#### Psychotropic Medications Explained:

### A Practical Overview for Mental Health Providers

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#### Objectives:

- Examine common medications used to treat:
  - Major Depressive Disorder (MDD)
  - Generalized Anxiety Disorder (GAD)
  - Bipolar Disorder
  - Post-Traumatic Stress Disorder (PTSD)
  - Attention-Deficit/Hyperactivity Disorder (ADHD)
- Identify the main classes of medications used to treat common psychiatric disorders: antidepressants
  (SSRIs, SNRIs), mood stabilizers, antipsychotics, benzodiazepines, and stimulants. Also, understand their
  primary indications, mechanisms of action, and therapeutic benefits.
- Review potential side effects and risks associated with commonly prescribed psychiatric medications.
- Examine the newest psychotropic medications and emerging treatments of Major Depressive Disorder (MDD), Anxiety disorders, Bipolar Disorder, Post-Traumatic Stress Disorder (PTSD), and Attention-Deficit/Hyperactivity Disorder (ADHD).

#### Drug Nomenclature:

- -Generic Name fluoxetine (not capitalized)
  - Most states require pharmacists to offer generic when available unless prescriber designates otherwise
- →Brand or Trade Name Prozac (capitalized, symbol R with a circle around it)

(Bloom, 2023)

### Pharmacological Classification:

- →Drugs are classified based on their mechanism of action (MOA)
- Drugs in a particular classification include only those drugs that have the same or similar MOA (Bloom, 2023)
  - Example: Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs): Inhibit the reuptake of serotonin and norepinephrine from the synapse into the presynaptic neuron

### Drugs in a Pharmacological Class Have Similar Attributes:

- ► FDA Indications
- **►**MOA
- Contraindications and precautions
- → Interactions
- Adverse reactions and side effects

### Psychotropics:

-Medications used to treat mental health disorders

Most commonly, psychotherapeutic medications work by altering the activity of neurotransmitters.

 Neurotransmitters are the body's chemical messengers, which transmit messages or signals from neuron (nerve cell) to neuron (NIH, 2023)

### Five Main Classes of Psychotropic Medications:

- Antidepressants
- Antipsychotics
- → Anti-anxiety
- Mood Stabilizers
- → Simulants

Treatments of Major Depressive Disorder

# Major Depressive Disorder (MDD): Antidepressants

- Neurotransmitters including dopamine, norepinephrine, and serotonin are key players in mood regulation
- Original Monoamine Hypothesis of Depression: Patients with depression are deficient in serotonin, norepinephrine, and dopamine
  - Contemporary research links depression to repeated exposure to stress/chronic stress
  - Stress increases cortisol levels in the brain
- Antidepressants may serve as a stimulus in activating brain- derived neurotrophic factor (BDNF)
  - This could explain why antidepressants can take two weeks or longer to take effect (Liu, et al., 2017; Wegmann, 2021)

# Major Depressive Disorder (MDD): Antidepressants

- Antidepressant Medications:
  - Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
  - Atypical antidepressants
    - → Tricyclic Antidepressants (TCAs)
    - Monoamine Oxidase Inhibitors (MAOIs)
    - Hybrids

### Major Depressive Disorder (MDD): Antidepressants – SSRIs

- Examples include: fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa), escitalopram (Lexapro)
- Mechanism of Action (MOA): Block the reuptake of serotonin
  - ➤ Well-tolerated
  - Safer in overdose
- → Side Effects:
  - Often transient (with exception of weight gain)
  - Activation, nausea, insomnia, sexual dysfunction
    - Often anorgasmia, impotence is rare
  - Late onset side effects: Apathy and decreased spontaneity
- Monitor for "serotonin syndrome" (hyperthermia, muscle rigidity, cardiovascular collapse)
- Also used to treat obsessive compulsive disorders, general and social anxiety disorders, panic disorder, post-traumatic stress disorder, premenstrual dysphoric disorder, and bulimia nervosa (Bloom, 2023; Preston & Johnson, 2019; Wegmann, 2021)

