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Master Class for Neuroscience Professional Development

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How to Proceed with Treatment-Resistant Depression When the Evidence-Base is Scant

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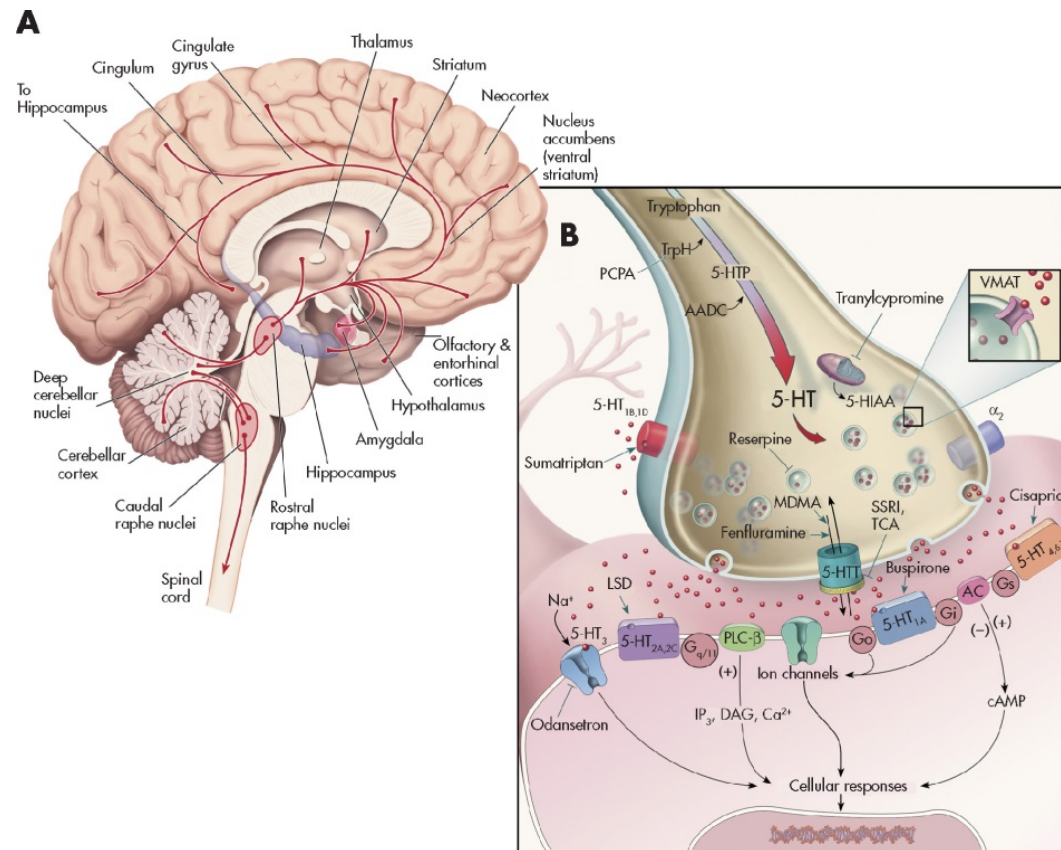


Learning Objective

Incorporate the effective use of ketamine into treatment strategies for TRD by examining dosing strategies, routes of administration, and duration of treatment.

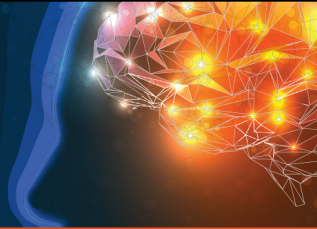


The Serotonergic System



Schatzberg A, et al. *The American Psychiatric Association Publishing Textbook of Psychopharmacology*. 5th ed. 2017.

Open-Label Psilocybin in Refractory Major Depression



- 12 treatment refractory depressives
- 10 mg. on day 1 and 25 mg. on day 8
- 8 of 12 patients responded at one week;
7 of the 12 maintained response at 3 months

Double-blind Studies of Psilocybin in Cancer Patients with Comorbid Depression and Anxiety



- Two positive double-blind studies
- Niacin or low dose psilocybin as controls
- Full doses of psilocybin were 0.3 mg./kg. or 22 to or 30 mg./70 kg.
- Both studies demonstrated sustained responses at full doses

Griffiths RR, et al. *J Psychopharm.* 2016;30:12(1181-1197); Ross S, et al. *J Psychopharm.* 2016;30(12):1165-1180.

