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OUTLINE

1. Medication updates

2. Updates on new treatments for refractory or challenging conditions

3. Drug interactions with psychiatric medications

UPDATES FOR DEPRESSION

Duloxetine (6) (Irenka): SNRI

- Indications: MDD, GAD, diabetic neuropathy
- Benefits: also relieves anxiety and other types of pain
- *Common* adverse events: drowsiness, nausea, constipation
- *Serious* adverse events: allergic or skin reaction, serotonin syndrome

UPDATES FOR DEPRESSION

Vortioxetine (5) (Trintellix): serotonin modulator

- Inhibits serotonin reuptake, antagonizes 5-HT3 receptors, agonizes 5-HT1A receptors
- Indication: MDD
- Benefits (6): less likely to cause weight gain than SSRIs, TCAs, MAOIs
- *Common* adverse events: nausea, vomiting, constipation.
- *Serious* adverse events: suicidality, serotonin syndrome, bleeding.

UPDATES FOR DEPRESSION

Brexanolone (5) (Zulresso): allopregnanolone analog

- positive allosteric modulator of GABA-A receptors
- Indication: postpartum depression
- Benefits: cost-effective compared with SSRIs
- *Common* adverse events (6): drowsiness, lightheaded, dry mouth, flushing
- *Serious* adverse events (5): CNS depression, loss of consciousness, worsening depression (6)
- Controlled substance: must enroll in the REMS program

UPDATES FOR DEPRESSION

Dextromethorphan / Bupropion HCl (5) (Auvelity)

- Dextromethorphan: MOA unknown, but antagonizes NMDA receptors, agonizes sigma-1 receptors
- Bupropion: NDRI (Norepinephrine-Dopamine Reuptake Inhibitor)
- Indication: MDD
- Benefits: 1st of its kind, efficacy as early as 1 week (12)
- *Common* adverse events (6): dizziness, diarrhea, dry mouth, sweating, headache, somnolence, sexual dysfunction
- *Serious* adverse events: seizures, HTN, mania, serotonin syndrome (???)

UPDATES FOR DEPRESSION

Aripiprazole (5) (Abilify): 2nd gen. antipsychotic, given orally

- MOA unknown, but partially agonizes D2 and 5-HT1A receptors, antagonizes 5-HT2A receptors
- Indications: schizophrenia, BP-I (manic/mixed), MDD (as adjunct)
- Benefits: efficacy similar to risperidone; less adverse events than olanzapine & risperidone (13)
- *Common* adverse events (6): blurry vision, sialorrhea, stiffness, weight gain, nausea, somnolence
- *Serious* adverse events: neuroleptic malignant syndrome, extrapyramidal sx, leukocytopenia, hyperglycemia, seizure, impulsivity

UPDATES FOR DEPRESSION

Aripiprazole lauroxil (5) (Aristada): 2nd gen. antipsychotic, given by injection

- MOA unknown, but partially agonizes D2 and 5-HT1A receptors, antagonizes 5-HT2A receptors
- Indications: schizophrenia (any for MDD?)
- Benefits: long-acting
- *Common* adverse events (6): akathisia, pain at injection site, weight gain, somnolence
- *Serious* adverse events: neuroleptic malignant syndrome, extrapyramidal sx, leukocytopenia, hyperglycemia, seizure, impulsivity, heat/cold intolerance

UPDATES FOR DEPRESSION

Brexpiprazole (5) (Rexulti): 2nd gen. antipsychotic.

- Partially agonizes D2 and 5-HT1A receptors, antagonizes 5-HT2A receptors
- Indications: MDD, schizophrenia, dementia-associated agitation
- Benefits (6): once-daily dosing
- *Common* adverse events: weight gain, somnolence, dizziness, restlessness
- *Serious* adverse events: neuroleptic malignant syndrome, extrapyramidal sx, suicidality

UPDATES FOR DEPRESSION

Cariprazine (5) (Vraylar): 2nd gen. antipsychotic

- MOA unknown, but partially agonizes D2 and 5-HT1A receptors, antagonizes 5-HT2A receptors
- Indications: schizophrenia, BP-I (manic/mixed or depressive), MDD (as adjunct)
- Benefits (6): once-daily dosing
- *Common* adverse events: myoclonus, nausea, vomiting, somnolence, akathisia
- *Serious* adverse events: neuroleptic malignant syndrome, extrapyramidal sx, leukocytopenia, hyperglycemia, seizure, CVA, agitation

