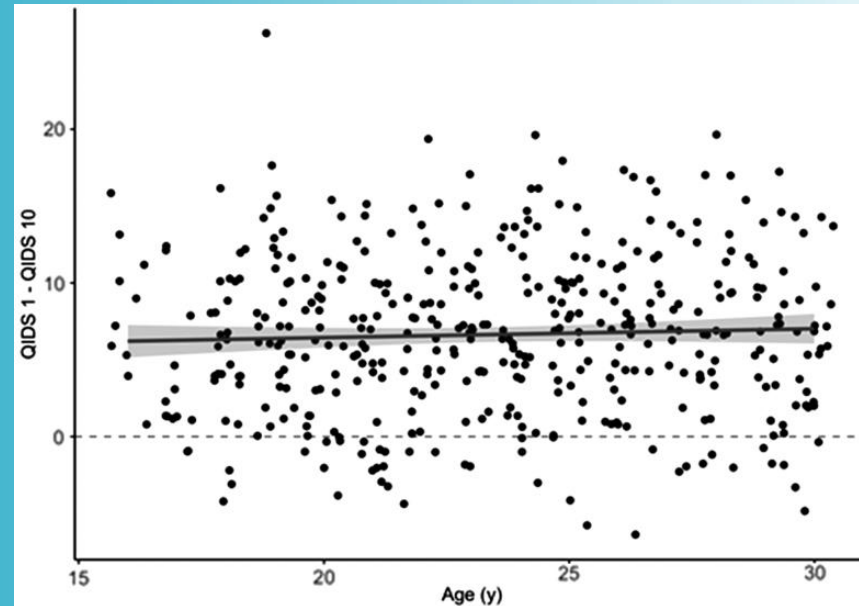
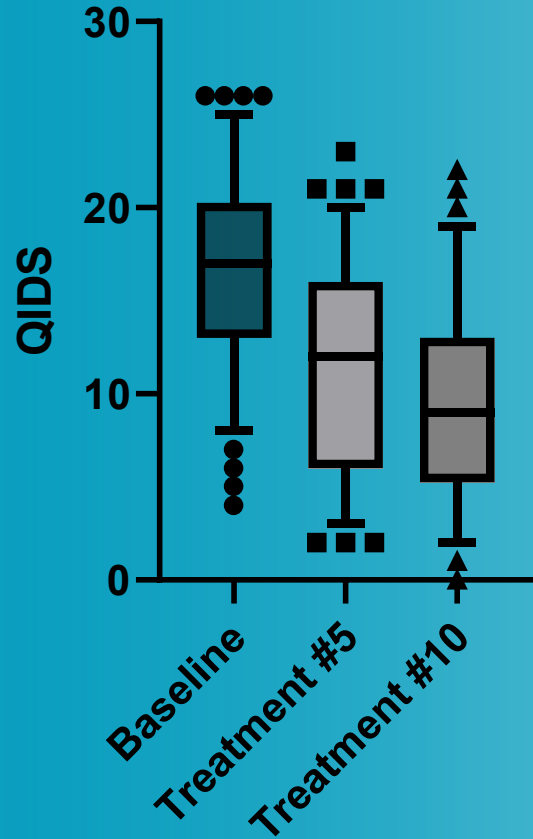


By: Francesca.pallone
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ECT: Electrical Parameters



