Methods in Research

Non-Invasive (Human)

- **Imaging**
  - **Computerized (Axial) Tomography** (*CT scan*): x-ray of the brain, static pictures, and high spatial resolution, horizontal plane only
  - **Magnetic Resonance Imaging** (*MRI*): hydrogen atoms in a magnetic field, detailed static picture of the brain. Shows all planes, more sensitive than the CT scan
  - **Positron Emission Tomography** (*PET scan*): (need tracer: 2-deoxyglucose radioactivity put into the patient) measure of metabolic activity, dynamic pictures of the brain in action, brain slices. See brain light up when patient is told to think about certain things or do certain actions (Brain action like moving fingers, brain areas that function differently, brain areas that ‘absorb’ a particular drug
    - **Autoradiogram**: invasive: brain sliced after 2-DG absorption. Image obtained after ‘photographic-development like’ process (killing the animal, used for research)
  - **Functional MRI** (*fMRI*): modified MRI. Higher temporal resolution (about 6-8 seconds), low spatial resolution, imaging brain in action
  - **Diffusion Tensor Imaging** (*DTI*): modified MRI. Visualize a bundle of axons and projection pathways, use of MRI data to compute the movement of water molecules (along the axon). Efferent projections.

- **Electrical**
  - **Electrical** (*EEG*): recording surface electrical signals with ‘macro-electrodes’. High temporal resolution, low spatial resolution. Sleep studies, seizure detection, shows waves on a screen like aroused vs. relaxed waves

- **Magnetic**
  - **Magnetoencephalography** (*MEG*): detect small magnetic fields generated by neurons. More temporally precise than fMRI. Need special equipment/room patient is seated, seizure foci
  - **Transcranial Magnetic Stimulation**: create a magnetic field to induce an electric current (stimulation). Mostly superficial brain (cortex)
    - Stimulate in motor cortex → motor evoked potentials
    - Stimulate in occipital cortex → phosphenes
  - Variant: repetitive TMS.

- **Genetic**
  - In humans: twins and adoption studies - nature vs. nurture
    - Monozygotic (identical twins): same chromosomes, genes
    - Dizygotic (fraternal twins): different chromosomes
  - Concordance for traits (like schizophrenia, obesity, alcoholism), assess the influence of the environment
- **In animals**: targeted gene mutation - changing or deleting a specific gene
  - Still non-invasive

**Invasive (Animals)**
- *In vivo (behaving)*
  - Ablation/lesion: mapping brain area to functions, and functions to behaviors
  - Suction (mechanical), radio frequency (heat), excitotoxic lesions (spare axons)
  - Requires surgery. Small damage due to insertion of the electrode. Use of ‘sham’ lesions for controls
  - Variant: reversible lesions → use of specific chemicals or cooling
  - Recording/stimulation. Use microelectrodes. Clinical purposes when the patient is awake and the brain is open being stimulated. (has been used on humans)
  - Cannula implantation (injecting a chemical substance) target particular receptors in a specific brain area
  - Microdialysis: measure the concentration of a specific chemical substance
    - Substance is collected and analyzed
  - Optogenetics
    - Inject a virus into the brain, the virus carries genes that will produce light sensitive ion channels
      - ChR2: sensitive to blue, depolarizes the cell
      - NpHR: sensitive to yellow, hyperpolarizes the cell
    - Implant an optical fiber that shines blue and/or yellow light with a laser
    - Manipulate the activity of specific brain area
      - High temporal resolution
      - High spatial resolution
      - Cell specific
  - Single-unit recordings: activity of neurons while animals doing activities. Behavior, conditioning, learning, and memorizing. (maze)
    - Drug addiction, decision-making learning, perception
  - Stereotaxic surgery: use of a map and skull landmarks. Also done on humans. Recording and stimulation
    - Study brain connectivity, single cell activity, sleep
  - Study of brain tissue (extracted from the animal
    - Acute: brain slices, study o live single cells and small network properties, calcium imaging
    - Culture: a study of live single cells, and intracellular mechanisms

**Lesions: Knife Cuts**
- Like split brains for epilepsy
- Neurosurgery: lesions of the corpus callosum, a case where lesions are therapeutic; healing the patient