Basic Concepts

Selective Action Drugs are selective in their action on the nervous system.

Sites of Action The location at which a drug interacts with the body to produce its effects.

Drug Action Terminology

Agonist A drug that mimics or enhances the effects of a neurotransmitter.

Antagonist A drug that blocks or inhibits the effects of a neurotransmitter.

Precursor A substance from which another substance is formed. AKA, the ingredients used to make a neurotransmitter.

Synthesis The process of creating a neurotransmitter from its precursors.

Storage The neurotransmitter is stored in vesicles until it is needed.

Release The neurotransmitter is released into the synaptic cleft when an action potential arrives at the axon terminal.

Binding The neurotransmitter binds to receptors on the post-synaptic neuron, causing a change in the neuron's activity.

Inactivation The neurotransmitter is removed from the synaptic cleft by reuptake or enzymatic degradation.

Mimetic Mimics the action of a neurotransmitter.

Direct Agonist Binds to the same receptor as the neurotransmitter and mimics its effects.

Indirect Agonist Binds to a different site on the receptor and enhances the effects of the neurotransmitter.

Direct Antagonist Binds to the same receptor as the neurotransmitter and blocks its effects.

Indirect Antagonist Binds to a different site on the receptor and blocks the effects of the neurotransmitter.

Inverse Agonist Binds to the same receptor as the neurotransmitter and produces the opposite effect.

Depolarizing or *Desensitizing Agent* A drug that causes the AP to stay in a depolarized state; refusing to let the neuron go through another AP, and it stays in the absolute refractory period. (Antagonist)

Neurotransmitter Classes and Related Molecules

Glutamate Synthesized from precursor glutamine by an enzyme called *glutaminase*. It is the most common excitatory neurotransmitter in the brain.

NMDA A type of glutamate receptor that is important for synaptic plasticity and memory formation.

Ketamine A drug that blocks NMDA receptors and is used as an anesthetic and antidepressant.

GABA Synthesized from precursor glutamate by an enzyme called *glutamic acid decarboxylase*. It is the most common inhibitory neurotransmitter in the brain.

Glycine An inhibitory neurotransmitter that is important for motor control and is synthesized from serine.

Excitatory Amino Acid Transporters (EAATs) Facilitates reuptake of glutamate from the synaptic cleft. Important to reduce excitotoxicity.

Excitotoxicity The process by which excessive stimulation of neurons by excitatory neurotransmitters leads to cell death. (ALS, Lou Gehrig's disease)

Amines (monoamines) Derived from amino acids.

- **Catecholamines** Derived from tyrosine. Includes dopamine, norepinephrine, epinephrine. Uses dopaminergic, noradrenergic, and adrenergic systems.
- **Indoleamines** Derived from tryptophan. (Serotonin, melatonin)

Peptides Endogenous opioids. (endorphins, enkephalins, dynorphins)

Acetylcholine (ACh) A neurotransmitter that is involved in muscle contraction, learning, and memory. It is synthesized from choline and acetyl-CoA by the enzyme choline acetyltransferase (ChAT).

Cholinergic Refers to neurons that use acetylcholine as their neurotransmitter.

Lipids Endocannabinoids.

- **Anandamide** An endocannabinoid that binds to cannabinoid receptors and is involved in pain modulation, appetite, and mood regulation. (Sanskrit for "bliss")

Gases Nitric Oxide (NO) diffuses across membranes and acts as neurotransmitters.

Nucleosides (adenosine) Involved in sleep regulation and has inhibitory effects on neurotransmission.

Colocalized When two or more neurotransmitters are released from the same neuron.

Enzymes and Proteins

Monoamine Oxidase (MAO) An enzyme that breaks down monoamines (dopamine, norepinephrine, serotonin) in the presynaptic neuron.

"Vagusstoff" The original name given to acetylcholine by its discoverer, Otto von Loewy.

Choline Acetyltransferase (ChAT) The enzyme that synthesizes acetylcholine from choline and acetyl-CoA.

acetylcholinesterase (AChE) Breaks down ACh into acetate and choline. The choline is taken back up by active transport and reused, and the acetate is broken down and eliminated.

