Acetylcholine
- Synthesis:
  - CoA (mitochondria) + Acetate (vinegar, food) = Acetyl-CoA
- Found Where?:
  - Pons (REM sleep)
  - Basal Forebrain (learning in cortex, longer-term memory)
  - Medial Septum (brain rhythms, short-term memory in the hippocampus)
  - Peripheral nervous system (muscle contraction)
- Receptors: Mostly excitatory
  - Nicotonic: Ionotropic (Na), stimulated by nicotine
  - Muscarinic: Metabotropic (intracellular effects)
- 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 occurring substance, used medically
    - Black widow venom promotes ACh release (convulsion, death)
    - Neostigmine (AChE inhibitor, does not cross BBB, PNS only) reduces myasthenia gravis symptoms
    - Atropine blocks Muscarinic receptors, response to nerve gas
    - Curare blocks Nicotinic receptors (paralysis, surgical procedures)

Mono Amines: Catecholamines

DOPAMINE
- Synthesis: Tyrosine $\rightarrow$ L-Dopa $\rightarrow$ Dopamine
- Found Where?:
  - Substantia nigra: projects to basal ganglia (movement): Nigro-striatal
  - Ventral Tegmental Area
    - projects to limbic cortex (reinforcement, desire, positive 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 $\rightarrow$ Caudate
      - Dopamine does not cross the BBB, L-Dopa does
    - Deep brain stimulation (prevents tremors)
  - Schizophrenia (high levels of DA)
    - Chlorpromazine block Dopamine D2/4 receptors
  - AMPT blocks the enzyme (Tyrosine $\rightarrow$ L-Dopa)
- Reserpine prevents the storage of monoamines in vesicles
  - Amphetamines and cocaine = DA reuptake inhibitors, addiction
    - Methamphetamine: ‘crystal meth’ (also affects 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 increase vesicle content of DA
  - Dopamine: very localized production, diffuse projections

**NOREPINEPHRINE**
- Synthesis: Tyrosine $\rightarrow$ L-Dopa $\rightarrow$ Dopamine $\rightarrow$ Norepinephrine
- Found Where?:
  - Norepinephrine: Locus Coeruleus (dorsal pons)
  - Epinephrine (hormone) produces in adrenal medulla (gland above the kidneys)
  - wide projection 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 and Dopamine
  - Reserpine prevents the storage of monoamines in vesicles, hypertension
  - Idazoxam blocks autoreceptors (ie stops the regulation of release)

**SEROTONIN**
- Synthesis: Tryptophan (food) $\rightarrow$ 5-HTP $\rightarrow$ 5-HYDROXYTRYPTAMINE (5-HT)
- Found Where?:
  - mainly: raphe nuclei (midbrain)
  - released at axonal varicosities (diffuse release)
- Receptors: excitatory or inhibitory
  - 9 kinds
- Psychopharmacology
  - mood, eating (5-HT3 $\rightarrow$ vomiting), sleep (dreaming), pain
  - PCPA blocks the Tryptophan $\rightarrow$ 5-HTP reaction
  - Fluoxetine (Prozac) inhibits 5-HT reuptake, St Johns Wart, Anti-depressants, anxiolytics
  - Fenfluramine inhibits 5-HT reuptake and stimulate release, appetite suppressant
  - LSD is a hallucinogenic, multiple sites of action on 5-HT, agonist for 5-HT2A
  - MDMA, invert reuptake transporters direction, long-term memory deficits

**Neuro Peptides**
- Synthesis:
  - in the soma, from many amino acids, need axoplasmic transport
  - 100 kinds (CCK, substance P, oxytocin)
  - Neurotransmitters: endogenous opioids
- Found Where?:
  - in many regions of CNS and PNS
  - released at synaptic boutons, and by volume transmission (ie leaking)
- co-released with other neurotransmitters (same vesicles)
- deactivated by enzymes (no re-uptake or recycling)

- Receptors: usually inhibitory
  - many
  - for enkephalines: u, o, k receptors
  - for opioid peptides: opiate receptors

- Psychopharmacology:
  - Opium, morphine, heroin (opiates): bind to/open opiate receptors, analgesics, reinforcers
  - Codeine: cough suppressant, converted in liver into morphine, binds to opiate receptors
  - Naloxone: competitive blocker of opiate receptors (prevents overdose)
  - Angiotensin: PNS: constricts blood vessels, CNS: thirst

**Lipids**
- Synthesis: anadamide (endo-Cannabinoids)
  - Found Where?:
    - non local, produced on demand not stored in vesicles
- Receptors: excitatory or inhibitory
  - many, Metabotropic: CB1, CB2

- Psychopharmacology
  - complex synaptic effects, THC is an agonist for CB1 and CB2
  - THC: analgesic, sedative, appetite enhancer, reduce nausea, decrease asthma attacks
  - THC: interfere with attention, distort perception (time + space), impairs learning and memory, may be addictive in some individuals, at high doses
  - Synthetic THC prescribed for chemotherapy and multiple sclerosis
  - Acetaminophen (Tylenol): activates CB1 receptors, analgesic
  - Rimonabant: blocks CB1 receptors

**Nucleosides**
- Synthesis: sugar molecule bound to other compounds, Adenosine
  - Found Where?:
    - non local, for adenosine: three types of receptors, inhibitory through a metabotropic K channel, triggered by low energy and oxygen signals

- Psychopharmacology:
  - physiological: increase blood flow
  - neural: decrease arousal (involved in sleep)
  - caffeine is an adenosine receptor blocker, addictive (withdrawal symptoms), crosses placenta
  - passes through the BBB
  - caffeine is fat-soluble, passes through membranes

**Soluble Gases**
- Synthesis:
  - Nitric oxide (NO): within neurons, no storage
  - Carbon Monoxide (CO)

- Found Where?:
  - non local
- Receptors:
  - none, diffuse directly into neighboring neurons
  - triggers second messenger cascades

- Psychopharmacology:
  - modulates intestine function (relaxation)
  - stimulate erection (vasodilator), Viagra is an NO-inhibitor blocker
  - involved in learning and memory