UPDATES FOR DEPRESSION

Lumateperone (5) (Caplyta): 2nd gen. antipsychotic

- MOA unknown, but antagonizes D2 and 5-HT2A receptors
- Indications: schizophrenia, BP (depressive)
- Benefits (14): lower risk of antipsychotic adverse events
- *Common* adverse events (6): nausea, dizziness, somnolence, dry mouth
- *Serious* adverse events: neuroleptic malignant syndrome, extrapyramidal sx, leukocytopenia, hyperglycemia, seizure

UPDATES FOR DEPRESSION

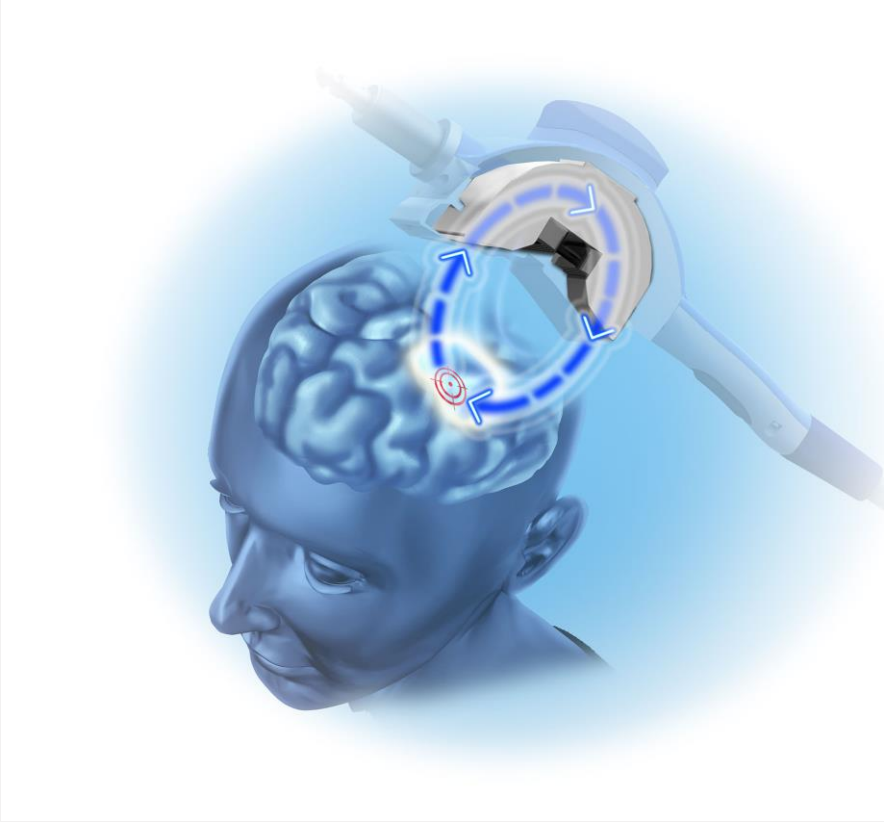
Olanzapine / Samidorphan (5) (Lybalvi): 2nd gen. antipsychotic

- Olanzapine MOA unknown, but antagonizes dopamine, 5-HT2
- Samidorphan antagonizes mu opioid receptors, partially agonizes delta & kappa
- Indications: schizophrenia, BP-I (manic/mixed)
- Benefit: decreased weight gain compared to olanzapine alone
- *Common* adverse events (6): somnolence, dry mouth, increased appetite
- *Serious* adverse events: CVA in elderly with dementia-related psychosis, neuroleptic malignant syndrome, respiratory depression

WHAT IS TMS?

