

Updates in Depression Management: Ketamine and Transcranial Magnetic Stimulation

Ananth Shenoy, MD, FACP

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Updates in Treatment Resistant Depression

- ▶ No financial disclosures. Will discuss off label use of ketamine
- ▶ Ketamine and Esketamine
- ▶ Repetitive Transcranial Magnetic Stimulation (rTMS)

Case 1

- ▶ 25F with history of unipolar vs bipolar depression, generalized anxiety disorder
 - ▶ Prior medication trials: Amitriptyline, fluoxetine, sertraline, citalopram, duloxetine, desvenlafaxine, mirtazapine
 - ▶ History of suicide attempt via overdose, questionable prior manic episode, cannabis dependency
 - ▶ Current medications: Clonazepam prn, quetiapine
 - ▶ Unable to see prior Psychiatrist due to insurance coverage
- ▶ She asks you about Ketamine!

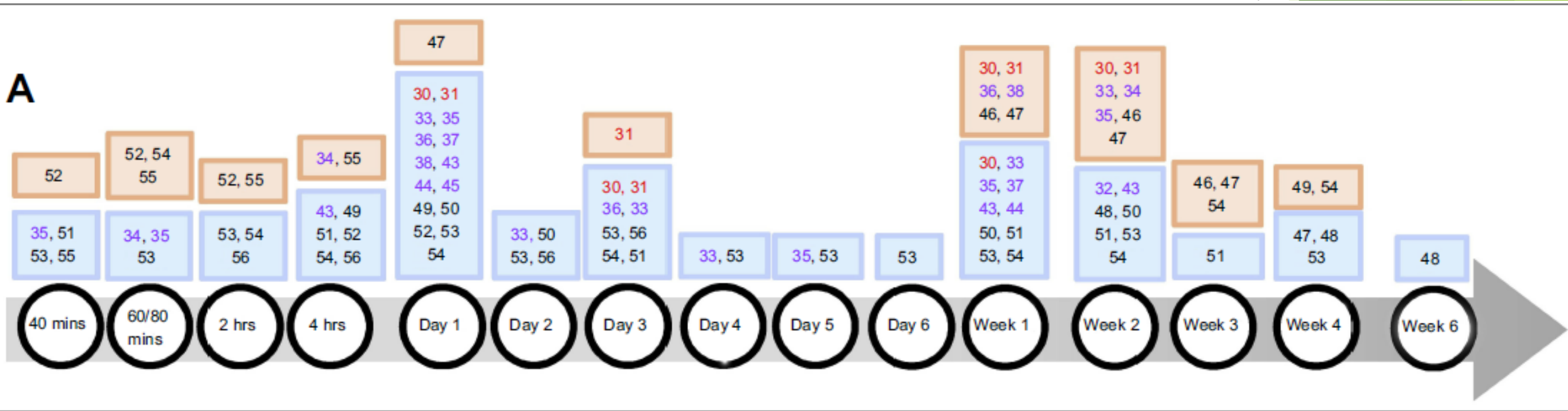
Ketamine

- ▶ Dissociative anesthetic, analgesic properties
- ▶ NMDA antagonist, **Mu agonist**, AMPA and mTOR pathways
- ▶ Schedule III, abuse potential
- ▶ Short half life, high first pass liver effect
- ▶ Routes for administration: **IV**, Nasal, Oral, IM
 - ▶ **Administered in monitored environment**
 - ▶ *Significantly lower dose than general anesthetic dosing*
- ▶ Racemic mixture - Esketamine the S-enantiomer - higher affinity
- ▶ Expensive \$\$\$

Ketamine and Esketamine

- ▶ Primarily compared to placebo in treatment resistant depression
- ▶ Variable quality of studies and sample sizes
- ▶ Significant improvement in depression scores *within hours to days*
 - ▶ NNT 2-4
- ▶ Duration of improvement short (1-2 weeks)
- ▶ Side effects dose dependent
 - ▶ Short term: dissociation, sedation, hypertension, tachycardia, anxiety.
 - ▶ Long term: dependency, cognitive effects, cystitis
- ▶ Dosing 2-3 times week initially, then 2/week for maintenance
 - ▶ Duration of treatment unclear - studies very short term (longest with follow up of 80 weeks)

