NEUR 1520 Neuroscience Study Guide for Exam 2: Lecture 13: Development of the Brain

Sources: the lecture slides and The Mind's Machine, Chapter 4. Nothing else.

Each heading is one book learning objective. [L13 s08] = Lecture 13, slide 8. [MM p124] = book page 124.

(teal italics) = plain meaning of the word before it. ⚠ **Do not mix up = a look-alike pair to keep apart.** **Amber dotted words** = names printed on the figure beside them.

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4.1.1 List the six stages of cellular processes needed for brain development

⚠ **Do not mix up: Neurons themselves do NOT divide: non-neuronal cells divide by mitosis to make neurons.** [L13 s08, MM p124]

Review: the rat with lever, catheter, and syringe pump is **drug self-administration**. [L13 s02, L13 s03]

Review: drug self-administration measures the **rewarding properties** of a drug. [L13 s03]

Mature human brain: more than **80** billion neurons and more than **100** trillion synapses. [MM p121]

Each person begins as a single microscopic cell, the **fertilized egg**. [MM p121]

Within **12** hours of fertilization, the single cell begins dividing. [MM p122]

The early cluster of dividing cells, like grapes, is **only 200** micrometers wide. [MM p122]

A human **embryo** *(earliest stage of a developing animal)* develops three cell layers: endoderm, mesoderm, **ectoderm**. [L13 s05, L13 s06, MM p122]

The three distinct cell layers appear within a week of fertilization. [MM p122]

The three layers are the beginnings of all the tissues of the body. [MM p122]

Ectoderm *(outer cell layer)*: becomes the nervous system and the skin. [L13 s05, MM p122]

The nervous system comes from the outermost layer, ectoderm, **NOT** from endoderm or mesoderm. [L13 s05, MM p122]

A thickening of the ectoderm forms the **neural plate**; then the **neural groove** develops. [L13 s06, MM p123]

The neural plate is a thickened midline strip of ectoderm. [L13 s06, MM p123]

The edges of the plate rise and fold inward to form the groove. [L13 s06]

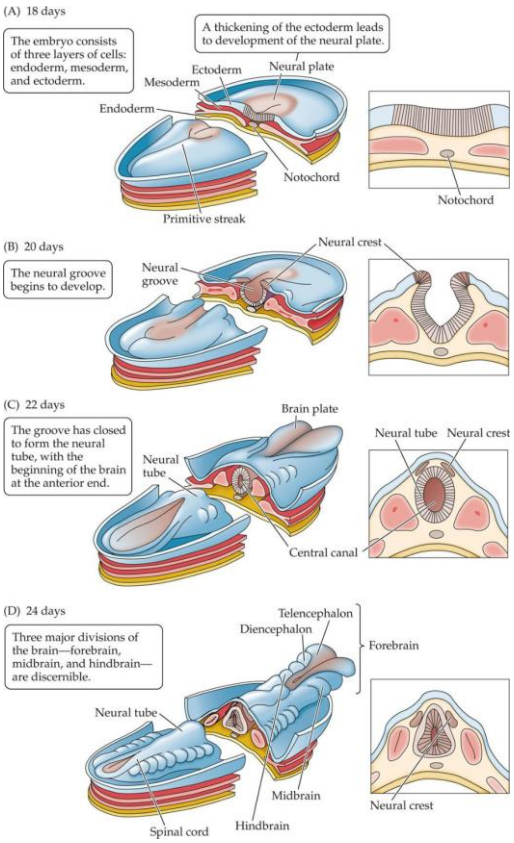
Neural crest: cells on the raised edges of the folding groove. [L13 s06, MM p123]

Neural tube *(tube that becomes brain and spinal cord)*: forms when the crests of the neural groove join. [L13 s05, L13 s06, MM p122]

The neural tube is the beginning of the **central nervous system** (CNS). [MM p122]

The anterior neural tube has three subdivisions: **forebrain**, **midbrain**, **hindbrain**. [L13 s05, L13 s06, MM p122]

