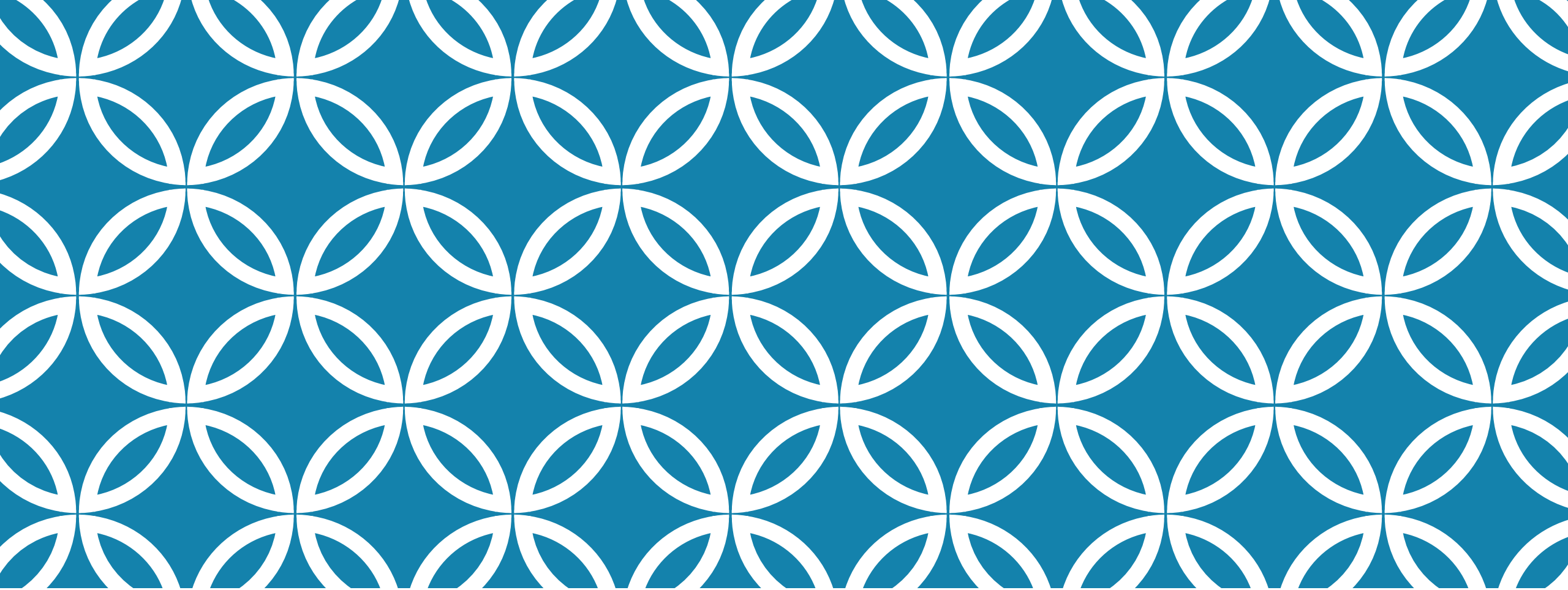


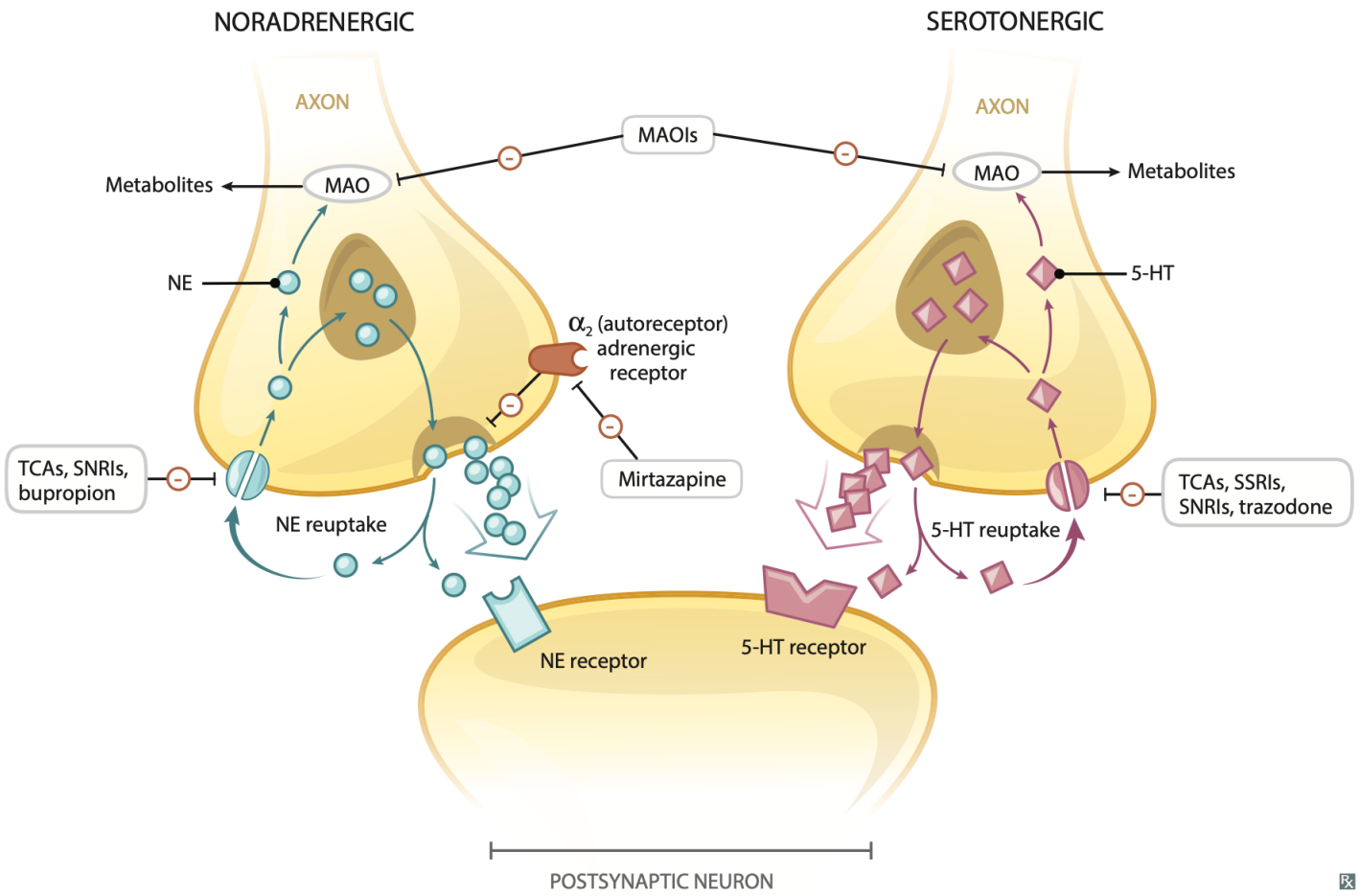
PSYCHOPHARMACOLOGY

DEPRESSION

The first major hypothesis of depression was formulated about 30 years ago and proposed that the main symptoms of depression are due to a functional deficiency of the brain monoaminergic transmitters norepinephrine (NE), 5-HT, and/or dopamine (DA), whereas mania is caused by functional excess of monoamines at critical synapses in the brain.

ANTIDEPRESSANTS

Antidepressants



ANTIDEPRESSANTS

Approximately 60 to 70% of patients with major depression will respond

to an antidepressant medication.

All antidepressants have similar response rates in treating major depression but differ in safety and side-effect profiles.

It usually takes 4 to 6 weeks on a given dose of an antidepressant for a

patient to fully beneit from a trial of the medication.