### Major Depressive Disorder (MDD): Antidepressants – SNRIs

- Examples include: duloxetine (Cymbalta), venlafaxine (Effexor), desvenlafaxine (Pristia), and levomilnacipran (Fetzima)
- MOA: Block the reuptake of serotonin and norepinephrine
- → Side Effects:
  - Less sexual dysfunction compared to SSRIs
  - → May increase blood pressure
- Duloxetine may be beneficial in patients who have co-occurring pain disorders (Wegmann, 2021)

### Major Depressive Disorder (MDD): Antidepressants – Atypical

- Bupropion (Wellbutrin)
  - → MOA: Blocks reuptake of norepinephrine and dopamine
  - May be added to SSRI as adjunctive treatment or to offset sexual side effects
  - FDA approved for smoking cessation
- Remeron (Mirtazapine)
  - → MOA: Works indirectly on norepinephrine and serotonin
  - Beneficial for sleep, anxiety, and increasing appetite
  - May cause weight gain (Wegmann, 2021)

# Major Depressive Disorder (MDD): Antidepressants – TCAs

- Examples include: amitriptyline, clomipramine, doxepin, imipramine, trimipramine, desipramine, nortriptyline
  - MOA: Primarily block reuptake of serotonin and norepinephrine
  - Block acetylcholine and histamine receptors
  - Inhibit sodium and calcium channels
- Second-line treatment due to less tolerable side effects and toxicity in overdose (Hirsh & Birnbaum, 2023)

### Major Depressive Disorder (MDD): Antidepressants – MAOIs

- Examples include: tranylcypromine (Parnate), phenelzine (Nardil), selegiline (Emsam)
  - MOA: Inhibit the enzyme monoamine oxidase, which breaks down serotonin, dopamine and norepinephrine
  - Most effective of the antidepressants, particularly for atypical depression
  - Prescribed as last resort due to severe side effects such as hypertensive crisis, food and drug interactions, potentially fatal drug-drug interactions, and withdrawal symptoms (Wegmann, 2021)

#### Major Depressive Disorder (MDD): Antidepressants – Hybrid Antidepressants

- Vilazodone (Viibryd)
  - MOA: Similar action of the SSRIs with added anxiolytic actions of buspirone (Buspar)
  - Fewer sexual side effects and less incidence of weight gain
- Vortioxetine (Trintellix)
  - → MOA: Similar to Viibryd
  - Fewer sexual side effects and less incidence of weight gain (Wegmann, 2021)

### Major Depressive Disorder (MDD): Additional Augmentation Strategies

- Lithium (Eskalith)
  - Primarily used in treatment of bipolar disorder
  - Effective in treatment resistant depression and reducing suicidal thinking
- Stimulants
- Liothyronine (Cytomel)
- Antipsychotics
  - Aripiprazole (Abilify), olanzapine/fluoxetine (Symbax), quetiapine (Seroquel), brexpiprazole (Rexulti), and cariprazine (Vraylar), most recently approved in 2021 (Heldt, 2017)

- Esketamine (Spravato) nasal spray (isomer of ketamine)
  - Approved in 2019 as adjunctive treatment in combination with antidepressants for treatment-resistant depression (TRD)
  - Schedule III controlled substance
  - Medication is self-administered intranasally under supervision of a provider
  - Patients must be monitored for 2 hours due to potential for increase in blood pressure
  - Patients are not permitted to drive on the day medication is administered
  - Benefits are immediate and maintained with continual use
  - Doses per week decrease as you get further into treatment. Maintenance is one dose every 1-2 weeks (Wegmann, 2021)

#### Intravenous Ketamine

- General anesthetic, NMDA receptor antagonist
- Used off-label for TRD
- Demonstrated effectiveness in multiple randomized controlled trials
- Three infusions week one, two infusions week two, then once per week for three weeks
- Dosed monthly for maintenance (Wegmann, 2021)

- Dextromethorphan-Bupropion (Auvelity):
  - MOA: Norepinephrine-dopamine reuptake inhibitor and NMDA receptor antagonist
  - Approved in 2022 for treatment of MDD in adults
  - May be difficult to get covered by insurance (UpToDate, n.d.)