Forebrain: front division; contains cerebral hemispheres (cortex), thalamus, hypothalamus. [L13 s05, MM p122]



Embryo layers, neural plate, groove, and tube, with the three brain divisions [L13 s06]

On the figure: ectoderm · neural plate · neural groove · neural crest · neural tube · forebrain · midbrain · hindbrain

Midbrain: the middle division of the brain. [L13 s05, MM p122]

Hindbrain: rear division; becomes the cerebellum, pons, and medulla. [L13 s05, MM p122]

Inside of the neural tube becomes the **cerebral ventricles** *(fluid-filled brain spaces)* and the spinal central canal. [MM p122]

The tube interior also becomes the passages that connect the ventricles and canal. [MM p122]

The tail end of the neural tube is labeled **spinal cord**. [L13 s06, MM p123]

Fetal brain from **10** to **41** weeks: **gyri** *(ridges)* and **sulci** *(grooves)* gradually emerge. [L13 s07, MM p123]

By the end of week **8,** the head is half the total size of the embryo. [MM p122]

The head is half the embryo size at week **8** because of **rapid brain growth**. [MM p122]

By the end of week **8,** the embryo shows the first beginnings of most body organs. [MM p122]

Embryo: first **10** weeks after fertilization; **fetus** *(developing individual after embryo stage)* thereafter. [MM p122]

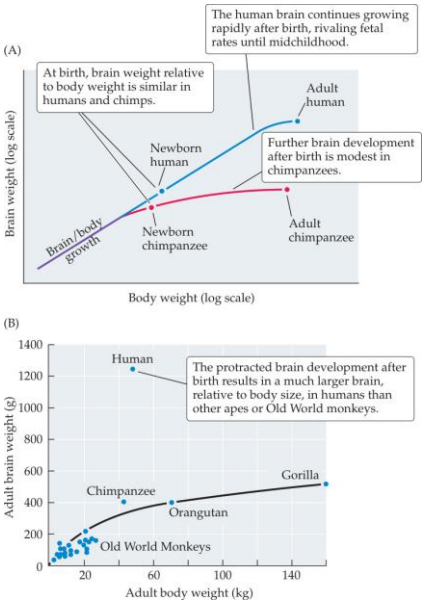
Humans are unique among primates in dramatic brain growth after birth. [MM p123]

At birth, brain weight relative to body weight is similar in humans and chimps. [MM p124]

Before birth, humans and chimps share one brain-to-body growth line. [MM p124]