Ketamine Trials



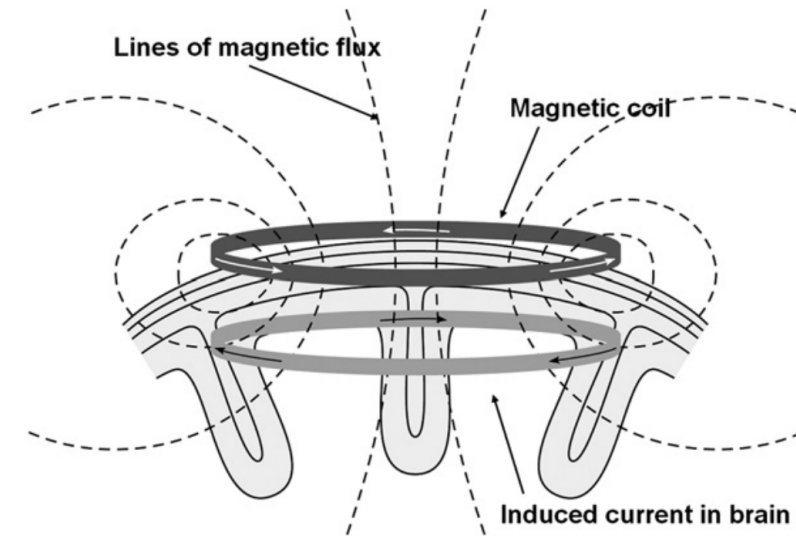
- ▶ Positive in blue, negative in orange, outcomes at different time points

Ketamine and esketamine

- ▶ Esketamine nasal administration FDA approved for treatment resistant depression, and **depression with suicidality** (Spravato)
 - ▶ Available through monitored clinic setting (REMS program)
- ▶ Ketamine use would be off label
 - ▶ Would need expertise, monitoring, likely IV administration
- ▶ **Likely out of pocket (\$\$\$)**
- ▶ Maybe a **bridge for severe depression and suicidality** while waiting for other pharmacotherapy to take effect
- ▶ Caution with history of substance dependency, other co-morbid behavioral health concerns or bipolar depression

Transcranial Magnetic Stimulation (TMS)

- ▶ Magnetic fields are generated by the device (like focused MRI)
- ▶ These induce electric currents in the brain - can target regions
 - ▶ Left dorsolateral prefrontal cortex
- ▶ Brief but repetitive bursts are applied
- ▶ Sessions ~30mins, several sessions per week for 1-2 months
- ▶ Measurable biochemical and physiologic changes in the brain
- ▶ Two FDA approved devices for repetitive TMS