- Cariprazine (Vraylar)
  - Antipsychotic with dual action at D2 and D3 receptors
  - Previously approved for treatment of schizophrenia and all poles of bipolar
  - 2022 received FDA approval as adjunctive treatment to antidepressants for treatment of MDD
  - Low risk of metabolic and motor side effects (Sachs et al., 2023)

### Treatments of Anxiety Disorders

#### Anxiety Disorders

- Most Common Anxiety Disorders
  - Generalized anxiety disorder (GAD)
  - Social anxiety disorder (SAD)
  - Panic disorder
  - Phobia related disorders

Antidepressants: SSRIs and SNRIs are considered first-line treatment when considering pharmacotherapy (NIH, 2024)

### Anxiety Disorders: Treatments

#### Benzodiazepines

- Examples include: lorazepam (Ativan), clonazepam (Klonopin), alprazolam (Xanax), temazepam (Restoril)
- ➤ MOA: Work on GABA receptor
- Used effectively short-term or while titrating antidepressant
- Not recommended for long-term use due to potential for tolerance, abuse addiction, and worsening symptoms
- Side effects: Sedation, cognitive and memory impairment, dizziness, and falls in elderly (Heldt, 2017)

#### Buspirone (Buspar)

- MOA: Serotonin receptor partial agonist
- Does not work on GABA receptors, thus, not sedating
- Minimal to no withdrawal effects or addiction potential
- Counsel patients it does not work immediately and may take several weeks (Heldt, 2017)

### Anxiety Disorders: Treatments

- Propranolol (Inderal)
  - MOA: Beta Blocker that crosses blood brain barrier
  - Used to treat hypertension, glaucoma and migraine headaches
  - Helpful in treating anxiety conditions, specifically performance anxiety (off-label)
- Gabapentin (Neurontin)
  - MOA: Anticonvulsant, similar to GABA, blocks calcium channels
  - Schedule V controlled substance
  - Works to reduce anxiety by acting as an anxiolytic (off-label)
  - Similar relief to benzodiazepines, with less risk of tolerance and abuse (Heldt, 2017)
- Hydroxyzine (Vistaril or Atarax)
  - → MOA: Antihistamine
  - Used off-label to treat anxiety
  - Side effect of sedation (Heldt, 2017)

### Treatments of Bipolar Disorder

#### Bipolar Disorders: Mood Stabilizers

- Lithium (Eskalith)
  - MOA: widely unknown
  - Single most effective medication available for treatment and prevention of both manic and depressive episodes in bipolar
  - One of two medications (clozapine) proven to have anti-suicide effect
  - Not used first- line due to extremely narrow therapeutic window
  - Harsh side effect profile that may permanently impact multiple organs in the body
  - → Teratogenic in pregnancy (Wegmann, 2021)

#### Bipolar Disorders: Anticonvulsants

- Examples include: divalproex (Depakote), lamotrigine (Lamictal), carbamazepine (Tegretol), and topiramate (Topamax)
- Divalproex (Depakote)
  - MOA: inhibits sodium channels, and increases GABA
  - Extremely effective in treating and preventing manic episodes
- Lamotrigine (Lamictal)
  - MOA: widely unknown, thought to inhibit sodium channels
  - Effective in treatment and prevention of bipolar depression, with little effect on mania
  - Well-tolerated
  - Risk of Steven-Johnson Syndrome
    - ➤ Life threatening dermatological disease that can result in sloughing of epidermis (medical emergency)
    - → To mitigate start dose low and increase slowly (Bloom & Amber, 2017; Wegmann, 2021)

