The Neurotransmitters

- **Acetylcholine**
  - **Synthesis**
    - CoA (mitochondria) → Acetyl-CoA → ChAT Choline Acetyl Transferase → ACh (destroyed by AChE)
  - found in
    - Pons (REM sleep)
    - Basal Forebrain (learning in cortex, LT memory)
    - Medial Septum (brain rhythms, ST memory in hippocampus)
    - PNS (muscle contraction)
  - **Receptors**
    - Mostly excitatory
    - Nicotinic: Ionotropic (Na⁺) stimulated by nicotine
    - Muscarinic: metabotropic (intracellular effects)
  - **Psychopharmacology**
    - 1st neurotransmitter discovered
    - Ach is involved in muscle contraction
    - Parasympathetic system: digestion, decrease in heart rate
    - Botulinum toxin blocks Ach release → paralysis, death, wrinkles
      - Produced by extremely poisonous bacteria
      - Naturally occurring
      - Used medically
    - Black widow spider venom promotes Ach release → convulsion, death
      - Agonist
    - Neostigmine (AChE inhibitor, does not cross BBB, PNS only) → reduces myasthenia gravis symptoms
      - Agonist
    - Atropine blocks Muscarinic receptors
      - Response to nerve gas
    - Curare blocks Nicotinic receptors → paralysis, surgical procedures

- **Mono Amines: Catecholamine**
- Synthesis
  Tyrosine (high protein foods) $\rightarrow$ enzyme $\rightarrow$ L-Dopa $\rightarrow$ Dopamine

- Found in
  - Midbrain
    - Substantia Nigra
      - Projects to Basal Ganglia (movement) = Nigro-striatal (Striatum = Caudate + Putamen)
    - Ventral Tegmental Area
      - Projects to limbic cortex (reinforcement, desire, emotions) = Mesolimbic
      - Projects to prefrontal cortex (planning, problem solving) = Mesocortical

- Receptors
  - Inhibitory or exhibitory

- Dopamine (DA)
  - Psychopharmacology
    - Pleasure system, positive reinforcement, drug addiction
    - Localized production, diffuse projections
    - Low levels $\rightarrow$ Parkinson’s Disease
      - Damage of the connections of Sub Nigra $\rightarrow$ Caudate
      - DA does not cross BBB
        - L-Dopa does
      - Deep brain stimulation (prevent tremors)
    - High levels $\rightarrow$ Schizophrenia
      - Chlorpromazine block Dopamine D$_{2/A}$ receptors
    - AMPT blocks the enzyme (Tyrosine $\rightarrow$ L-Dopa)
    - Reserpine prevents storage of monoamines in vesicles
    - Amphetamines & cocaine = DA reuptake inhibitors $\rightarrow$ addiction
      - Methamphetamine/crystal meth affects levels of NE
    - Methylphenidate/Ritalin treats Attention Deficit Disorders
    - Monoamine Oxidase destroys/oxidizes excessive monoamines
      - Found naturally in blood
      - Too much $\rightarrow$ depression
      - Destroyed by Deprenyl increasing vesicle content of DA
      - Inactivate free floating dopamine molecules

- Nor/Epinephrine (NE/E) aka Nor/Adrenalin
  - Synthesis
    - Tyrosine $\rightarrow$ L-Dopa $\rightarrow$ Dopamine $\rightarrow$ Norepinephrine
  - Found
    - Locus Coeruleus (dorsal Pons)
- Epinephrine (hormone) produced in adrenal medulla (gland above kidneys)
  - Wide projections throughout brain
  - Release at axonal varicosities (diffuse release)
    - Receptors
      - Excitatory or inhibitory
        - Metabotropic
    - Psychopharmacology
      - Vigilance and attention
      - Furasic Acid blocks synthesis of NE from Dopamine
      - Reserpine prevents storage of monoamines in vesicles $\rightarrow$ hypertension
      - Idazoxan blocks autoreceptors (stops regulation of release)

- Serotonin (5-HT)
  - Very localized production, diffuse projections
  - Synthesis
    - Tryptophan (food) $\rightarrow$ 5-HT $\rightarrow$ 5-Hydroxytryptamine (5-HT)
  - Found in
    - Raphe nuclei (midbrain)
    - Released at axonal varicosities (diffuse release)
  - Receptors
    - Excitatory or inhibitory
    - 9 kinds
  - Psychopharmacology
    - Mood, eating (5-HT3, vomiting), sleep (reaming), pain
    - PCPA blocks Tryptophan $\rightarrow$ 5-HTP reaction
    - Fluoxetine/Prozac inhibits 5-HT reuptake
      - Agonist
    - Fenfluramine inhibits 5-HT reuptake stimulating release $\rightarrow$ appetite suppressing
    - LSD has multiple sites of action
    - MDMA inverts reuptake of transporter’s direction
      - LT memory deficits

- (Neuro)Peptides
  - Synthesis
    - In the soma from many aminoacids
      - Need axoplasmic transport
    - 100 different kinds
    - Transmitters = Endogenous opioids (endorphins)
  - Found in
    - Many regions of CNS and PNS
    - Released at synaptic boutons & by volume transmission (leaking)
- Co-released with other neurotransmitters
- Deactivated by enzymes
  - No reuptake or recycling
- Receptors
  - Inhibitory
- Psychopharmacology
  - Opium, morphine, heroine (opiates) bind to/open opiate receptors
    - Analgesics, reinforcers
  - Codeine converted in liver into morphine binding to opiate receptors
  - Naloxone is a competitive blocker of opiate receptors preventing overdose
  - Angiotensin in the PNS to constrict blood vessels; in the CNS for thirst
- Lipids
  - Found
    - Non local
    - Produced on demand, not stored in vesicles
  - Receptors
    - Excitatory or inhibitory
      - Metabotropic
  - Psychopharmacology
    - Complex synaptic effects
    - THC is an agonist for CB1 and CB2
    - THC (analgesic, sedative, appetite enhancer, reduce nausea, chemotherapy) blocks 5-HT3
    - THC interferes with attention, distort perception of time and space, impairs learning and memory
    - Synthetic THC prescribed for chemotherapy and multiple sclerosis
    - Acetaminophen/Tylenol acts on CB1 receptors
    - Rimonabant blocks CB1 receptors
- Nucleosides
  - Synthesis
    - Sugar molecule bound to other compounds
      - I.e. Adenosine
  - Found
    - Non local
    - Adenosine released by astrocytes providing energy when needed
  - Receptors
    - Many
  - Psychopharmacology
    - Physiological = increase blood flow
    - Neural = decrease arousal (involved in sleep)
    - Caffeine is an adenosine receptor blocker


- **Soluble gases**
  - **Synthesis**
    - I.e. Nitric Oxide (NO) in neurons, no storage
  - **Round**
    - Non local
  - **Receptors**
    - None, they diffuse directly into neighboring neurons
    - Triggers second messenger cascades
  - **Psychopharmacology of NO**
    - Modulates intestine function (relaxation)
    - Stimulate erection (vasodilator)
      - Viagra is a no-inhibitor blocker
    - Involved in learning and memory