Acetylcholine (ACh)

1. **Synthesis**
   - \( \text{CoA} + \text{Acetate} \rightarrow \text{Acetyl-CoA} \) (mitochondria) (food, vinegar)
   - + Choline \( \rightarrow \text{ChAT} \rightarrow \text{CoA} + \text{ACh} \) (lipids, foods)
     - Destroyed by ACh-E

2. **Location**
   - Pons: REM sleep
   - Basal forebrain: learning cortex and long-term memory
   - Medial septum: brain rhythms and short-term memory (hippocampus)
   - PNS: muscle contraction

3. **Receptors:** Mostly Excitatory
   - Nicotinic: Ionotropic (\( \text{Na}^+ \))
     - Stimulated by nicotine and blocked by curare
   - Muscarinic: Metabotropic (intracellular effects)
     - Stimulated by muscarine and blocked by atropine

4. **Psychopharmacology**
   - First neurotransmitters discovered
- Involved in muscle contraction
- In PNS: ACh is responsible for digestion and lowering the heart rate
- Botulinum Toxin (BOTOX)
  i. Blocks ACh release
  ii. Antagonist
- Black widow venom
  i. Promotes ACh release
  ii. Agonist
- Neostigmine
  i. ACh-E inhibitor; reduces myasthenia gravis symptoms
  ii. Agonist
- Atropine
  i. Blocks muscarinic receptors; response to nerve gas
  ii. Antagonist
- Curare
  i. Blocks nicotinic receptors
  ii. Antagonist

Monoamines: Catecholamine: Dopamine (DA)
*localized production, diffused projections

1. Synthesis
   - Tyrosine \rightarrow \text{L-Dopa} \rightarrow \text{Dopamine}
     (high protein foods) (+ enzyme)

https://www.slideshare.net/siddharthadutta8/dopamine-dopaminergic-system-pharmacotherapy-and-modulation-70950944
2. **Location**
   - Midbrain
     i. Substantia nigra
        - Projects to basal ganglial nigrostratial pathway
     ii. Ventral tegmental area
        - Projects to limbic cortex and prefrontal cortex

3. **Receptors: Excitatory and Inhibitory**
   - D1, D2, D3, D4, D5

4. **Psychopharmacology**
   - “Pleasure” system, positive reinforcement and drug addiction
   - Parkinson’s disease: due to low levels of DA
     i. Damage connects to substantia nigra → caudate
     ii. Dopamine does not cross the BBB but **L-Dopa (agonist)** does
     iii. Deep brain stimulation, Prevents tremors
   - Schizophrenia: due to high levels of DA
     i. **Chlorpromazine (antagonist)** blocks dopamine D_{2/4} receptors
   - **AMPT**
     i. Blocks the enzyme that helps tyrosine turn into L-Dopa
     ii. **Antagonist**
   - **Reserpine**
     i. Prevents storage of DA monoamines in vesicles
     ii. **Antagonist**
   - **Amphetamines and Cocaine**
     i. DA re-uptake inhibitors: Addiction
        - I.E. methamphetamine and methylphenidate (Ritalin)
     ii. **Agonists**
   - Monoamine oxidase destroys (oxidizes) excessive monoamines
     i. Found naturally in blood, cheese and chocolate. Excess MAO is linked to depression.
     ii. **Deprenyl (agonist)** destroys MAO and increases vesicle content of DA
     iii. Inactivates “free-floating” dopamine

**Monoamines: Catecholamine: Nor/Epinephrine (NE/E)**
*very localized production, diffuse projections

1. **Synthesis**
   - Tyrosine → L-Dopa → Dopamine → Norepinephrine
2. **Location**
   - NE: locus coeruleus (dorsal pons)
   - E (hormone): produced in adrenal medulla (gland above the kidney)
   - Wide projections throughout the brain
   - Released at the axonal varicosities

3. **Receptors: Excitatory and Inhibitory**
   - Metabotropic: $\alpha$-adrenergic and $\beta$-adrenergic

4. **Psychopharmacology**
   - Vigilance and attention
   - **Fusaric acid**
     - i. Blocks NE synthesis from dopamine
     - ii. **Antagonist**
   - **Reserpine**
     - i. Prevents storage of NE monoamines in vesicles; hypertension
     - ii. **Antagonist**
   - **Idazoxam**
     - i. Blocks the autoreceptors
     - ii. **Agonist**