Synaptic Structures and Neural Pathways

Neuromusclar Junction The synapse between a motor neuron and a muscle fiber.

Paravertebral Ganglion A ganglion located next to the spinal cord.

Sympathetic Chain A chain of ganglia that runs parallel to the spinal cord. This is the reason for when you get anxious, ALL of your body gets anxious.

Basal Forebrain Activates the cortex and facilitates learning.

Nucleus Basalis Projects to the cortex

Medial Septal Nucleus and *Nucleus of Diagonal Band* Projects to the hippocampus through the fornix for memory and learning.

Pedunculopontine nucleus (PPT) and Laterodorsal Tegmental Nucleus (LDT) Projects to the pons and thalamus to facilitate REM sleep generation.

Receptors

Nicotinic Receptors Agonist at low doses, but antagonist at high doses. Also iontropic. They are found predominately at the Neuromusclar Function in the PNS.

Muscarinic Receptors Comes from a hallucinogenic mushroom (Amanita muscaria). Predominates in the CNS, but also found in the PNS. They are metabotropic receptors.

Drugs and Toxins Affecting Acetylcholine

Curare (direct antagonist) A drug that blocks nicotinic receptors, causing paralysis.

Muscarine (direct agonist) A drug that activates muscarinic receptors, causing hallucinations and other effects.

Atropine (direct antagonist) A drug that blocks muscarinic receptors, causing pupil dilation and increased heart rate. Comes from the belladonna alkaloids (deadly nightshade) plant.

Scopolamine (direct antagonist) A drug that blocks muscarinic receptors, causing sedation and amnesia. Comes from the belladonna alkaloids (deadly nightshade) plant.

Botulinum Toxin A waste product of *Clostridium botulinum*, which are bacteria who grows without oxygen. It interferes with Ca^{2+} influx channels, preventing the release of ACh. Because Botox causes paralysis, it can interfere with emotional *expression* because it paralyzes muscles like the orbicularis oculi. Additionally, since we know that expression influences experience, when we paralyze these muscles, then the emotional *experience* is also negatively affected.

Botox Derived from botulinum toxin, a neurotoxin that blocks the release of ACh at the neuromuscular junction, causing paralysis. It is used for cosmetic purposes to reduce wrinkles by paralyzing facial muscles. It can also be used to treat various medical conditions such as chronic migraines, hyperhidrosis (excessive sweating), and muscle spasms. The effects of Botox typically last for several months before the muscle activity gradually returns.

Black Widow Spider Venom A neurotoxin that causes the release of ACh at the neuromuscular junction, causing continual release of ACh and paralysis.

Cobra and Krait Venom A neurotoxin that blocks the binding of ACh to nicotinic receptors, causing paralysis.

AchE Blockers Comes into contact with the enzyme that breaks down ACh, causing an increase in ACh in the synaptic cleft.

- **Parathion** Insecticide. Crosses the blood-brain barrier and causes CNS effects.
- **DFP (Diisopropylfluorophosphate)** It is used as a chemical warfare agent and can cause paralysis and respiratory failure.
- **Sarin** It is highly toxic and can cause convulsions, paralysis, and death.

Pralidoxime A drug that reactivates AChE, allowing it to break down ACh again. Also used as an antidote for nerve gas poisoning.

Diseases and Related Treatments

Myasthenia Gravis A disease that causes muscle weakness and fatigue. It is caused by an autoimmune response that attacks nicotinic receptors at the neuromuscular junction, leading to a decrease in ACh receptor availability.

***Neostigmine*, *Physostigmine* (Prostigmin, Antilirum)** Drugs that inhibit AChE. Does not cross the blood-brain barrier. Used to treat myasthenia gravis.

***Donepezil*, *Rivastigmine* (Aricept, Exelon)** Drugs that inhibit AChE. Cross the blood-brain barrier. Used to treat Alzheimer's disease and Parkinson's disease (only the cognitive part).