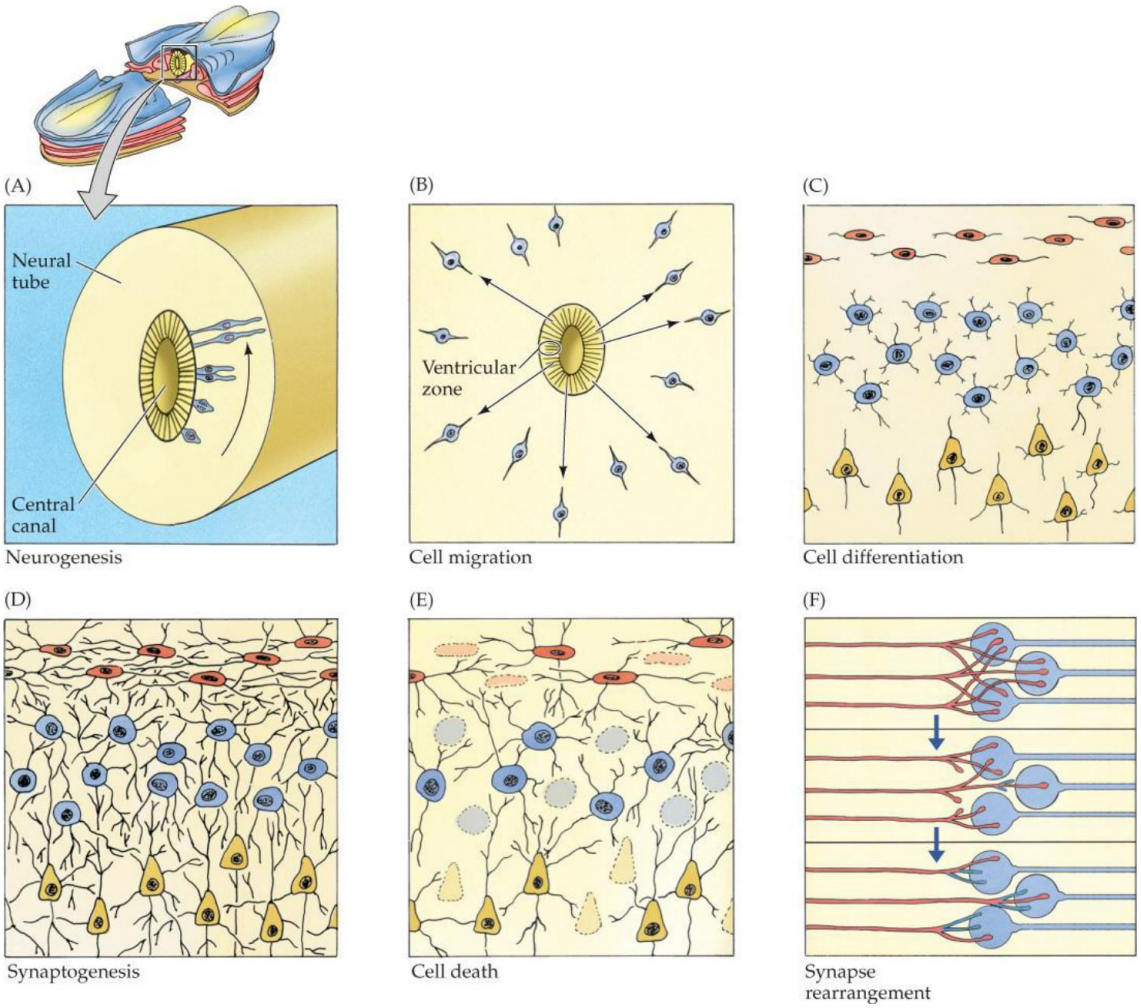
Human brains keep growing fast after birth, rivaling fetal rates until midchildhood; chimps grow modestly. [MM p124]

Humans have a much larger brain for body size than other apes or **Old World monkeys**. [MM p124]



Human and chimpanzee brain growth after birth, and brain size across apes and monkeys [MM p124]

On the figure: human · Old World monkeys



The six stages of neural development in order, from neurogenesis to synapse rearrangement [L13 s09]

On the figure: neural tube · central canal · ventricular zone · neurogenesis · cell migration · cell differentiation · synaptogenesis · cell death

> The six stages proceed at different rates and times in different nervous system parts. [MM p122]

Some stages may overlap, even within one region. [MM p122]

Formation of **myelin sheaths** for axons is another stage, outside the six. [MM p122]

Neurogenesis *(making new neurons)*: mitosis of non-neuronal cells produces neurons. [L13 s08, L13 s09, MM p124]

Mitosis *(cell division)*: division of somatic cells that involves duplication of DNA. [MM p124]

Dividing cells begin as a single layer along the inner surface of the **neural tube**. [MM p124]

Ventricular zone *(layer lining the ventricles)*: region inside the neural tube where mitosis happens. [L13 s08, L13 s09, MM p124]

Slides: neurogenesis forms the ventricular zone; book: mitosis takes place within it. [L13 s08, MM p124]

Ventricular zone (ependymal layer) gives neurons early in development and glial cells throughout life. [MM p124]

Cell migration: cells move out of the ventricular zone toward their destinations. [L13 s08, L13 s09, MM p124]

Migrating cells travel relatively long distances to fill out the brain. [MM p124]

Migration builds distinct cell groups: nuclei in the CNS, layers of the cerebral cortex. [MM p122]

Newly arrived cells look no more like nerve cells than like cells of other organs. [MM p124]

Gene expression *(using a gene to make protein)*: a cell makes an mRNA transcript of a gene. [MM p124]