ECT: Effectiveness for Depression

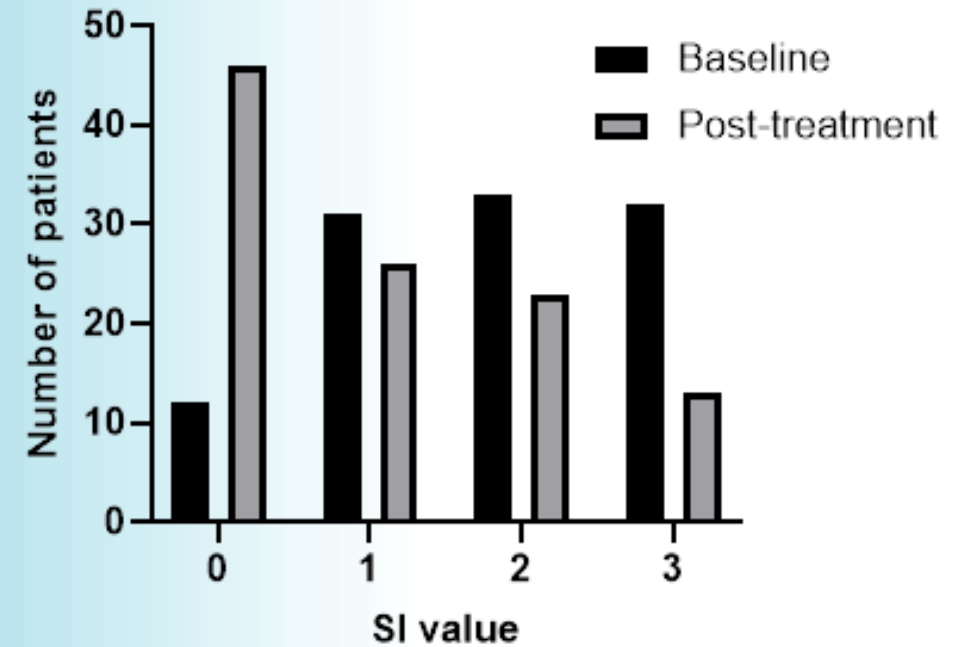
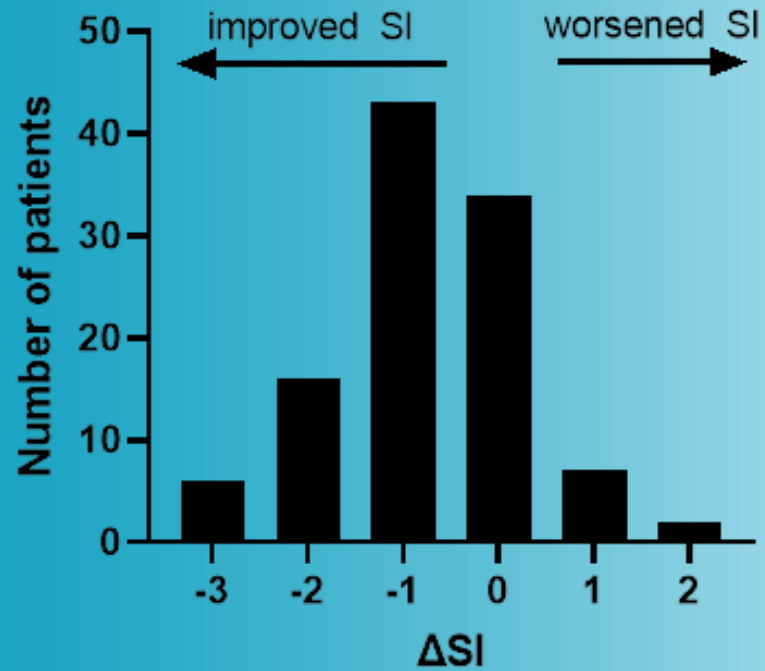


- 108 patients 16-19yo
- 306 patients 20-30yo
- QIDS-SR-16
 - Δ QIDS -6.7
 - Severe \rightarrow moderate
 - 10 treatments