ANTIDEPRESSANTS

SSRI

SSNRI

Heterocyclic antidepressants

MAOIs

Miscellaneous

SSRI

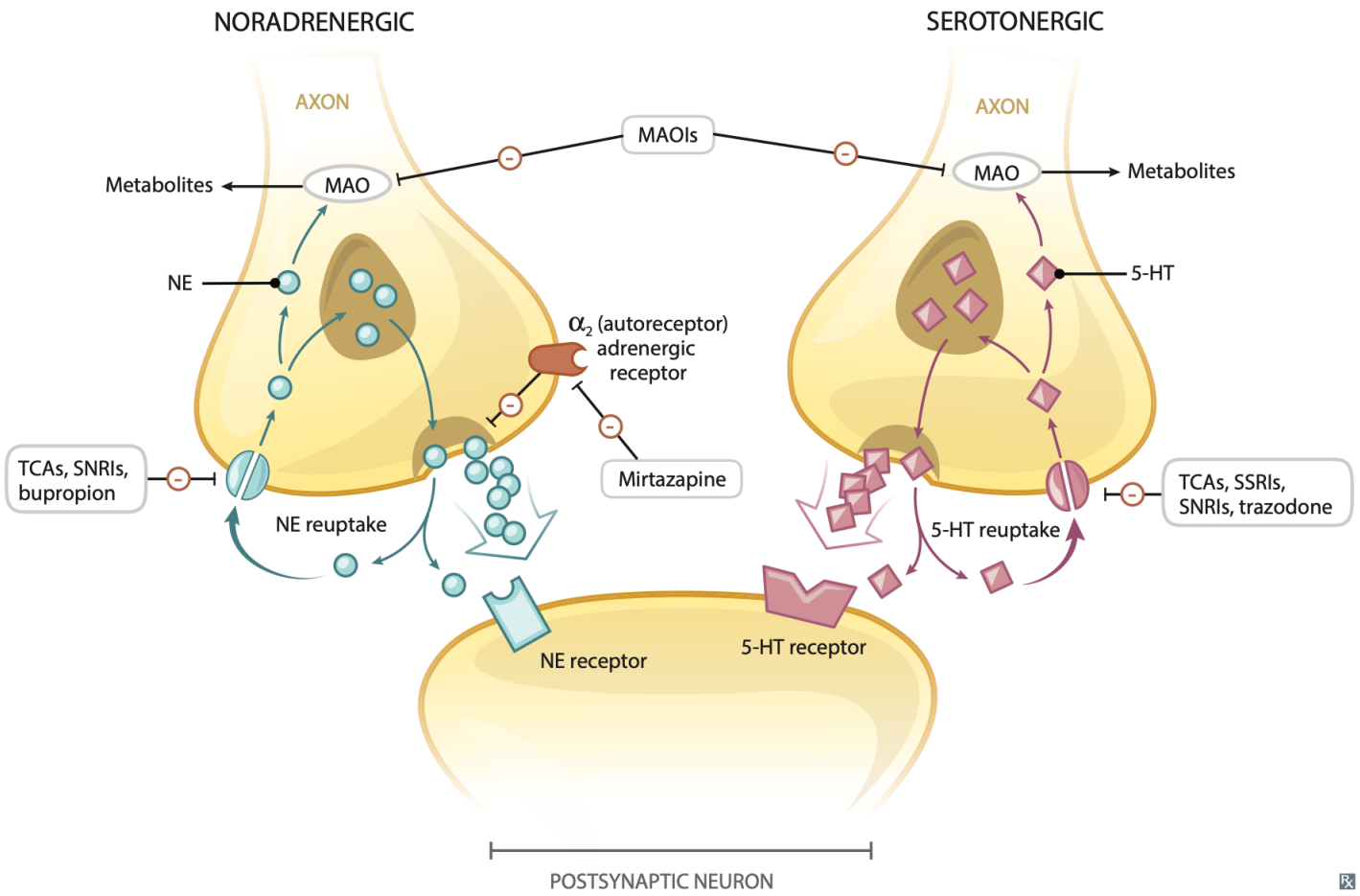
SSRIs inhibit presynaptic serotonin pumps that take up serotonin, leading to increased availability of serotonin in synaptic clefts. Additionally, SSRIs cause downstream effects increasing brain plasticity—this mechanism has been hypothesized to explain the delay to onset of antidepressant effect.

Usually dosed daily, except fluoxetine weekly.

Most commonly prescribed antidepressant due to low incidence of side effects, no food restrictions, and safer in overdose.

ANTIDEPRESSANTS

Antidepressants



SSRI

- Fluoxetine: Longest half life, safe in pregnancy.
- Sertraline: GI disturbances, few drug interactions
- Paroxetine: Inhibitor of CYP26, and anticholinergic side effects.
- Fluvoxamine: OCD
- Citalopram: QTc prolongation
- Escitalopram: QTc prolongation

SSRI

Side effects:

- GI disturbances
- Insomnia
- Headache
- Weight Change

- Sexual dysfunction
- Restlessness

- Serotonin Syndrome

SNRI

- Venlafaxine: MDD, GAD.