- TMS = Transcranial Magnetic Stimulation

- Consists of placing an electromagnetic coil on the patient's head, delivering magnetic pulses that pass into and either stimulate or inhibit the cortex, depending on pulse frequency. (8)



TRANSCRANIAL MAGNETIC STIMULATION (TMS)

TMS* TYPES & INDICATIONS

- *Repetitive* TMS (rTMS) indications include:
  - Treatment-resistant depression – focused on the L dorsolateral prefrontal cortex (2)
  - "anxious" depression
  - OCD – focused on the dorsomedial prefrontal cortex (2)

- *Deep* TMS (dTMS) indications include the same as for rTMS, plus smoking addiction

*TMS = Transcranial Magnetic Stimulation

TMS* TYPES

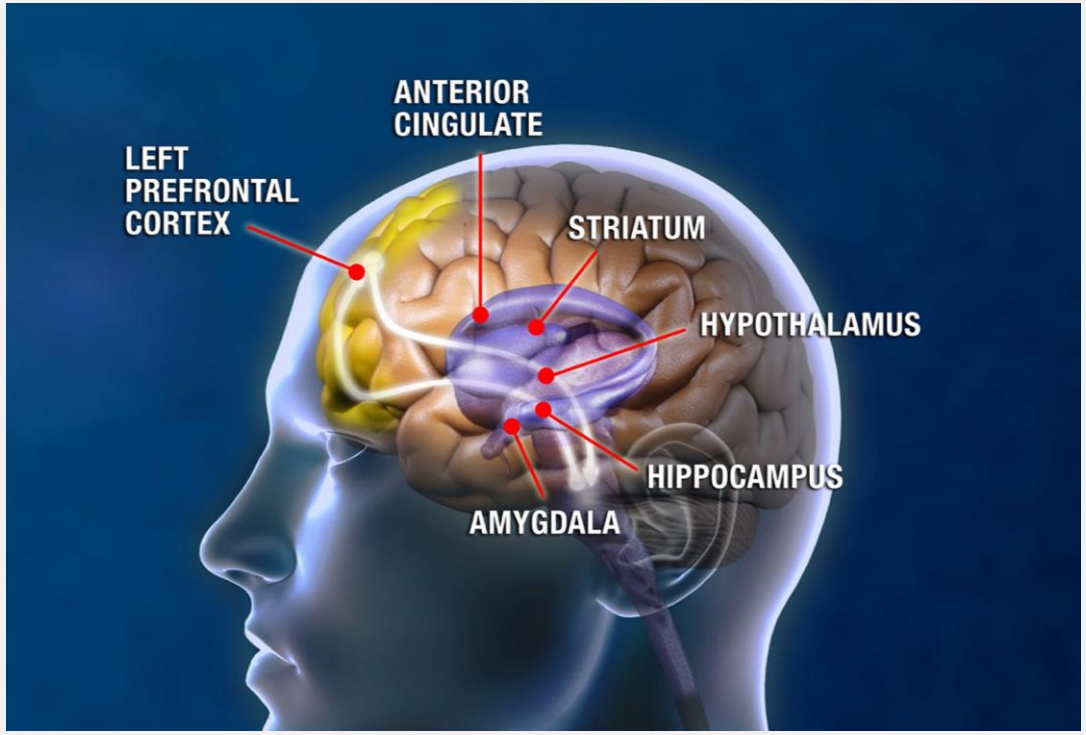
- *Repetitive* TMS (rTMS):
  - "TMS involves passing an electrical current through a coil placed against the scalp. The rapidly changing electrical current creates a time-varying magnetic field, which passes unimpeded through the scalp and skull and induces an electrical field in the cortex. This electrical field changes neuronal activity at the site of stimulation and within interconnected neuronal networks" (1)
- *Deep* TMS (dTMS):
  - dTMS uses an "[H-coil] to affect extensive neuronal pathways, including deeper cortical regions and fibers targeting subcortical regions, without a significant increase of the electric field induced in superficial cortical layers" (1)
- Contraindicated with seizure disorders and non-MRI-safe metal within the head or neck (eg pacemakers, spinal cord stimulators)

*TMS = Transcranial Magnetic Stimulation

TMS* BENEFITS & ADVERSE EVENTS

- Benefits
  - Non-drug, non-invasive, transient AEs (3)
  - Discontinuation rate due to AEs was only 4.5% (3)
  - Long-lasting symptom relief. “Among 120 patients who met IDS-SR response or remission criteria [for depression] at the end of acute treatment [with TMS], 75 (62.5%) continued to meet response criteria throughout long-term follow-up” (4)
- Adverse events
  - Most common AEs are transient headaches and treatment-site scalp discomfort (3)
  - Other AEs include sleepiness and seizures

