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Psychiatry and Addictions Case Conference

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NEUROSTEROIDS: NEW MEDICATIONS FOR POSTPARTUM DEPRESSION (AND, EVENTUALLY, MDD)

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GENERAL DISCLOSURES

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SPEAKER DISCLOSURES

✓ I get royalties from UpToDate for reviewing the anxiety disorder sections.

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose:

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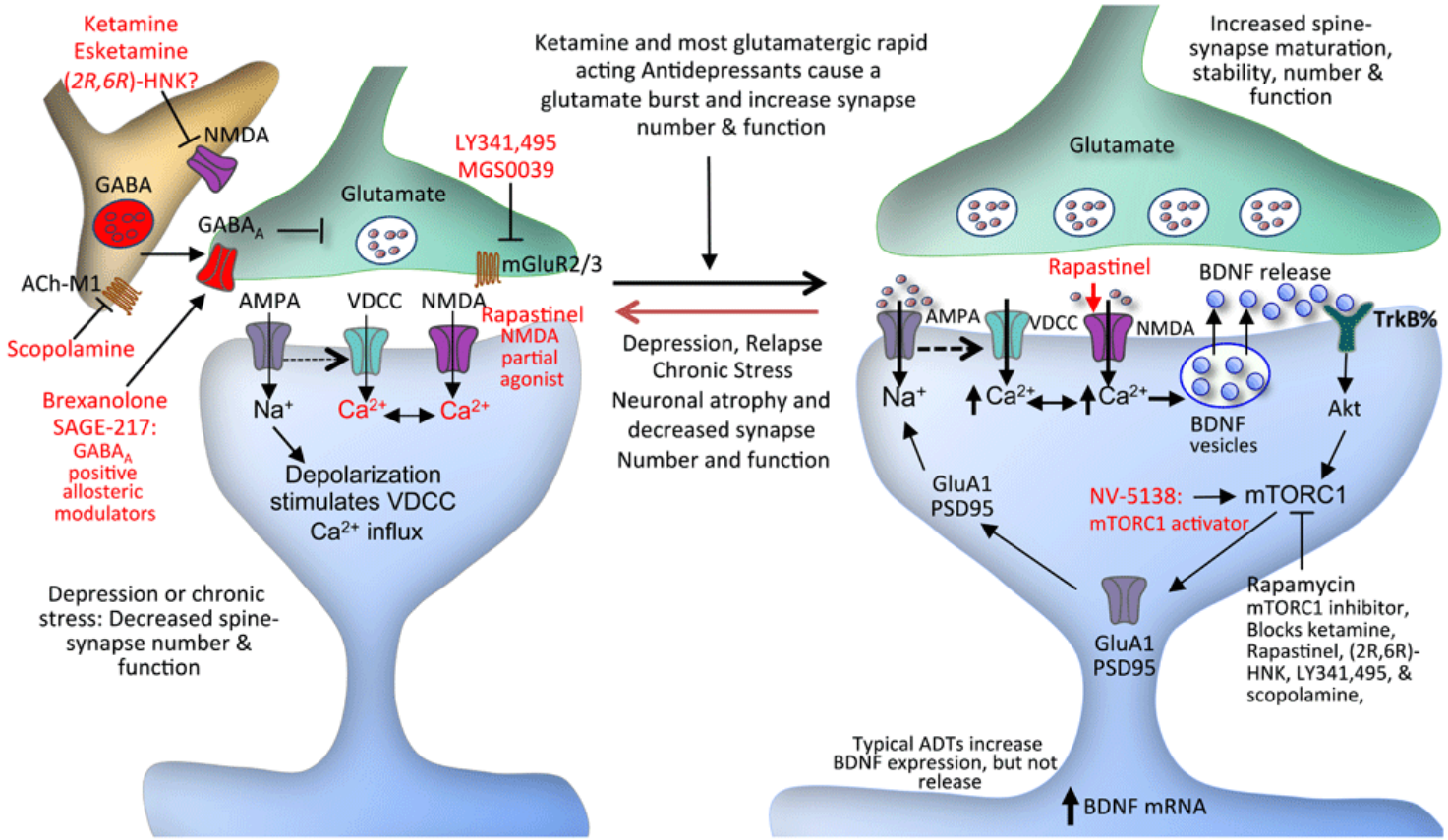
POSTPARTUM DEPRESSION (PREVALENCE AND ONSET)

- DSM-5 defines “peripartum onset” as during pregnancy or within 4 weeks of delivery. Other definitions define PPD as within 12 months after delivery.
- Prevalence is variable because we can’t agree on a definition, but is reported as 9-16%.
- Onset (Altemus et al., J Clin Psych, 2012)
  - Postpartum month 1 – 54 percent
  - Postpartum month 2 to 4 – 40 percent
  - Postpartum month 5 to 12 – 6 percent
- Good apps for providers are UpToDate and Lactmed

NEUROSTEROIDS AND BREXANOLONE (ZULRESSO) THEORY

- Brexanolone is an IV formulation of allopregnanolone, which is a naturally occurring metabolite of progresterone.
- Allopregnanolone rises in pregnancy, peaks in the 3rd trimester, then drops rapidly after parturition.
- In rats, chronic stress decreases levels of allopregnanolone.
- Allopregnanolone binds to the GABA-A receptor (but on a different part of the molecule than benzodiazepines)