Similar safety profile to SSRI in addition to increased BP

- Duloxetine: MDD, neuropathic pain, fibromyalgia.

Similar safety profile to SSRI in addition dry mouth and constipation.

HETEROCYCLIC ANTIDEPRESSANTS

TCAs inhibit the reuptake of norepinephrine and serotonin

HETEROCYCLIC ANTIDEPRESSANTS

Tricyclic antidepressants:

Tertiary amines: Amitriptyline, Imipramine, Clomipramine, Doxepin.

More Anti-HAM side effects

Secondary amines: Nortriptyline, desipramine.

Less Anti-HAM side effects

Tetracyclic antidepressants:

Amoxapine

They are rarely used as first-line agents due to a higher incidence of side effects, titration of dosing, and lethality in overdose

MONOAMINE OXIDASE INHIBITORS

MAOIs include: Phenelzine, Tranylcypromine, Isocarboxazid

MAOIs prevent the inactivation of biogenic amines such as norepinephrine, serotonin, dopamine, and tyramine (an intermediate in the conversion of tyrosine to norepinephrine).

Used in refractory depression

Side effects:

Serotonin syndrome

Hypertensive crisis

Orthostatic hypotension

MISCELLANEOUS ANTIDEPRESSANTS

Bupropion:

Norepinephrine-dopamine reuptake inhibitor.

Relative lack of sexual side effects as compared to the SSRIs.

Effective for smoking cessation.

Weight neutral.

Side effects:

- Increased anxiety
- Increased risk of seizures
- Contraindicated in patients with epilepsy or active eating disorders, and in those currently on an MAOI.

MISCELLANEOUS ANTIDEPRESSANTS

Trazodone and Nefazodone:

Serotonin Receptor Antagonists and Agonists

Used in MDD, insomnia

Side effects: sedation, priapism, orthostatic hypotension.

Nefazodone no longer used for risk of liver failure.

MISCELLANEOUS ANTIDEPRESSANTS

Mirtazapine:

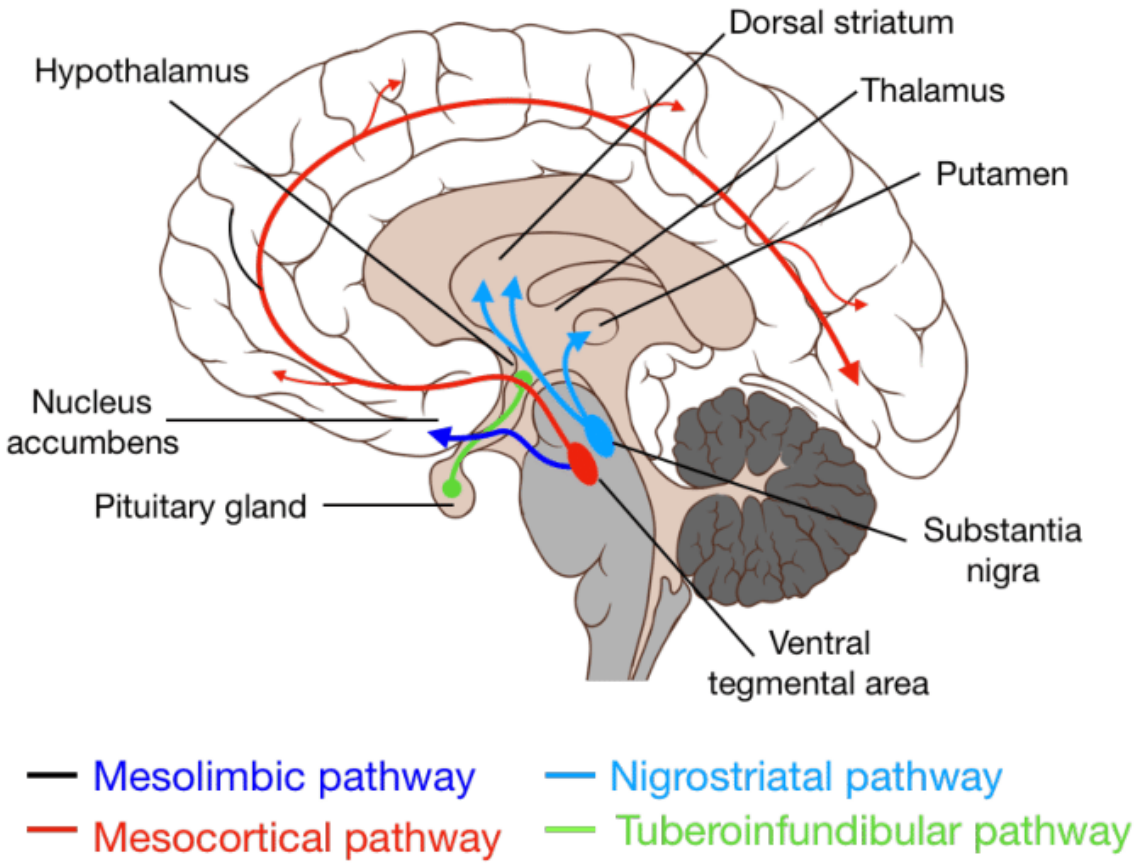
α2-Adrenergic Receptor Antagonists

Useful in the treatment of major depression, especially in patients

who have significant weight loss and/or insomnia.

Side effects: sedation, weight gain, anticholinergic effects, and (rarely) agranulocytosis.

DOPAMINE PATHWAYS



SCHIZOPHRENIA

This dopamine hypothesis attributes the positive symptoms of the illness to excessive activation of D2 receptors via the mesolimbic pathway, while low levels of dopamine in the nigrostriatal pathway are theorized to cause motor symptoms through their effect on the extrapyramidal system. Low mesocortical dopamine levels resulting from the mesocortical pathway are thought to elicit the negative symptoms of the disease.

ANTIPSYCHOTICS

Typical block dopamine receptors

Atypical block dopamine and serotonin receptors

Used primarily for positive symptoms

ANTIPSYCHOTICS

Typical antipsychotics differ in potency

Low potency antipsychotics: Chlorpromazine, Thioridazine

Mid potency: Loxapine, Thiothixene, Molindone, Perphenazine

High potency: Haloperidol, Fluphenazine, trifluoperazine, pimozide

Low potency have more anti-HAM side effects but less EPS

High potency have less anti-HAM side effects but more EPS

ANTIPSYCHOTICS

Side effects:

EPS: Akathasia, Dystonia, Parkinsonism, Tardive dyskinesia

Hyperprolactinemia

Anti-HAM

Neuroleptic malignant syndrome

ANTIPSYCHOTICS

Atypical antipsychotics: Clozapine, Olanzapine, Risperidone, Quetiapine,…..

Side effects:

Less likely to cause EPS, TD, or neuroleptic malignant syndrome.

Metabolic syndrome: weight gain, hyperlipidemia, hyperglycemia

Clozapine carries a risk of agranulocytosis

MOOD STABILIZERS AND ANTICONVULSANTS

Used for prevention and treatment of acute mania

Potentiation of antipsychotics

Treatment of aggression and impulsivity

Augmentation of antidepressants

LITHIUM

Lithium is the drug of choice in acute mania and as prophylaxis for both manic and depressive episodes in bipolar and schizoaffective disorders.