***Xanomelne*, *trospium chloride* (Cobenfy)** A drug that blocks the muscarinic receptors in the CNS, but not in the PNS. Used to treat schizophrenia.

Additional Neurotransmitter Synthesis/Metabolism and Neural Systems

Tyrosine Hydroxylase The rate-limiting enzyme in the synthesis of catecholamines.

Nigrostriatal System Starts in the substantia nigra and ends in the striatum (caudate nucleus and putamen).

Reserpine (**Raudixin**) Used to decrease blood pressure (Not in use anymore because it caused Parkinson's-like symptoms). Works by blocking monoamine transporters.

MPTP Neurotoxin for DA cells in the Nigrostriatal System (which is not endogenous).

MPPP Opioid analgesic drug.

Lewy Bodies Misfolded proteins that are found in the brains of people with Parkinson's.

Huntington's Chorea A genetic disorder that leads to uncontrolled movements and cognitive decline.

Pallidotomy A surgery that affects the Globus Pallidus to inhibit movement.

Choreoathetotic Movements Too much movement

Athetosis Slow continually writing movements

Choreic *to dance*; rapid, purposeless, involuntary movements.

Dopaminergic Drugs

***Deprenyl*, *Selegiline* (Eldepryl, Jumex)** Drugs that inhibit MAO, can slow down progression of the disease.

***Tetrabenazine* (Xenazine)** Drug that inhibits the DA vesicle transporters. It is used to treat Huntington's disease.

***Methylphenidate* (Ritalin)** A drug that increases DA and NE in the brain, used to treat ADHD, but can also be used for narcolepsy.

Neuropeptides and Sleep-Regulating Molecules

Hypocretine A neuropeptide that is involved in the regulation of sleep and wakefulness.

Orexin Another name for hypocretin; makes you want to eat.

***Suvorexant* (Belsomra)** An antagonist for the orexin receptor, which is used to treat insomnia.

TAK-994 OX2R (Orexin-2 receptor) agonist. Used to treat narcolepsy by stimulating the orexin receptors in the brain, promoting wakefulness and alertness.

Hcrt-1 Intranasal hypocretin-1 (orexin-1) agonist. Also treats narcolepsy by the same mechanism as TAK-994.

Opioids

Receptors

Mu Receptors Responsible for analgesia and euphoric effects.

Delta Receptors Responsible for analgesia.

Kappa Receptors Colocalized with certain catecholamines. Plays a role with analgesia and in learning and memory, emotional control, and stress response.

Endorphins Endogenous opioids that bind to mu receptors.

Enkephalins Endogenous opioids that bind to delta receptors.

Dynorphins Endogenous opioids that bind to kappa receptors.

Antagonists

***Naloxone* (Narcan)** An opioid antagonist that is used to reverse opioid overdoses. It works by blocking the effects of opioids at the mu-opioid receptors in the brain.

***Naltrexone* (Vivitrol)** An opioid antagonist that is used to treat alcohol and opioid dependence. It works by blocking the effects of opioids at the mu-opioid receptors in the brain, reducing cravings and withdrawal symptoms.

NonOpioid Pain Relief

VS-548 Used in acute post-surgical pain relief and has no addiction risk. It works by blocking Na^+ channels in PNS pain fibers.

NSAIDS

Proprionic Acid Derivatives These include Ibuprofen, naproxen, and ketoprofen.

Salicylates These include aspirin, diflunisal, and salsalate.

COX-2 Inhibitors These include celecoxib (Celebrex) and rofecoxib (Vioxx). They are used to treat arthritis and other inflammatory conditions. COX-2 is an enzyme that is involved in the production of prostaglandins, which are responsible for pain and inflammation.

Dopamine-Related Systems

Mesocortical System From ventral tegmental nucleus to prefrontal cortex, limbic CORTEX, hippocampus, all frontal lobes, and association areas of parietal and temporal lobes in primates. Involved with short-term memories, planning, and problem-solving.

Mesolimbic System (MLS) Responsible for reward and reinforcement. Runs from the ventral tegmental nucleus to the limbic system. Consists of the nucleus accumbens, amygdala, and hippocampus.