



UW PACC

Psychiatry and Addictions Case Conference

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UPDATES TO PTSD PSYCHOPHARMACOLOGY TREATMENT

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SPEAKER DISCLOSURES

- ✓ Any conflicts of interest?
 - None

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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OBJECTIVES

1. Describe first-line pharmacotherapy treatments for PTSD.
2. Understand evidence base for augmentation options for PTSD treatment
3. Apply appropriate decision-making to variety of clinical scenarios
4. Articulate the evidence base for emerging PTSD treatments

CASE STUDY

- Ms. J is a 43-year-old female presenting after referral from her PCP. Experienced a car accident in 2023 where her and her husband had to be hospitalized for months due to severe injuries.
- **Mood/Anxiety:** Has felt little enjoyment in hobbies for the past 2 years. Attributes to questioning what she could have done to prevent car accident. Sleeps poorly due to nightmares about nearly dying, being trapped. Often avoids driving (when she does, experiences increased HR, SOB, dizziness), has led to her working part time as public transportation to work takes 3 hours out of her day. Has been going on since she discharged from the hospital in 2023.
 - Denies SI; no history of suicidal thoughts/attempts
- **Psychosis:** Reports at times feeling like she can hear brakes screeching when riding in a car, reminds her of the accident. Otherwise denies AVH, paranoia.
- **Substance Use:** 2 glasses of wine per week, otherwise denies
- **Recent stressors:** Has had to work part-time, has led to financial stress in the family, though able to make ends meet.
- **Psychiatric History:** None
- **No known family history of psychiatric or substance use issues**
- **No previous medications trials**



WHAT DO YOU THINK IS GOING ON?

DSM-V-TR DIAGNOSIS FOR PTSD

- Exposure to actual or threatened death, serious injury, or sexual violence
- Presence of one or more intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred
- Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred
- Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two or more symptoms
- Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) symptoms
- Duration of the disturbance is more than 1 month.
- The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.
- Specify whether: with dissociative symptoms, depersonalization, derealization
- Specify whether: With delayed expression: If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).

STRONGEST EVIDENCE FOR PSYCHOTHERAPY > PHARMACOTHERAPY



- Evidence-base is strongest for exposure therapies
 - Cognitive Processing Therapy (CPT)
 - Eye Movement Desensitization and Reprocessing (EMDR)
 - Prolonged Exposure Therapy

Topic	Sub-topic	#	Recommendation	Strength ^a	Category ^b
(cont.)	Pharmacotherapy	15.	We recommend paroxetine, sertraline, or venlafaxine for the treatment of PTSD.	Strong for	Reviewed, New-replaced
		16.	There is insufficient evidence to recommend for or against amitriptyline, bupropion, buspirone, citalopram, desvenlafaxine, duloxetine, escitalopram, eszopiclone, fluoxetine, imipramine, mirtazapine, lamotrigine, nefazodone, olanzapine, phenelzine, pregabalin, rivastigmine, topiramate, or quetiapine for the treatment of PTSD.	Neither for nor against	Reviewed, New-replaced
	Pharmacotherapy (cont.)	17.	There is insufficient evidence to recommend for or against psilocybin, ayahuasca, dimethyltryptamine, ibogaine, or lysergic acid diethylamide for the treatment of PTSD.	Neither for nor against	Reviewed, New-added
		18.	We suggest against divalproex, guanfacine, ketamine, prazosin, risperidone, tiagabine, or vortioxetine for the treatment of PTSD.	Weak against	Reviewed, New-replaced
		19.	We recommend against benzodiazepines for the treatment of PTSD.	Strong against	Reviewed, New-replaced
		20.	We recommend against cannabis or cannabis derivatives for	Strong	Reviewed,

PHARMACOTHERAPY

- FDA approved for PTSD
 - Sertraline
 - Paroxetine
- Off-label
 - Mirtazapine
 - Amitriptyline
 - Venlafaxine

What would be your
recommendations for
Ms. J?



CASE STUDY- CONTINUED

Ms. J returns to your clinic 6 months after completing a course of Cognitive Processing Therapy. She has now been on sertraline 200 mg daily for 8 months. She still struggles with the following symptoms:

- Nightmares
- Little enjoyment of hobbies
- Is still avoiding driving
- Believes that she could've prevented the car accident from happening

What adjunctive medications could you consider?

PROPRANOLOL



Limited evidence for efficacy in hyperarousal, intrusive symptoms



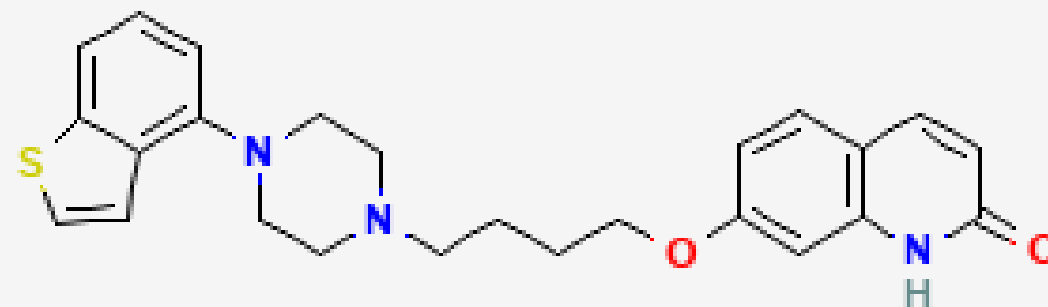
Combined use with therapy

Memory reconsolidation via exposure therapy + medication 60 minutes prior

- May decrease nightmare severity

ANTIPSYCHOTICS

- Brexipiprazole approved for use with sertraline
 - Dosage: 1-3 mg added to sertraline
 - Re-experiencing, avoidance, negative cognition, depression, hyperarousal, and reactivity
- Risperidone, quetiapine, and other SGAs
 - Mixed evidence, weak to no support
 - May specifically help with intrusion and hyperarousal symptoms