J. Child Adolesc. Psychopharm., 2021; 31: 538-44



ECT: Suicidal Ideation

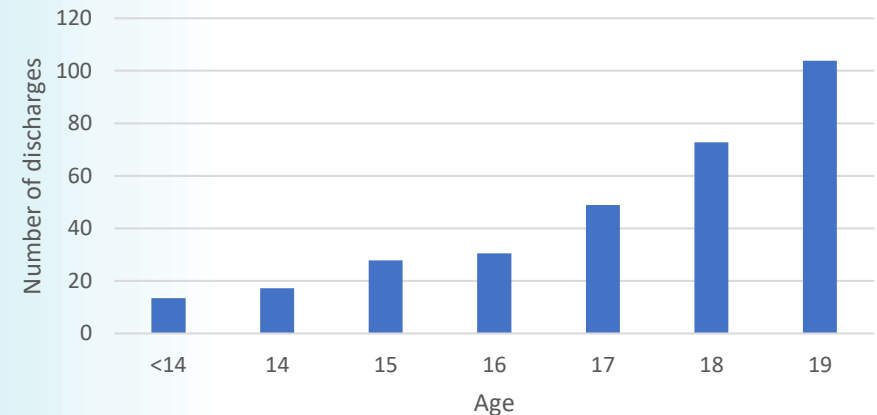


Brain Stim., 2022; 15: 1181-3



ECT: Recipients

- Pediatric patients <0.5% of ECT recipients nationally
- F > M
- Diagnosis
 - Major Depressive Disorder
 - Psychosis (including catatonia)
 - Bipolar disorder





ECT: Side effects

Memory Impairment

- Anterograde
- Retrograde

Physical Effects

- Headache
- Muscle aches

Disruption to Home/School

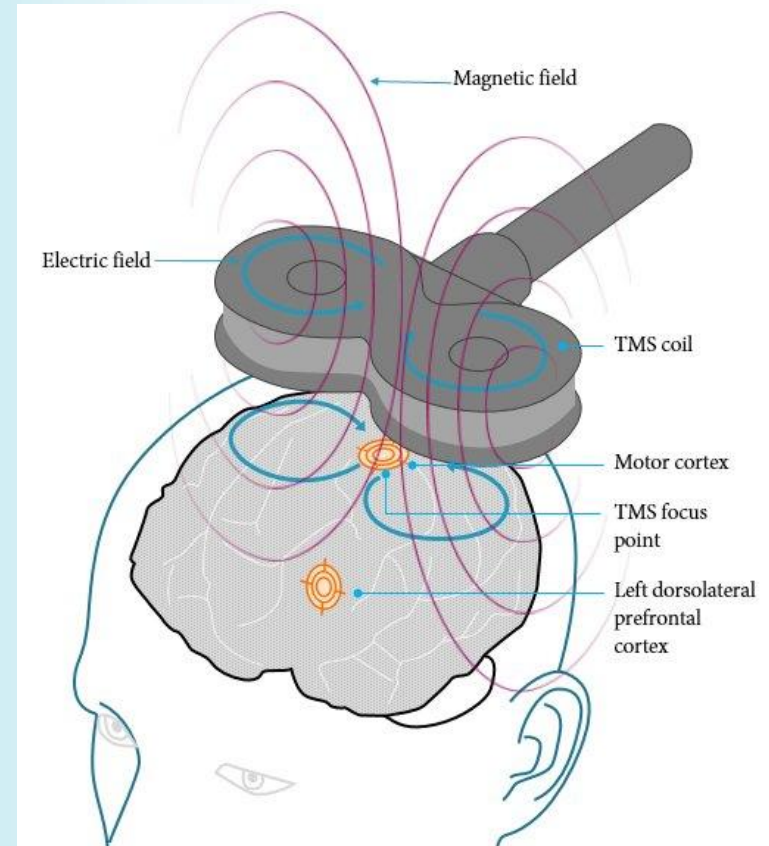
- 2-3x/week sessions

Very Rare

- Fracture
- Death

TMS: Background

- Externally-applied magnetic field induces cortical electrical pulse
- Provides *focal* stimulation
 - Can be excitatory or inhibitory
- No anesthesia required
- Typically 5x/week for ~6 weeks
- Insurance coverage can be challenging