Once cells reach their destinations, they begin expressing particular genes. [L13 s08, MM p124]

Cell differentiation *(becoming a specific cell type)*: cells become distinctive neuron or glial types. [L13 s08, L13 s09, MM p124]

Differentiation happens through **cell-cell interactions** *(cells signaling their neighbors)* and expressing particular genes. [L13 s08, MM p124]

Synaptogenesis *(making synapses)*: synaptic connections form as axons and dendrites grow. [L13 s08, L13 s09, MM p124]

Cell death: selective death of many neurons early in development. [L13 s08, L13 s09, MM p125]

Synapse rearrangement: many early synapses retract while other, later synapses form. [L13 s08, L13 s09, MM p125]

Synapse rearrangement refines connections and extends throughout the lifespan. [MM p122]

In the embryo figure the **forebrain** has two parts: **telencephalon** and **diencephalon**. [L13 s06]

Embryo timeline

Embryo age	What the figure shows
18 days	Three layers; thick ectoderm forms neural plate
20 days	Neural groove begins to develop
22 days	Groove closes into neural tube
24 days (slides); 25 days (book)	Forebrain, midbrain, hindbrain discernible

Table source: [L13 s06, MM p123]

Six stages of brain development, in order

Stage	What happens
1. Neurogenesis	Mitosis of non-neuronal cells makes neurons
2. Cell migration	Cells leave ventricular zone for destinations
3. Cell differentiation	Cells become specific neuron or glia types
4. Synaptogenesis	Axons, dendrites grow; synapses form
5. Cell death	Selective death of many neurons
6. Synapse rearrangement	Some synapses lost, others formed; fine-tuning

Table source: [L13 s08, L13 s09, MM p122, MM p125]

4.1.2 Describe the two phases of brain development characterized by the loss of structures

⚠ **Do not mix up: Neurons dying in development are NOT defective: they actively commit suicide (apoptosis).** [MM p127]

Two classes of brain structures lost during development: **neurons** and **synapses**. [MM p128]

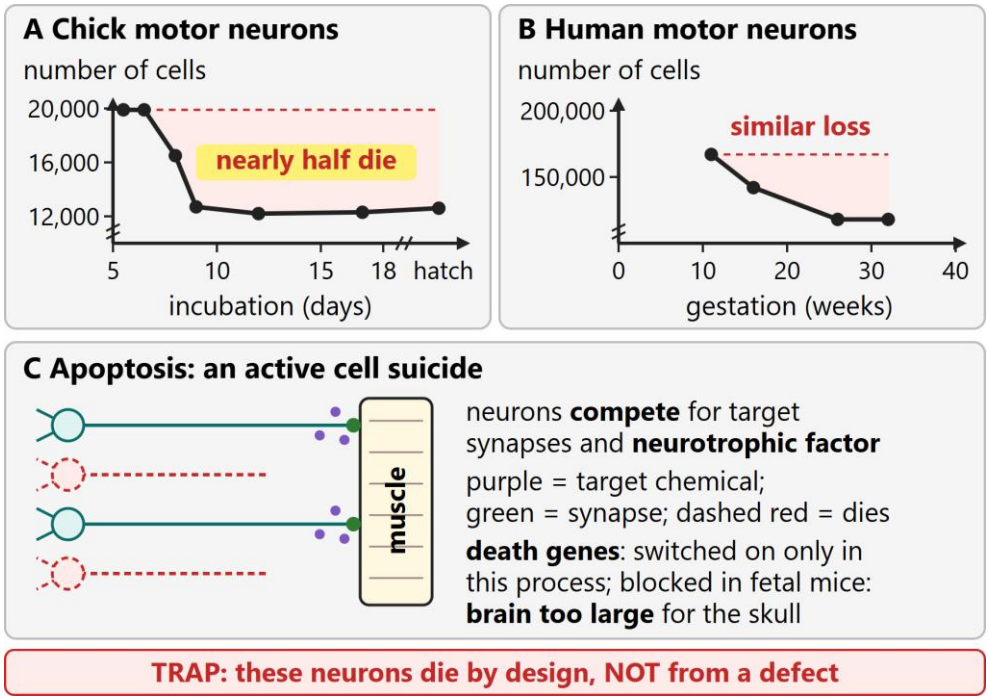
Cell death (**apoptosis** *(programmed cell death)*) is an important, normal part of brain development. [L13 s11, MM p126]