PRAZOSIN

- Mixed evidence
 - 15-week positive RCT in 2013, large base of clinical use
 - 26-week negative RCT in 2018
 - AASM supports use for nightmares
 - Doxazosin?



MOOD STABILIZERS

- Mixed evidence for adjunctive use
 - Lamotrigine
 - Low, but high acceptability
 - Topiramate
 - Low evidence, limited small trials
 - Valproic acid
 - Negative, no recent evidence
 - Lithium
 - Least evidence

ALPHA-2 AGONISTS



- Clonidine
 - Limited RCT support
 - Some evidence for improved sleep, nightmares, daytime hyperarousal
- Guanfacine
 - No studies found for adults
 - No RCT, though case studies support use in pediatrics

BENZODIAZEPINES



- Not recommended for use by VA
- Few recent RCTs or meta-analyses
- 2 recent meta-analyses do suggest that use worsens symptoms, including in exposure therapy setting

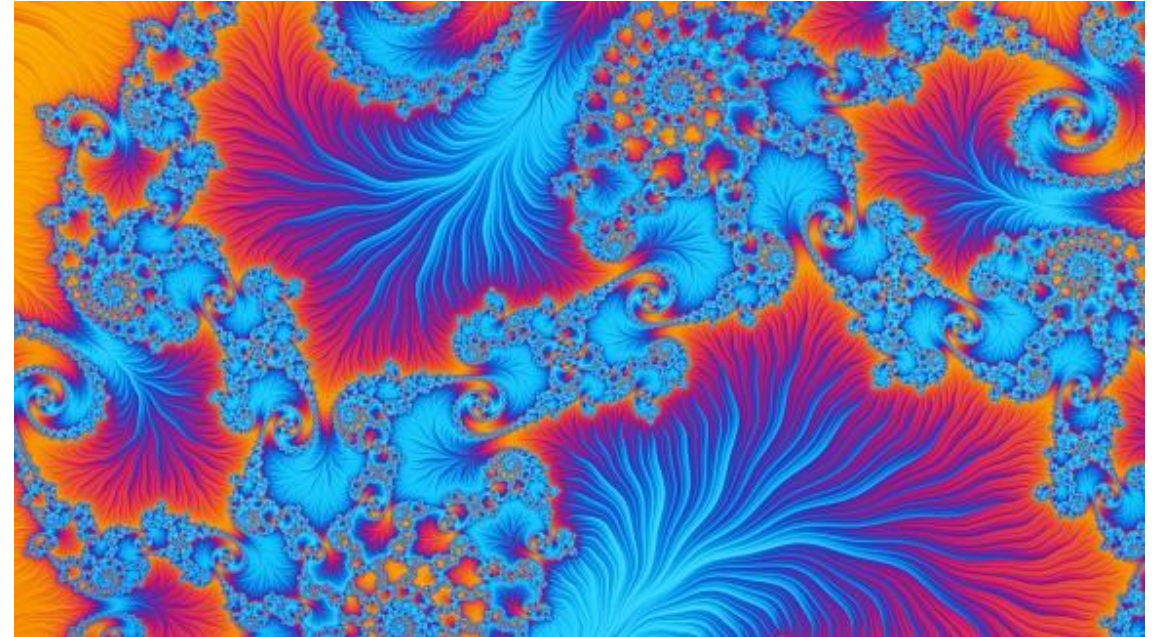
CASE STUDY- CONTINUED

Ms. J returns to your clinic in 3 months. She still has trouble with blaming herself for the car accident and intrusive thoughts, despite the addition of brexipiprazole to sertraline. She's heard about psilocybin for PTSD and is interested to hear more about new treatments for PTSD.



EMERGING PTSD TREATMENTS

- Psychedelics
 - 3,4-Methylenedioxymethamphetamine (MDMA)
 - Most researched, RCTs, failed FDA approval
 - Combined with manualized therapy
 - Symptom improvement up to 12-months
 - Phase 3 trial design flaws
 - Psilocybin
 - Pilot studies and theoretical mechanisms



EMERGING PTSD TREATMENTS

- Ketamine
 - Mixed evidence, most recent meta-analysis was negative
- Cannabis
 - Insufficient evidence
 - Possible short-term benefits vs chronic risk



EMERGING PTSD TREATMENTS (CONT.)

TMS

- Multiple meta-analyses with conflicting evidence
 - One with evidence for particular kind of TMS (rDLPFC)
 - Two suggest no difference compared to placebo

Stellate Ganglion Blocks

- Limited, mixed evidence and few RCTs

Hydrocortisone

- Some evidence for IV administration immediately post trauma or in first 3 months after trauma
- Little evidence for effectiveness in chronic PTSD

THANK YOU!

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