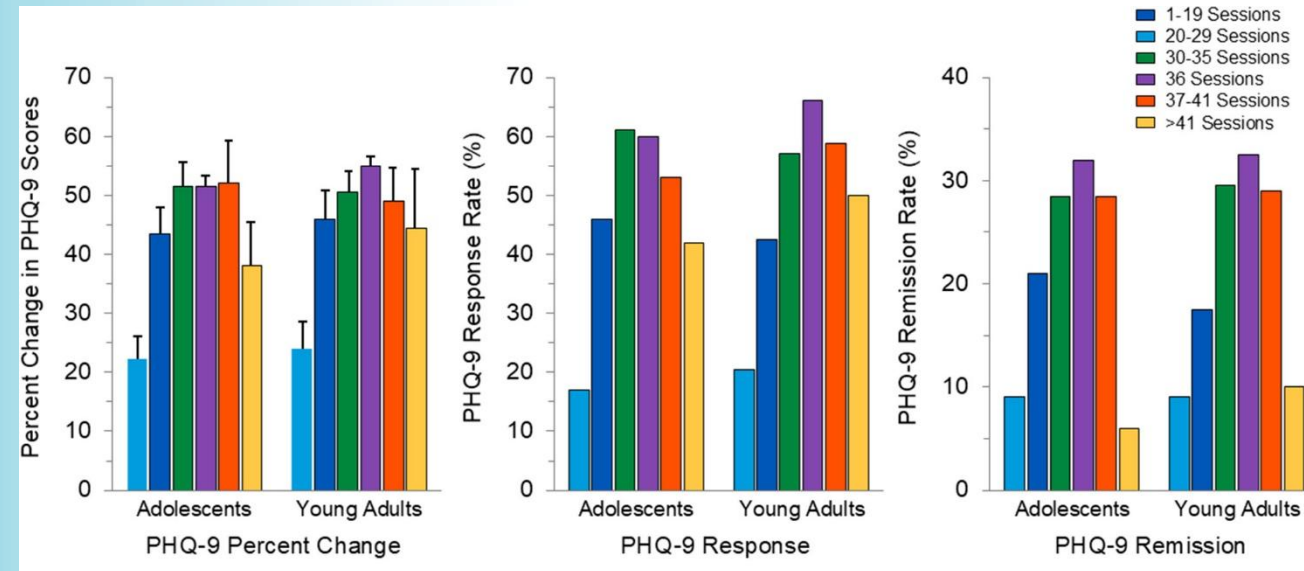
TMS: Evidence

- Multiple approved devices and protocols
 - MDD (ages 15 and older)
 - OCD (adults)
 - Smoking cessation (adults)
 - Anxiety symptoms in depression (adults)
- Because of diversity of devices and stimuli, difficult to generalize findings to other contexts



TMS: Evidence

- N=682 (12-19), N=601 (20-21)
- Naturalistic follow-up in real world settings
- L DLPFC stimulation
- Adolescents with equivalent outcomes to young adults