EVERYBODY HATES SLIDES LIKE THESE
(BUT JUST FOCUS ON THE TOP LEFT CORNER AND TRUST ME FOR A SECOND)



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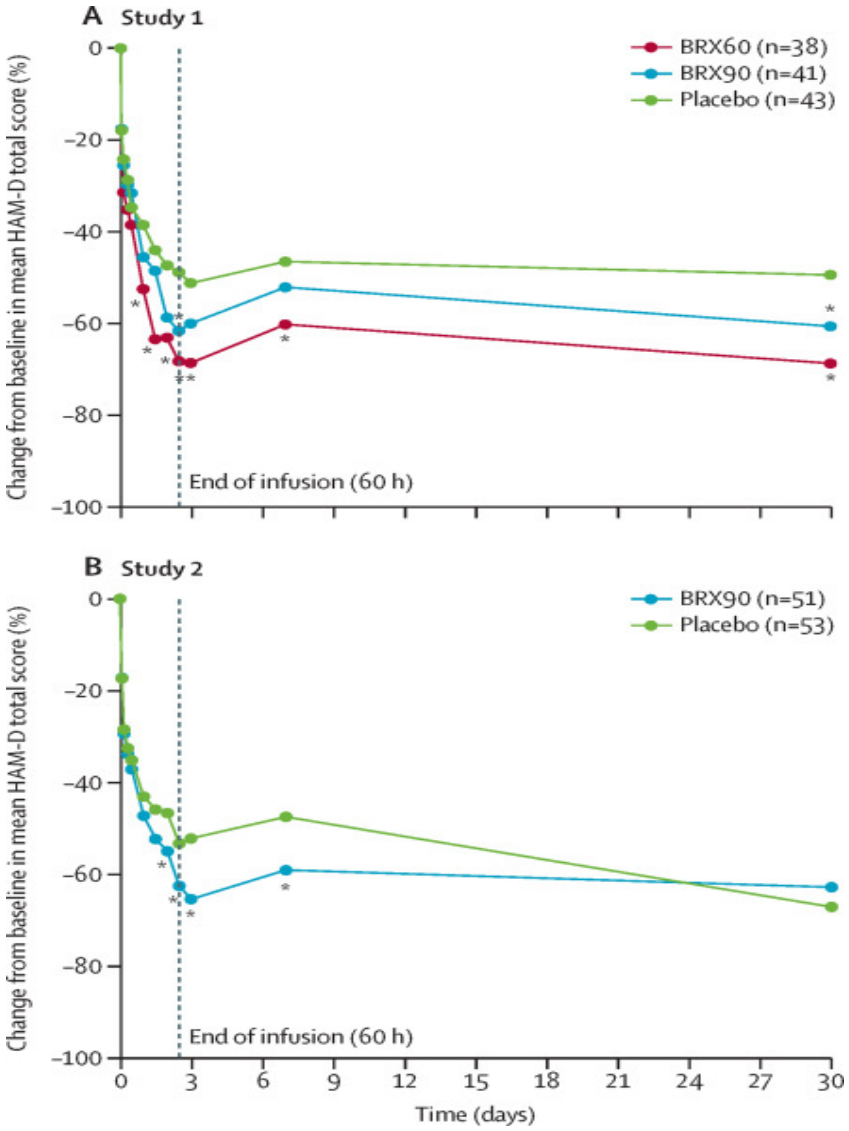
BREXANOLONE PRECAUTIONS AND PRICE

- There is a Zulresso-REMS program because of the pulse-oximetry monitoring, need for continuous observation, and need for supervision while caring for children, that is required during medication delivery
- 60-hour continuous infusion
- Can cause excessive sedation and sudden loss of consciousness
- Half life is ~9 hours
- Over 60 hours, most patients will require 5 vials, which cost a total of ~$35,000 (not including the cost of the hospital admission)

SPEED AND DURATION OF EFFECT



CGI much improved or very much improved

- Study 1
  - 82% vs. 84% vs. 56% at 60 hours (NNT = 4)
- Study 2
  - 80% vs. 56% at 60 hours (NNT = 4)
  - Difference from placebo at 7 but not 30 days

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THE NEXT NEUROSTEROID: SAGE-217

- Development for MDD is based on the theory of decreased GABA and glutaminergic tone in patients with depression.
- Phase III trials (the final stage before it is submitted to the FDA for review) are nearly complete for both MDD and PPD. It is still probably several years off from approval.
- It is a once-daily, oral formulation, rather than continuous IV.
- The results of an 89-patient, double-blind, placebo-controlled trail was published in NEJM in September of 2019 (first author Gunduz-Bruce).

THINGS THAT WORRY ME
(THESE COULD BE UNFOUNDED WORRIES)

- Duration of effect for any “rapid-acting” treatment of depression
- Abuse potential of sedating medications
- Potential for “rebound depression”
- FDA-indications for medications for PPD could devalue screening for, and treatment of, psychosocial contributors and psychiatric co-morbidities.

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