#### Bipolar Disorders: Anticonvulsants (cont'd)

- Carbamazepine (Tegretol)
  - MOA: Inhibits sodium channels and impacts GABA
  - Effective in treatment and prevention of manic episodes
  - High incidence of drug-drug interactions
  - Not recommended in pregnancy
  - May cause Stevens-Johnson Syndrome (Wegmann, 2021)

#### Bipolar Disorders: Antipsychotics

- Examples include: Olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), paliperidone (Invega), ziprasidone (Geodon), lurasidone (Latuda), aripiprazole (Abilify), cariprazine (Vraylar), and clozapine (Clozaril)
  - MOA: Block dopamine and select serotonin receptors
  - Mainstay of treatment for schizophrenia
  - May be sedating
  - Metabolic side effects: weight gain, hyperlipidemia, hyperglycemia
  - Motor side effects such as Parkinson like symptoms, akathisia, tardive dyskinesia, and dystonia (Wegmann, 2021)

#### Bipolar Disorders: Updates in Bipolar Treatment

- Antipsychotic: Lumateperone (Caplyta)
  - →Approved in 2020 for the treatment of schizophrenia and bipolar depressive episodes
  - Lower risk of weight gain and motor side effects

# Treatments of Post-Traumatic Stress Disorder (PTSD)

#### Post-Traumatic Stress Disorder (PTSD)

- Trauma Focused Psychotherapy is still the mainstay of treatment
- Medications are used to target symptoms such as nightmares and hyperarousal
- ► Antidepressants
  - Examples include: SSRIs-paroxetine (Paxil) and sertraline (Zoloft) are FDA approved to treat PTSD
- Mood Stabilizers
  - Potential benefit with the use of mood stabilizers in conjunction with other treatment modalities
- Atypical antipsychotics
  - May assist in reducing flashbacks, anxiety, and improving sleep

### Post-Traumatic Stress Disorder (PTSD) (cont'd)

- Benzodiazepines
  - Commonly prescribed, although benefits are not well proven clinically
  - May be used at low doses to assist in sleep
  - Caution advised due to high prevalence of co-occurring substance use disorders in this population
- Steroids
  - ► It is hypothesized people who have lower cortisol levels post trauma may benefit from cortisone treatment immediately after trauma
- MDMA and ketamine
  - These drugs have psychedelic properties that may reduce anxiety, improve relaxation, promote feelings of euphoria and well-being
  - May assist in tolerance of exposure therapy (Wegmann, 2021)

# Treatments of Attention-Deficit Hyperactivity Disorder (ADHD)

### Attention-Deficit Hyperactivity Disorder (ADHD)

- Attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed behavioral disorder in children, and the numbers are expected to rise
  - → The CDC reported that in 2022, over 7 million (11.4%) U.S. children ages 3–17 years were diagnosed with ADHD, an increase of 1 million compared to 2016
    - The elevated numbers aren't limited to children.
    - According to a 2021 report in the Journal of Managed Care & Specialty Pharmacy, 8.7 million adults in the U.S. have ADHD

#### -Psychostimulants

Two main classes: methylphenidate (MPH) and amphetamine (AMP)

#### Attention-Deficit Hyperactivity Disorder (ADHD)

#### Psychostimulants

- Two main classes: methylphenidate (MPH) and amphetamine (AMP)
- Both are delivered into the body and reach the brain through various delivery mechanisms
  - ▶ Immediate-release
  - Osmotic-release
  - ▶ Time- release
  - ▶ Transdermal system
  - ▶ Pro- drug release

- ► Immediate- Release Delivery Mechanism
  - Examples include: Ritalin, Focalin, Dexedrine, and Adderall
  - Pill formulation
  - Absorbed rapidly in 30 minutes
  - Peak serum levels attained in 60-90 minutes
  - ► Last for about 2-3 hours
  - Dose at least three times per day