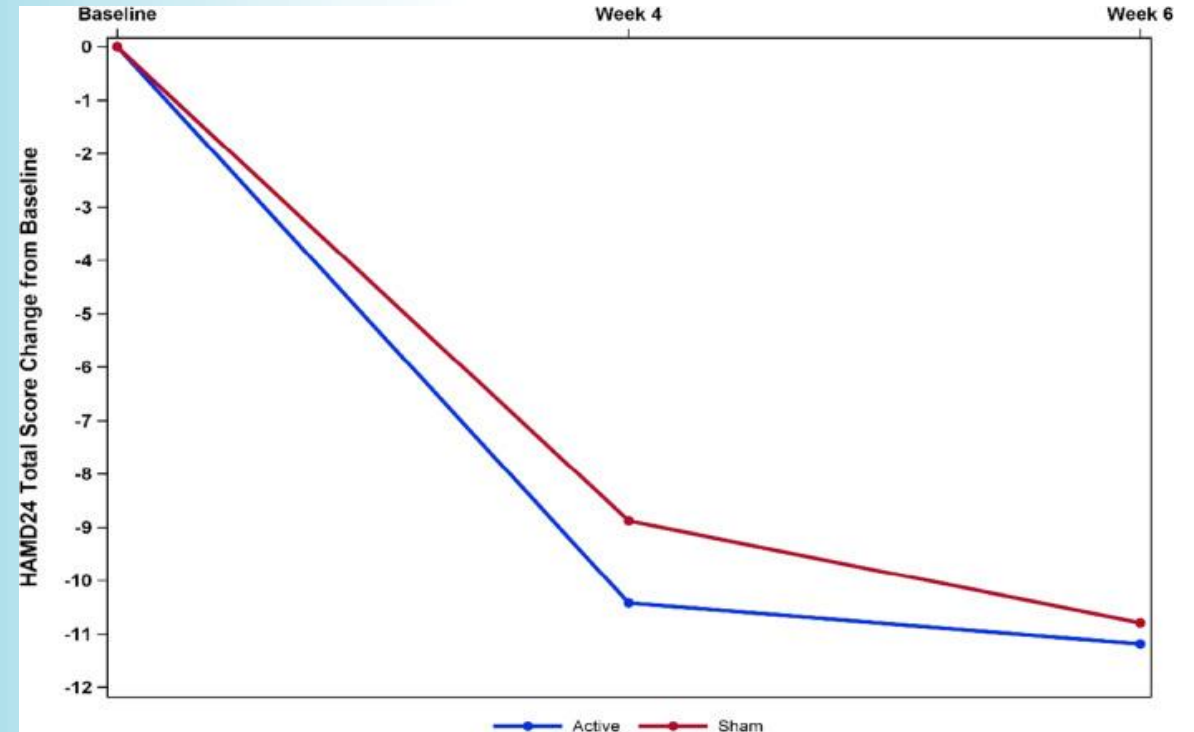


JAACAP Open, 2025; 3: 1246-1258



TMS: Evidence

- N=103
- Mean age 17
- 6 weeks of daily TMS vs. sham
 - 10Hz, 37.5 min
 - Left prefrontal target
- TMS was not superior to sham



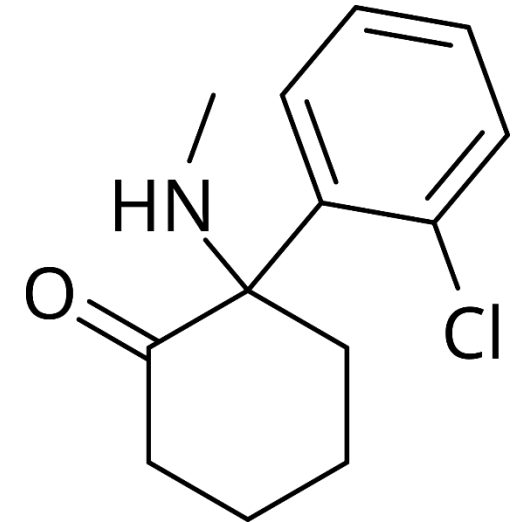
Neuropsychopharmacology, 2021; 46: 462-469



Ketamine: Background

- Approved for general anesthesia (1970)
 - NMDA antagonist
 - Also active at many other receptors
- Absorbed in multiple routes (PO, IV, IM, IN)

- Clinical effects
 - Dissociation
 - ↑HR, ↑BP
 - Rare respiratory depression

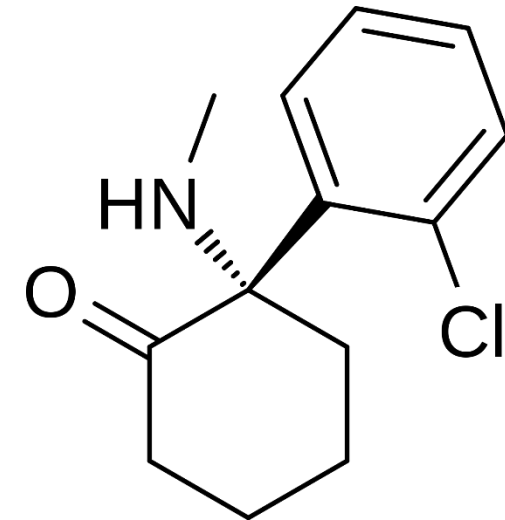


ketamine
(racemic)