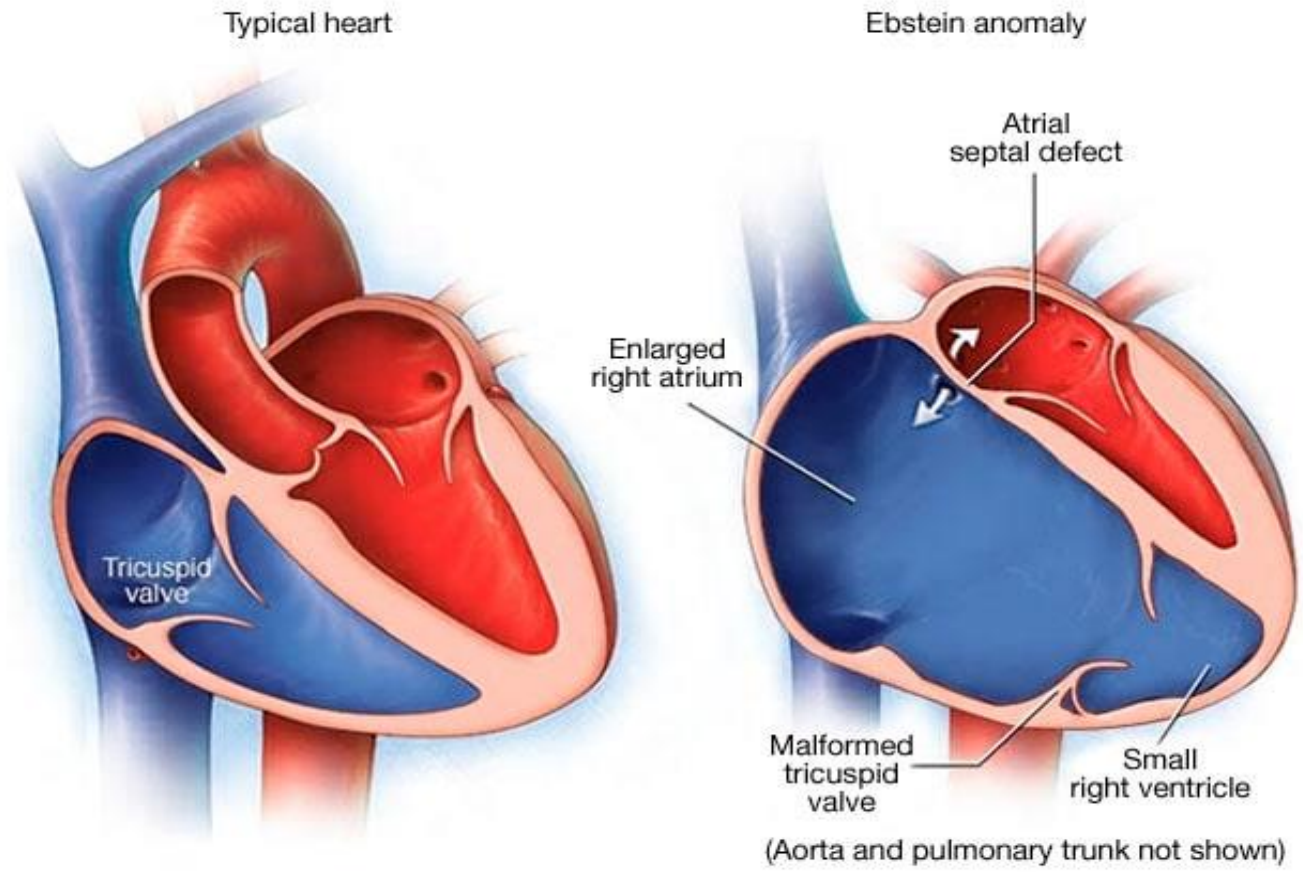
Narrow therapeutic index: therapeutic range: 0.6–1.2, Toxic: >1.5, Potentially lethal: >2.0

Renal metabolism

Prior to initiating, patients should have an ECG, basic chemistries, thyroid function tests, a complete blood count (CBC), and a pregnancy test.

Side effects: DI, tremor, thyroid imbalance, ecg changes, Ebstein anomaly

EBSTEIN ANOMALY



ANTICONVULSANTS

Carbamazepine: works by blocking sodium channels.

Side effects: SIADH, benign leukopenia, aplastic anemia, teratogenic neural tube defects, SJS.

Valproic acid: works by blocking sodium channels and increases GABA concentrations.

Side effects: teratogenic.

Lamotrigine: modulates glutamate and aspartate.

Side effects: SJS

Topiramate: helps with weight loss

ANXIOLYTICS

Benzodiazepines:

Potentiate GABA by increasing frequency of receptor opening

Barbiturates:

Potentiate GABA by increasing time of receptor opening

Buspirone:

Partial agonist at 5HT-1A receptor, thereby decreasing serotonergic activity.

Propranolol:

Beta-blocker

BENZODIAZEPINES

Long acting: Diazepam, Clonazepam.

Intermediate acting: Alprazolam, Lorazepam, Oxazepam, Temazepam

Short acting: Midazolam.