Buprenorphine



- Partial mu opioid agonist
- Kappa antagonist
- Used in addiction treatment
- Open-label, positive data in refractory depression
- Improves mood in opioid abusers (RCT data)
- Being developed (in combination with samidorphan, a mu antagonist) for treatment of refractory major depression

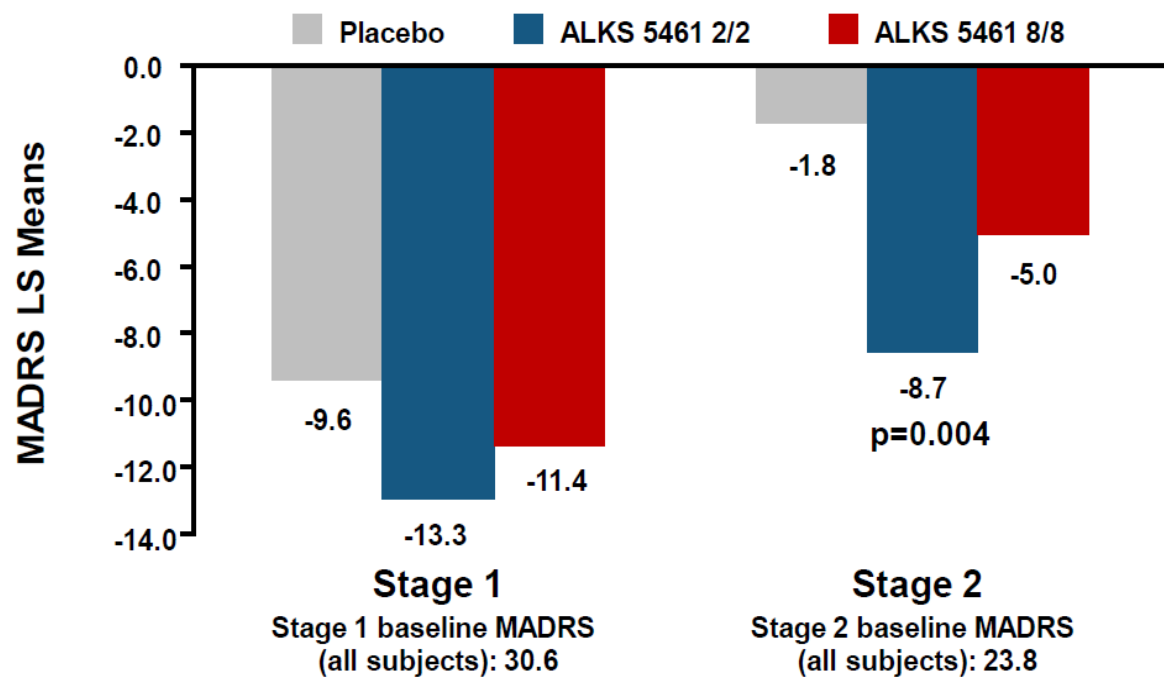
Low-Dose Buprenorphine Reduces Suicidal Ideation



- 88 patients with clinically significant suicidal ideation
- Buprenorphine 0.1-0.8 mg/day (mean dose 0.44 mg/day) or placebo for 4 weeks
- Buprenorphine superior to PBO for reducing suicidal ideation at 2 and 4 weeks
- No withdrawal symptoms after treatment discontinuation

RCT of ALKS 5461 (Buprenorphine Plus the Mu Antagonist Samidorphan) in SSRI Non-Responders

Figure 4: MADRS Change from Baseline at Week 4



Fava M, et al. *Am J Psychiatry*. 2016;173(5):499-508.

ALKS-5461 as Adjunct in MDD*



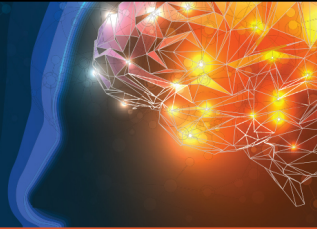
- FORWARD-4 and FORWARD-5
- 792 patients in DB, PBO controlled 11 week trials in antidepressant non-responders
- Doses of buprenorphine/samidorphan (0.5/0.5 mg and 2/2 mg)
- Both doses not superior to PBO
- FORWARD-5 (1/1 mg and 2/2 mg): 2/2 mg. superior to placebo

*On 2/4/19, FDA rejected NDA of ALKS-5461 as adjunctive treatment for MDD.

Fava M, et al. *Mol Psychiatry*. 2018 Oct 29.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Personalize the management of your patients with TRD by understanding the potential effective use of ketamine, psilocybin, and buprenorphine in appropriate patients

Questions & Answers

Don't forget to fill out your evaluations to collect your credit.

