Pharmacokinetics

- Psychopharmacology:
  - Study of the effects of drugs on behavior
- Pharmacokinetics
  - Study of the 'fate'/movement' of substances administered to the body
    - Administered
    - Absorption
      - Entering the body or a body compartment (e.g. brain)
    - Distribution
      - Being carried to specific target organs
    - Metabolism
      - Being broken down by enzymes
    - Excretion

Routes of administration

- Intravenous
  - Fast, precise, direct access to the brain
    - Example: Drug abuse, adrenaline
- Interpretational: fast. Indirect access to the brain
  - Example: Chemotherapy (cancer)
- Intramuscular
  - Slower (capillaries) direct access
    - Vaccines, antibiotics
- Subcutaneous
  - Slow absorption (fat tissue) in direct
    - Insulin
- Oral
  - Easy, delayed (has to go through stomach/ intestines and the liver)
    - Aspirin
- Sublingual
  - Easy (for humans) by pass digestive system, capillaries of the tongue
    - Steroids, cardiovascular (hypertension, vasodilator)
- Intrarectal
  - Slow bypass the stomach
    - Suppositories
- Inhalation
  - Fast, easy requires volatile substance
    - Nasal decongestion, drug abuse (MJ) asthma
- Topical administration
  - Fast local (skin, mucous)
    - Nasal spray, eye drops, ear drops (herpes, glaucoma)
- Intracerebral
  - By passing the BBB, local (specific brain area) mostly research
- Intra(Cerebro)/ventricular
  - By [ass the BBB, global effect emergency
- FDA considered 111 routes of administrations valid
- Epidural, intracardiac, transdermal

- Kinetics of absorption
  - Study of the effect on some specific brain areas
  - Movement through the BBB
  - Lipid-soluble (e.g. heroine) substance pass the BBB
  - Water-soluble substances (e.g. morphine) do not
  - Chart 4.1 in the book

- Effectiveness: Does-Response curve
  - If the effect was proportional to the number of drugs: linear curve
  - Most drugs: non-linear curve
  - Chart 4.2 in the book

- Effectiveness: affinity
  - Affinity = strength of the binding
  - Drugs may have the same end-results, but may vary in effectiveness
  - Different sites of action
  - Morphine
    - Analgesic: Inhibits pain perception neurons
  - Aspirin
    - Analgesic: suppress chemical signal from damaged cells to the nervous system
  - Different affinity
    - Drug binds to receptors

- Margin of safety
  - Drugs have multiple effects at different concentrations: morphine
• Therapeutic index
  ○ TI: measure of drug safety
  ○ Therapeutic index = LD50 / ED50
  ○ LD = lethal dose for 50% of the animals
  ○ ED = effective dose for 50% of the animals
  ○ Valium (tranquilizer, anxiety reducer): TI = 100
  ○ Barbiturates (anesthesia, anticonvulsants): TI = 3 requires measurements in the blood and monitoring

• Drug misuse / abuse
  ○ What kind of long term effects do drugs have?
  ○ Effects decrease with repeated (prolonged) use
    • **Tolerance**: need more drugs: compensatory mechanisms counteracting the effect of the drug
      ▪ e.g. decrease in affinity, decrease in receptor numbers
    • **Withdrawal**: symptoms compensatory mechanism alone. Opposite behavioral/emotional effects
      ▪ e.g. euphoria to depression
  ○ Effect increases with repeated (prolonged) use: **sensitization**
    • e.g. antidepressants need time to be effective
  ○ Effects can be psychological: **placebo effect**
    • Used mainly in research
      ▪ e.g. control for anxiety (in humans)
      ▪ e.g. Control for the effect of drug administration (animals)
  ○ Drug reinforcing effect depends on environment
    • e.g. nicotine and cues

• How do drugs work? Agonists, antagonist
  ○ An **agonist** has the same postsynaptic effect as a neurotransmitter
    • e.g. it opens receptors
    • Chart 4.5 in the book

○ Direct agonist > competitive binding = competes with neurotransmitter molecules
○ Indirect agonist > noncompetitive binding > does not compete with neurotransmitter molecules

• Drugs can interfere with reuptake and degradation
  ○ Reuptake
- e.g. prevent reuptake (treating depression)

- **Neurotransmitters**
  - Goal of neurotransmitters release
    - Post synaptic potentials (EPSP/ IPSPS)
  - Transmitter ID card
    - Synthesis and deconstruction
    - Pathway of release
    - Receptors
    - Disease + action of prescription drugs

- **Amino acids**
  - **Glutamate (glu, glutamic acid)**
    - Synthesis: from protein in food
    - Found where: everywhere in the CNS
    - Receptors
      - Always excitatory
      - Ionotopic for NA (AMPA, Kainite)
      - Ionotopic for Na and CA (NMDA)
      - Metabotropic glutamate receptor
    - Psychopharmacology
      - NMDA involved in learning and memory
      - AP% blocks the glutamate binding site on NMDA receptor
      - Alcohol blocks NMDA receptor
      - PCP (angel dust) blocks NMDA and blocks calcium entry in the cell.
        - Hallucinations and aggression
          - Also, animals model for schizophrenia
      - Too much glutamate binding results in excito-toxicity (cell death)
  - **GABA**
    - Synthesis: from glutamate
- Found where: everywhere in CNS
- Receptors
  - Always inhibitory
  - Ionotropic from Cl (GABAa)
  - Metabotropic for K (GABAg) Exists presynaptic (Autoreceptors)
- Psychopharmacology
  - Controls spread if excitation (epilepsy, seizures)
  - opens and bicollinear blocks GABAa
  - Benzodiazepines (anxiolytic, sleep promoter’s seizure reducers) opens GABAa
  - GABAa is blocked by picrotoxin (convulsions)
  - Barbiturates (low doses = anesthesia higher does = respiratory arrest, low TI) opens GABAa
  - Gamma-hydroborate (GHB, date rape drug) GABA agonist
- **Glycine**
  - Synthesis: found in sugar cane
  - Endogenous productions unknown. Non-essential (can be synthesized by the body, no need for external source)
  - Found where: mainly in the spinal cord
  - Receptors
    - Always inhibitory
    - Ionotropic for Cl
  - Psychopharmacology
    - Prevents excessive muscle contraction
    - Tetanus: bacteria produces a chemical that blocks Glycine release
    - Strychnine blocks the Glycine receptor (convulsion and death) used by animal accordingly