Esketamine: Approval

- Esketamine approved for TRD and MDD with suicidal ideation (2019 and 2020)
- Approved for pts 18+
- Nasal spray device
 - Only offered under REMS (2hr monitoring)
- Dosing:
 - 2x/week for 4 weeks
 - 1x/week for 4 weeks
 - 0.5-1x/week thereafter
- Generally covered by insurance (adults)

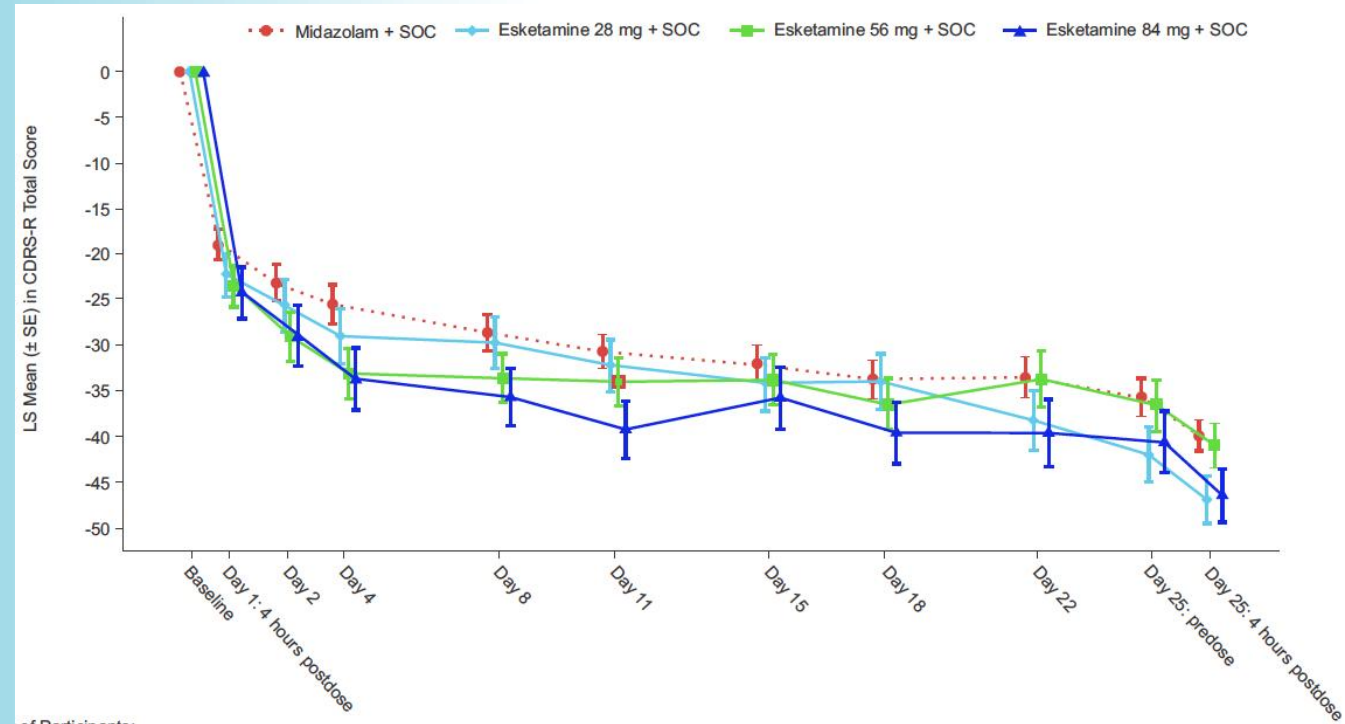


esketamine



Esketamine: Evidence

- Esketamine IN 2x/wk x4wk
- N=147; mean age 15
- Inpatient with SOC medications and therapy
- Esketamine > midazolam at 24hours (effect size 0.36)
- High response in all groups at day 25 (not powered for difference)

