Neurotransmitters

- **Acetylcholine**
  - **Found where**
    - Pons (REMS sleep)
    - Basal forebrain (learning in cortex, long-term memory)
    - Medial septum (brain rhythms, short term in the hippocampus)
    - Peripheral nervous system (muscle contraction)
  - **Receptors**
    - Mostly excitatory
    - Nicotinic: ionotropic (Na+), stimulated by nicotine
    - Muscarinic: metabotropic (intracellular effects)

- **Psychopharmacology**
  - The first neurotransmitter discovered
  - Ach is involved in muscle contractions
  - In the parasympathetic systems: digestion, decrease in heart rate
  - *Botulinum toxin* blocks ACh release (paralysis, death... wrinkles)
    - Produced by a bacteria. Extremely poisonous
    - Naturally occurring substance
    - Used medically
  - *Black widow spider venom* promoted ACh release (convulsion, death)
  - *Neostigmine* (AChE inhibitor, does not cross BBB, PNS ONLY)
  - *Atropine* blocks Muscarinic receptors
    - Response to nerve gas
  - *Curare* blocks nicotine receptors (paralysis, surgical procedures)

**Mono Amines**

- **Dopamine**
  - **Synthesis**
    - Tyrosine (high protein foods)
    - L-dopa
    - Midbrain
  - **Found where**
    - Substantia Nigra
      - Projects to Basal ganglia (movement): Nigro-striatal
    - Ventral tegmental 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, D5
  - **Psychopharmacology**
    - Pleasure system: positive reinforcement, drug addiction
    - Parkinson's disease (low levels of DA)
      - Damage of the connections: Sub nigra --> Caudate
      - Dopamine does not cross BBB. *L-Dopa* does
- Deep brain stimulation (prevent tumors)
- Schizophrenia (high levels of DA)
  - Chlorpromazine blocks Dopamine D2/4 receptors
- AMPT blocks the enzyme (Tyrosine → L-Dopa)
- Reserpine prevents the storage of monoamines in vesicles
- Amphetamines and cocaine = DA reuptake inhibitors. Addiction
  - Methamphetamine: 'crystal meth' (also affect levels of NE)
  - Methylphenidate: (= Ritalin) treat attention deficit disorders
- 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 vesicle content of DA

- Catecholamines
  - Synthesis
    - Comes from dopamine
  - Found where
    - Norepinephrine: locus Carolus (dorsal Pons)
    - Epinephrine (hormone) produced in the adrenal medulla (gland above the kidneys)
    - Wide projections throughout the brain
    - Release at axonal varicosities (diffuse release)
  - Receptors
    - Excitatory or inhibitory
    - Metabotropic: a-adrenergic, and B-adrenergic
  - Psychopharmacology
    - Vigilance and Attention
    - Fusaric Acid blocks the synthesis of NE from dopamine
    - Reserpine prevents the storage of monoamines in vesicles. Hypertension
    - Idazoxan blocks auto receptors (i.e. stops the regulation of release)

- Serotonin
  - Synthesis
    - Come from tryptophan to 5-HTP to 5-HT
  - Found where
    - Mainly: Raphe nuclei (midbrain)
    - Released at axonal varicosities (diffuse release)
  - Receptors
    - Excitatory or inhibitory
    - 9 kinds: labeled 5-HTxx. Ex. 5-HT2A
  - Psychopharmacology
    - Mood, eating (5-HT3 → vomiting), sleep (dreaming), pain
    - PCPA blocks the Tryptophan → 5-HTP reaction
    - Fluoxetine (Prozac) inhibits 5-HT reuptake. St. johns Wort. Anti-depressors and anxiolytics
    - Fenfluramine
      - inhibits 5-HT reuptake, and stimulate release
      - Appetite suppressing
    - LSD (aka acid)
      - is a hallucinogenic
- Multiple sites of action on 5-HT
- **Agonist** for 5-HT2A
- **MDMA (aka 'ecstasy')**
  - Invert reuptake transporters direction
  - Long-term memory deficits

- **Peptides**
  - **Synthesis**
    - In the soma, from many amino acids. Need axoplasmic transport
    - 100 kinds (ex: CCK, substance P, oxytocin)
    - Neurotransmitters: Endogenous opioids (e.g. Enkephalins, Endorphins)
  - **Found where**
    - In many regions of the CNS and PNS
    - Released at synaptic boutons, and by volume transmission (i.e 'leaking')
    - Co-released with other neurotransmitters (same vesicles)
    - Deactivated by enzymes (no re-reuptake or recycling)
  - **Receptors**
    - Usually inhibitory
    - MANY!
    - For enkephalins: mue, delt, kap receptors
    - For opioid-peptides: opiate receptors
  - **Psychopharmacology**
    - **Opium, morphine, heroine (opiates)**
      - binds to/open opiate receptors
      - Analgesics, reinforcers
    - **Codeine**
      - Cough suppressants
      - Converted in liver into morphine
      - binds opiate receptors
    - **Angiotensin**:  
      - PNS: constrict blood vessels, CNS: thirst

- **Lipids**
  - **Synthesis**
    - Anandamine (endo-Cannabinoids)
  - **Found where**
    - (non local)
    - Produced on demand, not stored in vesicles
  - **Receptors**
    - Excitatory or inhibitory
    - Metabotropic: CB
  - **Psychopharmacology**
    - Complex synaptic effects. THC is an agonist for CB1 and CB2
    - **THC** (marijuana, hashish)
      - Analgesics, sedative, appetite enhancer, reduce nausea
      - interferes with attentions
      - Distort perception of time (time+ space)
      - Impairs learning and memory
      - May be addictive in 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
    - Adenosine
  - **Found where**
    - Don’t know
    - Released by astrocytes (provide energy when needed)
  - **Receptors**
    - MANY
    - for adenosine: 3 types of receptors Inhibitory thought metabotropic K+ channels
      - Triggered by low energy and low oxygen signals
  - **Psychopharmacology**
    - **Physiological**: increase blood flow
    - **Neural**: decrease arousal (involved in sleep)
    - **Caffeine** is an adenosine receptor blocker.
      - Addictive (withdrawal symptoms)
      - Cross placenta
      - Passes through the BBB
      - Fat-soluble

- **Soluble gases**
  - **Synthesis**
    - E.g. nitric oxide (NO): within neurons, no storage
    - Carbon Monoxide (CO)
  - **Found where**
    - Non local
  - **Receptors**
    - None
    - Diffused directly into neighboring neurons
    - Triggers second messenger cascades
  - **Psychopharmacology (NO):**
    - Modulates intestine function (relaxation)
    - Stimulate erection (vasodilator)
      - **Viagra** is a NO-inhibitor blocker
    - Involved in learning and memory