**Monoamines: Serotonin (5-HT)**
*localized production, diffuse projections

1. **Synthesis**
   - Tryptophan $\rightarrow$ 5-HP $\rightarrow$ 5-HT
2. **Location**
   - Mainly in the raphe nuclei (midbrain)
   - Released at the axonal varicosities (diffuse release)

3. **Receptors:** *Excitatory and Inhibitory*
   - 9 different kinds; They are labeled 5-HT<sub>x</sub> (i.e. 5-HT<sub>2A</sub>)

4. **Psychopharmacology**
   - Responsible for mood, eating (5-HT<sub>3</sub>; vomiting), sleep and pain
     - **PCPA**
       i. Blocks tryptophan
       ii. *Antagonist*
     - **Fluoxetine (Prozac)**
       i. Inhibits re-uptake of 5-HT
       ii. *Agonist*
     - **Fenfluramine**
       i. Inhibits the re-uptake of 5-HT
       ii. stimulates release of 5-HT
       iii. Suppresses appetite
       iv. *Agonist*
     - **LSD (acid)**
       i. Stimulates 5-HT<sub>2A</sub> receptors
       ii. *Agonist*
     - **MDMA (ecstasy)**
i. Inverts the re-uptake transporters direction
ii. Stimulates release of 5-HT
iii. Long-term memory deficits
iv. Agonist

(Neuro)peptides

1. Synthesis
   - In soma, from many amino acids; Axoplasmic transport is necessary
   - 100 different kinds (i.e. CCK, Substance P)
   - Transmitters: endogenous opioids (peptides released from brain that act like opiates)

2. Location
   - CNS and PNS
   - Released at synaptic boutons and through volume transmission (“leaking”)
   - Co-released with other neurotransmitters of the same vesicles
   - Reactivated by enzymes (re-uptake)

3. Receptors: Inhibitory
   - MANY!
   - Enkephalins: μ, δ, κ receptors
   - Opioid peptide: opiate receptors

4. Psychopharmacology
   - Opium, morphine, heroine
     i. Bind to and open the opiate receptors
     ii. Agonist
   - Codeine
     i. The liver converts it to morphine and it then binds opiate receptors
     ii. Agonist
   - Naloxone
     i. Competitive blocker of opiate receptors; Prevents overdose
     ii. Antagonist
   - Angiotensin
     i. PNS: constricts blood vessels
     ii. CNS: thirst

Lipids

1. Synthesis
   - Anandamide (endocannabinoids)

2. Location
   - ?
• Non-local
• Produced on demand
• Not stored in vesicles

3. Receptor: *Excitatory and Inhibitory*
   • Many metabotropic receptors
   • Named CB₁, CB₂… etc.

4. Psychopharmacology
   • Complex synaptic effects: THC is an agonist for CB₁ and CB₂
     • *THC*
       i. Sedative, appetite enhancer, reduces nausea, distorts time and perception, interferes with attention and impair learning and memory
       ii. Blocks the 5-HT₃ receptor
       iii. Stimulates CB₁ receptors
       iv. *Agonist*
     • *Acetaminophen*
       i. Acts on the CB₁ receptor
       ii. Stimulates release of DA
       iii. *Agonist*
     • *Rimonabant*
       i. Blocks the CB₁ receptor
       ii. *Antagonist*

*Nucleosides*

1. Synthesis
   • Sugar molecules bound to other compounds (i.e. adenosine)

2. Location
   • ?
   • Non-local
   • Adenosine is released by astrocytes

3. Receptors
   • MANY!
   • Adenosine: 3 types of receptors, Inhibitory through metabotropic K⁺

4. Psychopharmacology
   • Physiological
     i. Increases blood flow
   • Neural
     i. Decreases arousal
   • *Caffeine*
     i. Passes the BBB, fat soluble, passes through cell membranes
ii. Blocks adenosine receptors

iii. *Antagonist*

**Soluble Gases**

1. **Synthesis**
   - Nitric Oxide (NO): found within neurons and is not stored
   - Carbon Monoxide (CO)

2. **Location**
   - ?
   - Non-local

3. **Receptors**
   - NONE: diffuses directly
   - Triggers the second messenger cascades

4. **Psychopharmacology: For NO**
   - Modulates intestine function (relaxation)
   - Stimulates erection (vasodilator), NO is an inhibitor blocker (i.e. Viagra)
   - Learning and memory