Chapter 5: Methods and Strategies Research

- Methods in Brain Research
  - Non-invasive (human):
    - Imaging:
      - CT Scan: computerized (Axial) Tomography (x-rays). Static pictures and high spatial resolution. Horizontal plane only.
        o Detailed 2-D pictures of the brain.
        o All planes
        o More sensitive than CT scan
        o Dynamic picture of the brain in action
        o Variant: Autoradiography (brain slices)
      - Functional MRI (fMRI): Modified MRI. Higher temporal resolution (~6-8 seconds), low spatial resolution.
      - DTI: Diffusion Tensor Imaging: Modified MRI. Image of bundles of axons and projection pathways.
    - MRI/fMRI
      - Imaging the brain 'in action'
      - Normal (research) and abnormal (clinical) functions
    - 2-DG
      - autoradiogram: invasive: brain sliced after 2-DG absorption
    - PET scan
      - Brain in action (e.g. movement)
        o Red= most active
        o Violet = least active
      - Brain areas that function differently (e.g. depression)
      - Brain areas that 'absorb' a particular drug (e.g. L-Dopa in Parkinson’s disease)
    - Diffusion Tensor Imaging (DTI)
      - Use of MRI data to compute the movement of water molecules (along the axon). Efferent projections.
  - Non-Invasive (human)
    - Electrical
      - Electroencephalography (EEG): recording surface electrical signals with macro-electrodes. High temporal resolution, low spatial resolution.
        - Sleep studies; seizure detection
      - Note: electrical and imaging:
- Optical recordings open skull, imaging electrical activity—used for research.

- **Magnetic**
  - Magnetoencephalography: detect small magnetic field generated by neurons.
  - More temporally precise than fMRI.
  - Need special equipment/room
  - Patients are seated
  - Seizure foci
  - Transcranial Magnetic Stimulation (TMS): create a magnetic field to induce an electrical current (stimulation). Mostly superficial brain (cortex).
    - Motor cortex → motor evoked potentials
    - Occipital cortex → phosphenes
    - Variant: repetitive TMS. Effects outlaw the period of stimulation. Research tool. Clinical tool (treat depression, mania, PTSD)

- **Genetic**
  - In humans: twin and adoption studies—Nature vs. Nurture
    - Monozygotic (identical): same chromosomes and genes
    - Dizygotic (fraternal): different chromosomes
      - Concordance for traits (e.g. schizophrenia, obesity, alcoholism), assess the influence of environment.
  - In Animals: Targeted gene mutation: changing or deleting a specific gene.

- **In vivo: behaving**
  - Ablation/ Lesion: Mapping brain areas to functions and functions to behaviors
  - Suction (mechanical), radio frequency (heat), excitotoxic lesions (spare axons)
  - Requires surgery. Small damage to insertion of electrode. Use of sham lesions for controls.
  - Variant: reversible lesions (use of specific chemicals, or colling).
    - Anesthesia: shut neurons off for a while
    - Lesions: knife cuts
      - E.g. split brains, epilepsy
      - Neurosurgeon: lesion of corpus callosum
    - Ultimate goal is the map the brain
  - Electrode implementation: wires lowered into particular area of interest of the brain

- **Invasive (Animals)**
- In vivo: behaving
  - Cannula implementation (injecting a chemical substance). Target particular receptors in specific brain areas.
  - Micro-dialysis: measuring the concentration of a specific chemical substance (e.g. neurotransmitter)
  - Optogenetics: Inject a virus in a brain area. The virus carries genes that will produce light sensitive proteins.
    - ChR2: sensitive to blue, depolarized the cell
    - NpHR: sensitive to yellow, hyperpolarize the cell
  - Implant an optical fiber that sines blue and/or yellow light with a laser
  - Manipulate the activity of specific cell types in specific brain area.
    - High temporal resolution
    - High spatial resolution
    - Cell specific
  - Single-unit recordings. Behavior: conditioning, learning and memory (maze)
    - E.g. learning, memory, drug addiction, decision-making, perception, etc.

- Animal – Anesthetized:
  - Stereotaxic surgery: use of an atlas and skull landmark (e.g. Bregma). Recording/stimulation. Also done in humans (local anesthesia).
  - Micro dialysis
    - E.g. study brain connectivity, single cell activity