*TMS = Transcranial Magnetic Stimulation



TMS*, THE TREATMENT

- Electromagnetic pulses focus on the left dorsolateral prefrontal cortex (9)

- Treatment is 2x weekly for first 4 weeks, then reassess
  - If continuing, change to weekly for 4 more weeks, then reassess
  - If continuing, change to every other week

*TMS = Transcranial Magnetic Stimulation

ESKETAMINE INDICATION

- An **NMDA** receptor antagonist (5)
- The **nasal spray** form is **indicated** for Treatment-Resistant Depression (TRD) and acute suicidality (when taken with an oral antidepressant) (7)
- *The infusion form is not FDA-approved for the above.*

ESKETAMINE ADVERSE EVENTS

- *Common* AEs:
  - dissociation, dizziness, nausea, sedation (5)
  - all resolve typically within that same day (7)

- *Serious* AEs: sedation, dissociation, dependence, suicidality, HTN, cognitive impairment (5), bladder problems (7)

ESKETAMINE ADMINISTRATION [7]

- REMS*-approved, making it a controlled substance
- Patients must enroll in the REMS program to monitor effects and prevent misuse
- Must receive treatment in clinic
- Treatment is followed by 2 hours of monitoring for BP or EKG changes, dissociation, sedation

*REMS = Risk Evaluation and Mitigation Strategy

ESKETAMINE, AFTER TREATMENT [7]

- Patients must not drive or operate machinery until *after* a full night's sleep.
- This means planning for transport to and from treatments.

DRUG INTERACTIONS: CYP1A2 (10,11)

Substrates	Inhibitors	Inducers
Caffeine	*Fluvoxamine*	Phenytoin
Haloperidol	Fluoxetine	Phenobarbital
Olanzapine, clozapine	Paroxetine	Carbamazepine
Duloxetine	Sertraline	Tobacco
TCAs	Cimetidine	Modafinil
Mirtazapine		Rifampin
Asenapine		

DRUG INTERACTIONS: CYP2C9 (10,11)

Substrates	Inhibitors	Inducers
Warfarin	*Fluoxetine*	Rifampin
ARBs	Valproic acid	Carbamazepine
NSAIDs	*Fluconazole*	
Glipizide	*Miconazole*	
	Amiodarone	

DRUG INTERACTIONS: CYP2C19 (10,11)

Substrates	Inhibitors	Inducers
BZDs	*Fluvoxamine*	Carbamazepine
PPIs	Fluoxetine	Valproic acid
SSRIs (citalopram)	Cimetidine	Phenytoin
Amitriptyline	Omeprazole	Phenobarbital
	Ketoconazole	Rifampin

DRUG INTERACTIONS: CYP2D6 (10)

Substrates	Inhibitors	Inducers
Beta blockers (S-metoprolol, timolol)	*Fluoxetine, Paroxetine*	None ???
TCAs (eg amitriptyline)	Clomipramine	
Antipsychotics (eg haloperidol, risperidone, aripiprazole)	Haloperidol	
Amphetamine	Cimetidine	
Dextromethorphan	Methadone	
Duloxetine	Duloxetine	
	Ritonavir	
	Bupropion	
	Quinidine	

DRUG INTERACTIONS: CYP3A4 (10)

Substrates	Inhibitors	Inducers
HIV antivirals (eg ritonavir)	*Ritonavir, indinavir*	*Carbamazepine*
Macrolides (eg erythromycin, but NOT azithromycin)	Erythromycin, *clarithromycin*	Phenobarbital
Quinidine	Amiodarone, diltiazem, verapamil	Phenytoin
Benzodiazepines (eg alprazolam, diazepam)	Fluvoxamine	Rifabutin
Immune modulators (eg cyclosporine, tacrolimus)	*Ketoconazole*, *itraconazole*	*Rifampin*
	Grapefruit juice	St. John's wort
		Troglitazone

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