Acetylcholine:

→ **How it is Synthesis:**

→ **Found where?**
- Pons (REM sleep)
- Basal forebrain (learning in cortex, long term memory)
- Medial septum (brain rhythms, short-term memory in the hippocampus)
- Peripheral nervous system (muscle contraction)

**Receptors:** mostly excitatory
- Nicotinic: inotropic (Na^+^+) stimulated by nicotine
- Muscarinic: meta botropic

**Psychopharmacology:**
- The first neurotransmitter discovered
- Ach is involved in muscle contractions
- In the parasympathetic system: digestion, decrease in heart rate

→ Botulinum toxin **blocks** Ach release (paralysis, death…wrinkles)
- Produced by bacteria, extremely poisonous, naturally occurred substance, used medically
→ AchE **destroys** Ach

→ Black Widow venom promotes

  - Ach release (convulsion, death)

→ Agonist

**Neostigmine** (AchE inhibitor, does not cross BBB, PNS only)

  • Reduces Myasthenia gravis symptoms

**Atropine** blocks muscarinic receptors (paralysis, surgical procedures)

**MonoAmines: Catecholamines**

**Dopamine**

**Synthesis:**
**Found where?**

↓**Midbrain (Mesencephalon)**

**Substantia nigra**
- Projects to basal ganglia (movement): Nigro - Striatal ←→ Striatum = Caudate + Putmen

**Ventraltegmental Area:**
- Projects to limbic cortex (reinforcement, desire, emotions): mesolimbic
- Projects to prefrontal cortex (planning, problem solving, mesocortical)

**Receptors**: excitatory or inhibitory
D1, D2, D3, D4

**Dopamine (aka DA)**

**Psychopharmacology:**
‘Pleasure system’, positive reinforcement: drug addiction, parkinson’s disease (low levels of dopamine)
→ damage to the connection: sub. Nigra → caudate
→ Dopamine does not cross BBB. L. Dopa does
→ deep brain stimulation:

  **Schizophrenia**
  
  High levels of dopamine
  → Chlorpromazine block dopamine D2/D4 receptors
  • AMPT blocks the enzyme (tyrosine → L. Dopa)
• Reserpine prevents the storage of monoamines in vesicles

→ Amphetamines & cocaine: DA reuptake inhibitors, addiction.
→ Methamphetamine = ‘crystal meth’ also effect levels of NE
→ Methylphenidate = ‘ritalin’ treat attention deficit disorder

-MonoAmine oxidase destroys (‘oxidizes’) excessive monoamines. Found naturally in blood (cheese / chocolate control)
   - Too much MAO is linked with depression
- deprenyl destroys MAOs and increases versicle content of DA

**MonoAmines: Catecholamines**

**Nor/epinephrine (NE/E)**

**Synthesis**
Tyrosine → L. Dopa → Dopamine → Norepinephrine

**Found Where?**
• Norepinephrine: Locus Coeruleus (dorsal Pons)

• Epinephrine (hormone) produced in adrena medulla gland above kidneys)

• Wide projections throughout the brain

• Release at axonal varicostilles (diffuse release)

**Receptors:** Excitatory or inhibitory
• Metabotropic: α - adrenergic, and β- adrenergic
• **α** (alpha)

• **β** (beta)

• They are linked to G proteins to activate a secondary messenger which binds and opens ion channels. There are 2 groups of adrenergic receptors, the alpha (α) and beta (β) which are divided in different subtypes.

**Psychopharmacology:**
• Vigilance and Attention

• *Fusaric Acid* blocks the synthesis of NE from dopamine

• *Reserpine* prevents the storage of monoamines in vesicles.

