Cogs17 Neurobiology of Cognition

Lecture 3: Development

Embryonic Development

A new embryo develops three cell layers, outer layer = **Ectoderm**; mid-layer = **Mesoderm**; inner layer = **Endoderm**
- Ecto ==> Nervous system, skin; Meso ==> Bones, muscles, blood vessels; Endo ==> organs, glands
- Over first 2 weeks, embryo changes from a sphere of cells to an elongated "worm", still 3 layered
  - Then dorsal Ectoderm (along "back" of worm) begins to thicken and forms hard **Neural Plate**
  - Edges of plate form ridges (**Neural Folds**) that curl toward each other along a longitudinal line
    i.e from Rostral (head) end to Caudal (tail) end, until they touch and then fuse
- By week 4, edges of Neural Folds have fused, forming **Neural Tube** lined with Ectoderm, embedded in Mesoderm
  - **Spina Bifida** = Neural Folds fail to fuse => serious brain & cord defects: deformation, retardation, death
  - Rostral end of Neural Tube >> Brain, dividing into Forebrain, Midbrain & Hindbrain - Caudal end >> Spinal Cord
  - Surface of ridges (**Neural Crest**) later breaks away from tube >> Ganglia of ANS & Peripheral Neurons & Glia
  - Hollow center of tube will form 4 chambers (**Ventricles**) in brain & Central Canal of Cord, later filled w/CSF

Proliferation, Migration, Differentiation

Proliferation = Growth of new cells (Neurons and Glia Cells); Occurs primarily prenatally, some in infancy
- **Stem Cells** = Ectodermal cells that line the inside of the Neural Tube (the **Ventricular Zone)**
  - The Stem Cells that give rise to Neurons (or Glia) first proliferate by undergoing Symmetrical Division
    - That is, each Stem Cell divides, producing two identical cells, continuously increasing size of the V. Zone
  - ~Week 7, these cells shift to Asymmetrical Division, producing one identical Stem Cell and one Neuron
    - Asymmetrical Division lasts about 3 months producing ~100 billion Neurons in cortex alone!
    - Rate, type, and location of proliferation varies for what will become different areas of the brain
  - Stem Cells stay put, to divide again, but Neurons begins to **migrate** to their final destinations
- Some Stem Cells become Glia Cells, including **Radial Glia** that extend fibers out from V Zone like wheel spokes
  - These fibers have cup-like feet that extend/attach to Ecto/Meso boundary & lengthen as cortex expands

Migration - Some Neurons migrate by "crawling" along Radial Glia fibers, often aided by Glycoproteins
- Other Neurons may migrate by following chemical trails laid down by Glia Cells or by other Neurons

Differentiation - While and/or after Neurons migrate, they differentiate, to vary widely in structure and function
- Per **Cell-Autonomous (**genetic**)** and **Induction** (chemical influences from local environments) factors

Synaptogenesis, Cell Death & Neuron Competition

Synaptogenesis - Developing junctions (Synapses) between cells
- After migration, Neurons grow **Axons** (branch for outgoing info) and, later, **Dendrites** (branches for incoming info)
- Axons must "find" appropriate Post-Synaptic Target cells with which to communicate (i.e. on which to "synapse")
  - **Growth Cone** at end of elongating Axon has many Filopodia that detect surrounding chemical gradients
  - Some Axons are directed by **Guidepost Cells**, Glia cells that adhere to growing Axon and direct it toward Target cell
  - Others depend on Chemical Trails produced by Glia cells or other migrating Neurons/Axons
- **Neurotrophins** = chemicals that attract/repel and promote survival and activity of Neurons
  - e.g. Muscles/organs produce **NGF** (Nerve Growth Factor) that attract & promote survival of SNS Axons
  - e.g. In CNS, **BDNF** (Brain-Derived Neurotrophic Factor) promotes Axon survival and later Axonal branching

Apoptosis (**Cell Death**) - All Neurons have **suicide genes** – brain chemistry & activation patterns determine if activated/not
- During fetal development, nervous system massively overproduces cells (up to 50% more than survive!)
  - As cells compete for connections, "losers" die off (suicide genes are activated)
    - e.g. Axons that arrive too late to find space on Post-Synaptic cell, cannot compete for Neurotrophins, die
    - Axons often begin by branching widely, connecting to many sites; Only a few are strengthened, maintained
      - So, each cell makes fewer, more selective connections as prenatal development progresses
    - Redundancy probably serves to assure correct connections & allows for flexible adapting to local conditions
- Post-development, most remaining Stem Cells also die by the activation of their suicide genes
  - Few Stem Cells survive in lining of Ventricles; Later in life may produce new Glia or (rarely!) Neurons
- Note Apotosis different from Necrosis from injury or toxins; Latter can contaminate, inflame; Former neat

"**Cells that Fire Together, Wire Together**"

- **Patterns of co-activity** often determine outcome of competition:
  - e.g. When Spontaneous release of Neurotransmitter by developing Pre-Synaptic Axon produces a Post-Synaptic response, active Post-Synaptic cell will release Neurotrophins that promote Pre-Synaptic cell survival
  - So, if researchers block spontaneous firing, brain will develop more cells and more connections than normal!
  - Neurotrophin release is only (most) effective on *active* Pre-Synaptic cells, so the more correlated the Pre&Post activity of a given pathway, the more likely it is to srengthen, and other less correlated connections die off
  - When out-competed die, remaining active ones will produce **Collateral Sprouts** that will take over synapses
- Adjacent Pre-Synaptic cells tend to correlate their bursts of activity, so tend to develop connections to adjacent Targets
  - This often results in **Topographic Map**, e.g. where spatial relationships along a receptor surface are preserved in brain

Further Development

- Brain growth in humans continues after birth, especially during first 4 years of life (plus later spurt during adolescence)
  - Newborn brain weighs about 350 grams, by 1 year 800-1000 grams, adult 1200-1400 grams
  - NOTE: Post-natal increase mainly due to increase in size of existing cells, and to Axonal and Dendritic branching
    - New neurons rare (few exceptions in parts of Cerebellum, Olfactory Receptors, Hippocampus)
- **Dendrites**, which receive input from other Neurons, continue to develop with experience, increasing "receiving" surface area
  - Dendrite development usually begins after migration & axonal growth, Dendritic branching continues with experience
    - e.g. Rats in enriched (vs. deprived) environment show significantly more **Dendritic Spines**
    - e.g. Musicians that finger string instruments (e.g. violins), trained from childhood, show expanded somatosensory (Parietal Lobe) map for fingers of left hand (probably from inc. dendritic branching)
- Post-natal experience continues to shape **Synaptogenesis**, esp in infancy, but even into adulthood
  - e.g. Kittens exposed only to vertical lines >> developed connections in visual cortex (e.g. V1) responsive to vertical stimuli, but could NOT, as cats, detect horizontal lines (cells normally responding to horizontals were out-competed)
- Glia Cells also continue to develop and differentiate, many different structures and functions
  - e.g. **Myelination** begins in Spinal Cord then in Hindbrain then Midbrain, then Forebrain, then PNS
    - Some myelination still forming at age 20; In a few brain areas, continues into adult life
- **Learning**! Our highly plastic brains continue to develop new connections, although NOT new neurons
    - More on this to come!