Risk of dependence

Overdose treated with flumazenil

HYPNOTICS

Zolpidem, Zaleplon, Eszopiclone: Selective binding to GABA-A which is responsible for sedation.

Diphenhydramine: Anti-histamine

Ramelteon: Melatonin agonist with no risk of dependency.

PSYCHOSTIMULANTS

Used in ADHD and refractory depression.

- Dextroamphetamines and amphetamines
- Methylphenidate
- Atomoxetine
- Modafinil: used in narcolepsy

Risk of abuse

COGNITIVE ENHANCERS

Acetylcholinesterase inhibitors:

Donepezil, Rivastigmine, Galantamine

NMDA antagonist:

Memantine

ASSORTED MEDICATIONS

Procainamide, quinidine: Confusion, delirium.

Albuterol: Anxiety, confusion.

Isoniazid: Psychosis.

Tetracycline: Depression.

Nifedipine, verapamil: Depression.

Cimetidine: Depression, confusion, psychosis.

Steroids: Aggressiveness/agitation, mania, depression, anxiety, psychosis.

PSYCHIATRIC EMERGENCIES

	CAUSE	MANIFESTATION	TREATMENT
Serotonin syndrome	Any drug that ↑ 5-HT. Psychiatric drugs: MAOIs, SSRIs, SNRIs, TCAs, vilazodone, vortioxetine, buspirone Nonpsychiatric drugs: tramadol, ondansetron, triptans, linezolid, MDMA, dextromethorphan, meperidine, St. John's wort	3 A's: ↑ activity (neuromuscular; eg, clonus, hyperreflexia, hypertonia, tremor, seizure), autonomic instability (eg, hyperthermia, diaphoresis, diarrhea), altered mental status	Cyproheptadine (5-HT_2 receptor antagonist) Prevention: avoid simultaneous serotonergic drugs, and allow a washout period between them
Hypertensive crisis	Eating tyramine-rich foods (eg, aged cheeses, cured meats, wine, chocolate) while taking MAOIs	Hypertensive crisis (tyramine displaces other neurotransmitters [eg, NE] in the synaptic cleft → ↑ sympathetic stimulation)	Phentolamine
Neuroleptic malignant syndrome	Antipsychotics (typical > atypical) + genetic predisposition	Malignant FEVER: Myoglobinuria, Fever, Encephalopathy, Vitals unstable, ↑ Enzymes (eg, CK), muscle Rigidity ("lead pipe")	Dantrolene, dopaminergics (eg, bromocriptine, amantadine), benzodiazepines; discontinue causative agent

PSYCHIATRIC EMERGENCIES

Delirium tremens	Alcohol withdrawal; occurs 2–4 days after last drink Classically seen in hospital setting when inpatient cannot drink	Altered mental status, hallucinations, autonomic hyperactivity, anxiety, seizures, tremors, psychomotor agitation, insomnia, nausea	Longer-acting benzodiazepines
Acute dystonia	Typical antipsychotics, anticonvulsants (eg, carbamazepine), metoclopramide	Sudden onset of muscle spasms, stiffness, and/or oculogyric crisis occurring hours to days after medication use; can lead to laryngospasm requiring intubation	Benztropine or diphenhydramine
Lithium toxicity	↑ lithium dosage, ↓ renal elimination (eg, acute kidney injury), medications affecting clearance (eg, ACE inhibitors, thiazide diuretics, NSAIDs). Narrow therapeutic window.	Nausea, vomiting, slurred speech, hyperreflexia, seizures, ataxia, nephrogenic diabetes insipidus	Discontinue lithium, hydrate aggressively with isotonic sodium chloride, consider hemodialysis
Tricyclic antidepressant toxicity	TCA overdose	Respiratory depression, hyperpyrexia, prolonged QT Tricyclic's: convulsions, coma, cardiotoxicity (arrhythmia due to Na^+ channel inhibition)	Supportive treatment, monitor ECG, $NaHCO_3$ (prevents arrhythmia), activated charcoal

NON-PHARMACOLOGICAL THERAPIES

Electroconvulsive Therapy:

Deep Brain Stimulation

Repetitive Transcortical Magnetic Stimulation

Light Therapy