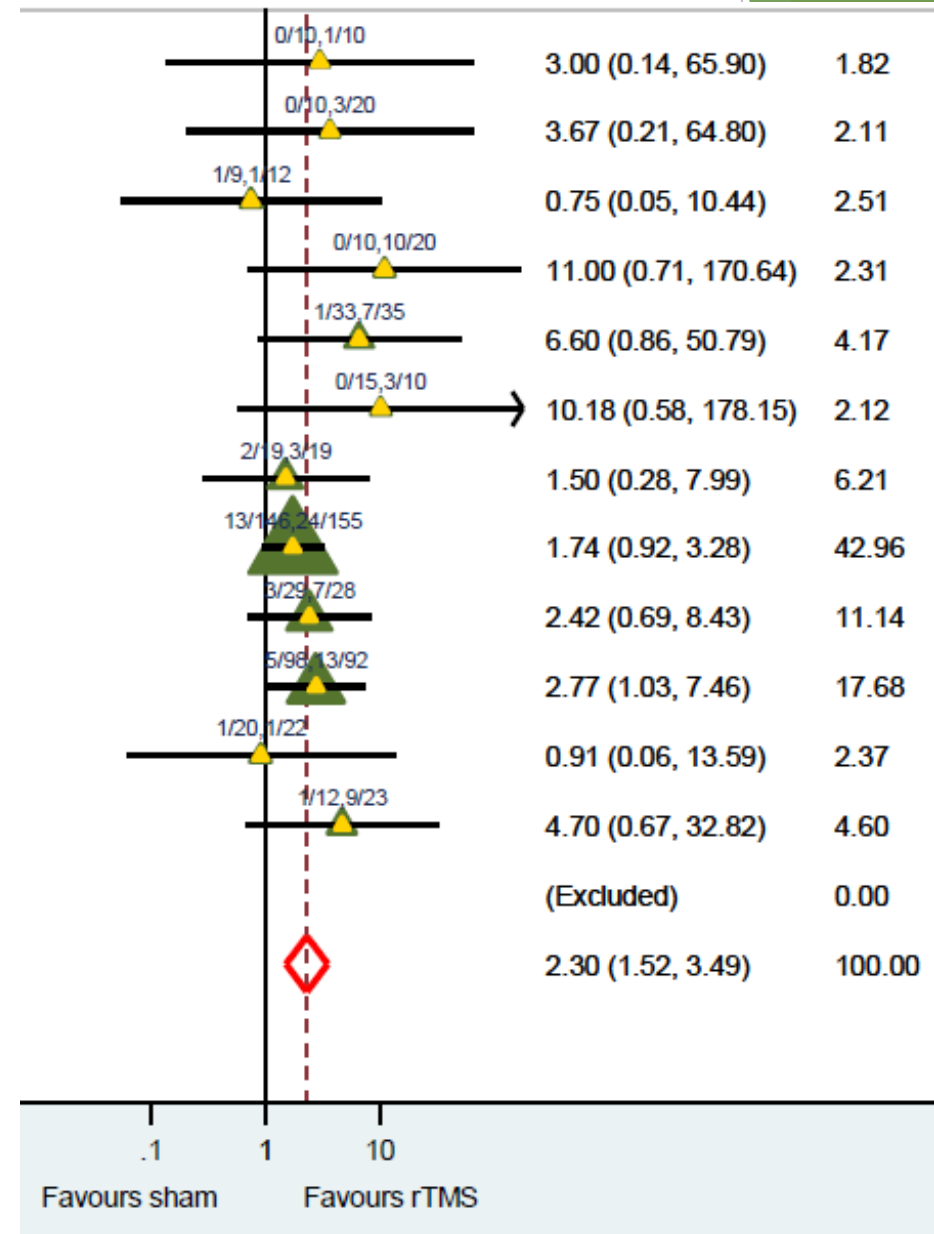


PMID: 17640522



TMS

- ▶ Primary comparisons to sham treatments and Electroconvulsive Therapy (ECT) in *treatment resistant depression*



PMID: 27099642

TMS

- ▶ *Generally well tolerated, low risk of seizure (0.01%)*
 - ▶ Headaches, scalp pain, nausea, syncope
- ▶ Primarily studied for short term use - follow up weeks to months
- ▶ Probably not as robust an effect as ECT, but still efficacious compared to sham
 - ▶ **NNT 5-10**
- ▶ Dedicated centers, insurance plans may cover
- ▶ A role in treatment resistant depression
- ▶ **Same contraindications as MRIs** (implanted devices) and those at **risk for seizures**

Summary

- ▶ Options for unipolar depression
 - ▶ Ketamine and Esketamine for acute symptoms, **maybe as bridge to another pharmacologic agent**
 - ▶ TMS as another option for resistant depression, compare to ECT => less barriers than ECT

- ▶ Questions?

Ananth.Shenoy@VirginiaMason.org

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