#### Osmotic-Release

- Referred to as osmotic- release oral system (OROS)
- Example: Concerta (only available as MPH)
- ► MOA: Osmotic pump system
- Comprised of an outer layer immediate-release drug overcoat methylphenidate, with an inner core that releases methylphenidate at a steady rate over 6-8 hours via an osmotic pump
- ► Taken once daily, but mimics three times per day dosing with immediate release
- ▶ Due to slow- release mechanism, Concerta is good for patients who need greater control of symptoms later in the day compared to morning hours

- ▶ Time-Release
  - Available as MPH and AMP
  - Examples include: Ritalin LA, Focalin XR, Metadate CD, and Adderall XR
  - Capsule formulation containing the active ingredient in form of coated beads
    - ▶ Beads dissolve at different times over 8 hours, making the medication timereleased
    - Capsules can be opened and sprinkled on food
  - ► Also available in liquid formulations
    - Example includes: Quillivant XR (methylphenidate ER suspension)
    - Similar to long-acting Ritalin, but in liquid from making dosage titration easier
    - Great for children who have trouble swallowing solid formulations

- Transdermal
  - Available as MPH
  - Example: Daytrana patch
  - Patch applied each morning and removed at 5pm to allow drug to eliminate from body
  - May cause permanent depigmented skin
- Pro-Drug
  - Available as AMP
  - Examples include: Vyvanse (the only pro-drug available)
  - ▶ MOA: Similar to Adderall XR, however, Adderall can be open, crushed and snorted
  - ▶ Vyvanse remains inactive until swallowed and absorbed in stomach. Once absorbed, it converts to active ingredient dAMP which then enters bloodstream

- Stimulant Side Effects
  - Generally well tolerated, even with long-term use
  - Common side effects: loss of appetite, weight loss, headache, nausea, anxiety, irritability, motor tics, muscle tension, and insomnia
  - Abuse potential due to increase in dopamine in the reward center of brain
    - ▶ This is rare when taken appropriately in pill or capsule form

## Attention-Deficit Hyperactivity Disorder (ADHD): Non-Stimulant Options

- Antidepressants
  - ► Bupropion (Wellbutrin)
    - ► MOA: Enhance actions of norepinephrine and dopamine in the prefrontal cortex
    - ► Simulants are still superior in clinical trials
    - ► May be used to treat co-occurring depression
    - ▶ Not a controlled substance
  - Atomoxetine (Strattera)
    - ► MOA: Norepinephrine reuptake inhibitor
    - ▶ Black box warning pertaining to risk of suicide in children and adolescents
    - ► Simulants are still superior in clinical trials
    - ▶ No long- term safety data available in children
    - ▶ Has been linked to liver damage

## Attention-Deficit Hyperactivity Disorder (ADHD): Non-Stimulant Options

- Alpha-2 Agonists
  - Guanfacine ER (Intuniv)
    - ► MOA: Antihypertensive medication that works on prefrontal cortex to improve executive function
    - ▶ Used to treat anxiety, aggression, irritability, tics, and Tourette's syndrome
    - Approved to treat children/adolescents (ages 6-17)
    - ➤ Side effects: often mild, but may be related to low blood pressure (headache, nausea, drowsy, and changes in cardiac rhythm)

#### Attention-Deficit Hyperactivity Disorder (ADHD): New Treatments in ADHD

- Mydayis (AMP)
  - Similar to Adderall XR, but has a longer duration of 16-hours compared to 12 with Adderall
- Aptensio XR (MPH)
  - Similar to Concerta, but more rapid onset
- ► Jornay PM (MPH)
  - ► Taken at bedtime, and starts working 8-10 hours later
  - Good for children who have trouble remembering to take medication in the morning, and those who struggle with symptom management early in the morning

#### Attention-Deficit Hyperactivity Disorder (ADHD): New Treatments in ADHD

- Qelbree
  - ► Approved in 2020 for patients ages 6 and older
  - Non-stimulant option that inhibits the reuptake of serotonin and norepinephrine
  - ▶ Black- box warning for suicidal thoughts and behaviors
  - Side effect of sedation, but generally well-tolerated

(Nasser et al., 2022)

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