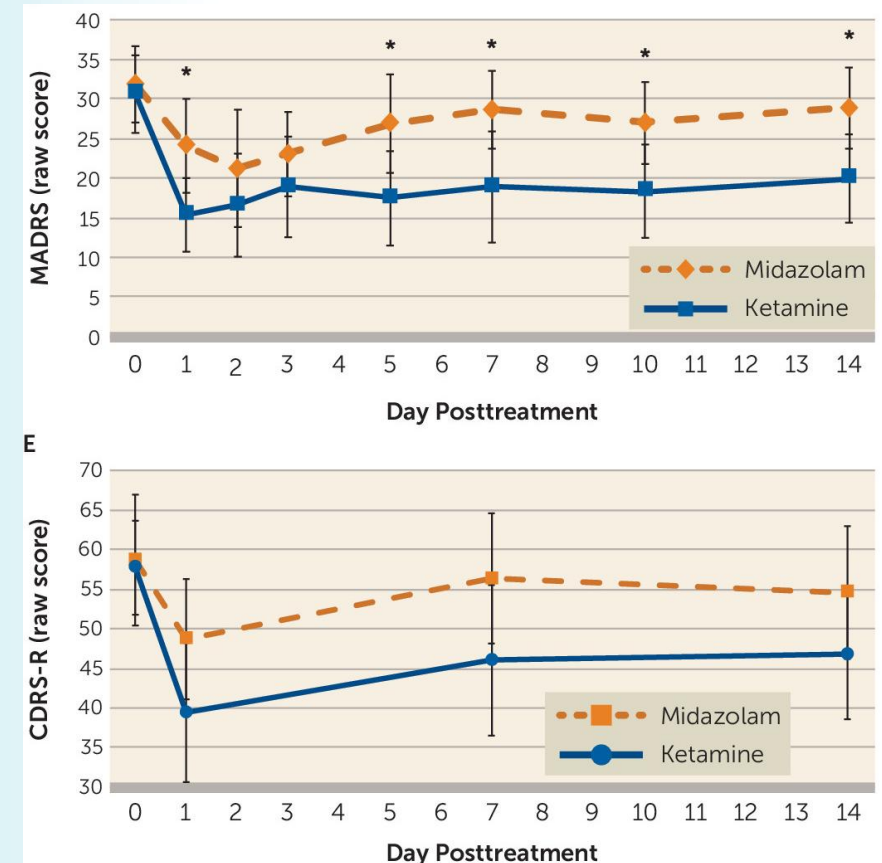


JAACAP, 2026; 65: 42-55



Ketamine: Evidence

- N=17, crossover IV infusion (ketamine vs. midazolam)
- Multiple additional studies underway for IV racemic ketamine
 - NOT industry-funded
- Almost never covered by insurance



Am. J. Psych., 2021; 178: 352-362



Future Techniques

- Modifications to ECT (magnetic seizure therapy)
- Pending prospective esketamine/ketamine trials
- TMS studies with new targets and protocols (SAINT)

- Ongoing research into alternate techniques (invasive and non-invasive)
- Psychedelics??



Summary

- Numerous non-medication options exist for pediatric depression
- With more than 80 years of research ECT remains the most evidence-based treatment
- TMS recently FDA-cleared in adolescents; optimal protocols remain under development
- Ketamine/esketamine are promising, but pediatric data are limited
- Given limited evidence for medications in TRD in youth, consider consultation for neuromodulation after 2 failed medication trials