**Hypertension**

• *Idazoxan* blocks autoreceptors (i.e stops the downregulation of release)

**MonoAmines:**

**Serotonin (5-HT)**

Synthesis:
Tryptophan (food) → 5- HTP → 5- Hydrpxyptamine (5-HT)

Found where?
→ Mainly: Raphe nuclei (midbrain)
→ Released at axonal varicosities (diffuse release)
Receptors:
9 kinds: Labeled 5-HTxx

Psychopharmacology:
→ Mood, eating (5HT3 → vomiting) sleep (dreaming, pain)
  • PCPA blocks the tryptophan → 5 HTP reaction
  • Fluoxetine (prozac) inhibits 5 HT reuptake, St. Johns Wort, Anti-depressants and anxiolytics.
  • Fenfluramine inhibits 5- HT reuptake and stimulates release, Appetite suppressing.
  • LSD (aka ‘acid’ is a hallucinogenic multiple sites of action on 5-HT agonist for 5-HT 2A)
- MSDMA (aka 'ecstasy') invert reuptake transporters direction. Long term memory deficits

(Neuro) Peptides

**Synthesis:**
- In the soma, from many aminoacids. Need axoplasmic transport

- 100 kinds (ex: CCK, substance P, Oxycontin…)

- Neurotransmitters: Endogenous opioids (e.g Enkephalins, Endorphins)

**Found Where?**
- In many regions of the CNS and PNS

- Released at synaptic boutons, and volume transmission (i.e ‘leaking’)

- Co-released with other neurotransmitters (same vesicles)

- Deactivated by enzymes (re-uptake or recycling)

**Receptors:** Usually inhibitory
- Many!

- For enkephalins: \( \mu, \delta, \kappa \) receptors
• For opioid-peptides: opiate receptors

**psychopharmacology:**
• Opium, Morphine, Heroine (opiates): bind to/open opioid receptors. Analgesic, reinforcers


• Naloxone: competitive blocker of opiate receptors (prevents overdose)

• Angiotensin: PNS constrict blood vessels, CNS: thirst.

**Lipids**

**Synthesis**
• E.g. Anandamide (endo-CannaBinoids)

**Found where?**
• (non local) Produced on demand, not stored in vesicles.

**Receptor:** Excitatory or inhibitory
• Many metabotropic: CB1, CB2…

**psychopharmacology**
• Complex synaptic effects. THC is an agonist for CB1 and CB2
• THC (marijuana, hashish): Analgesic, sedative, appetite enhancer, reduce nausea,
  ◦ (chemotherapy), blocks 5-HT, (anti-vomiting), decrease asthma attacks

• THC interferes with attention, distort perception (time + space), impairs learning and memory
  ◦ MAY BE ADDICTIVE TO SOME INDIVIDUALS AT HIGH DOSES

• Synthetic THC prescribed for chemotherapy and Multiple Sclerosis

• *Acetaminophen* (Paracetamol, Tylenol): activates CB1 receptors. Analgesic

• *Rimonabant*: blocks CB1 receptors

---

**Nucleosides**

**Synthesis**

• Sugar Molecule bound to other compounds

• Ex: Adenosine

---

**Found Where?**
• Non local

• Adenosine: released by astrocytes (provide energy when needed)

**Receptors:**
• Many!

• For adenosine: 3 types of receptors. Inhibitory through a metabotropic $K^+$ channel
  
  ◦ Triggered by low energy and low oxygen signals

**Psychopharmacology:**
• Physiological: increase blood flow

• Neutral: decrease arousal (involved in sleep)

• *Caffeine* is an adenosine BLOCKER. Addictive (withdrawal symptoms), crosses placenta.

**Caffeine is not (yet?) illegal…**
• Caffeine passes through the BBB

• Caffeine is fat-soluble. Passes through cell membranes

**Soluble Gases**

**Synthesis:**
• E.g Nitric Oxide (NO): within neurons, no storage

• E.g carbon Monoxide (CO)

**From where?**
Non Local

**Receptors:**
None, diffuse directly into neighboring neurons
Triggers second messenger cascades

**Psychopharmacology (NO):**
• Modulates intestine function (relaxation).

• Stimulate erection (vasodilator. Viagra is an NO- inhibitor blocker

• Involved in learning and memory