Apoptosis comes from the Greek apo, away from, and ptosis, act of falling. [L13 s11, MM p126]

Apoptosis also sculpts other tissues in both animals and plants. [MM p126]

The number of neurons that die during early development is large. [L13 s11, MM p127]

In some brain and spinal cord regions, most young nerve cells die before birth. [MM p127]



Chick and human motor neuron loss, and apoptosis as active suicide [MM p127]

On the figure: motor neurons · apoptosis · death genes · neurotrophic factor

Chicks: nearly half of spinal **motor neurons** die before hatching. [MM p127]

The chick motor neuron count drops steeply early in incubation, then stays fairly stable. [MM p127]

Developing humans show a similar loss of spinal motor neurons. [MM p127]

Cells die from complex interactions with surrounding cells, not from a defect. [MM p127]

Death genes *(suicide genes)*: genes expressed **only** when a cell undergoes **apoptosis**. [L13 s11, MM p127]

Fetal mice with blocked death genes grow brains too large to fit in the skull. [MM p127]

Neurons compete for synaptic connections and **neurotrophic factors** *(target chemicals that keep neurons alive)*. [L13 s11, MM p127]

Targets are other nerve cells or end organs, such as muscle. [MM p127]

Neurons that make adequate synapses survive; those without a place for synapses die. [MM p127]

Neurotrophic factors (trophic factors): target-derived chemicals that act as if they feed neurons. [L13 s11, MM p127]

Trophe is Greek for nourishment, so these factors seem to feed neurons. [MM p127]

Neurons receiving enough **neurotrophic factor** survive; those that do not, die. [MM p127]

1. Different target cell groups produce different **neurotrophic factors**. [L13 s12, MM p128]

2. Innervating neurons take up the factors and transport them to their **cell bodies**. [L13 s12, MM p128]

3. At the cell body, factors regulate gene expression, shaping the neuron's development. [L13 s12, MM p128]

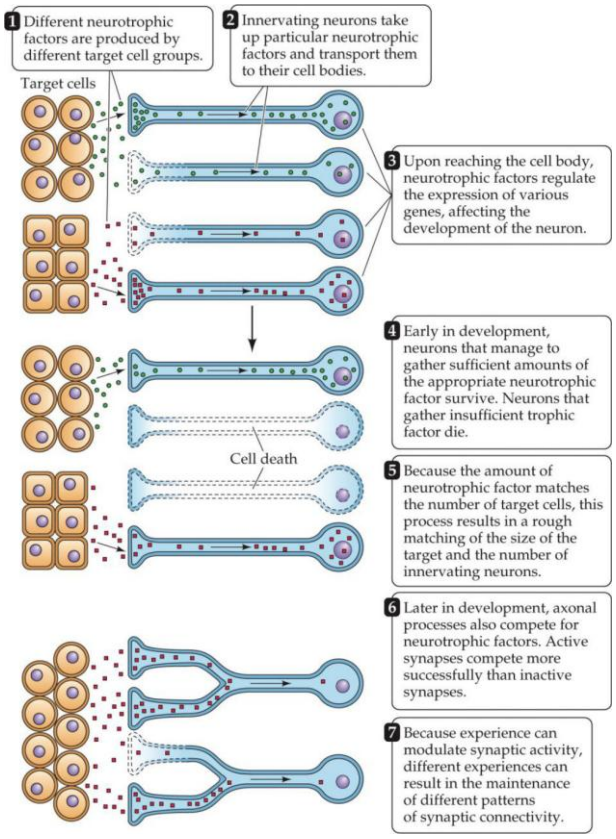
4. Early: neurons gathering enough factor survive; those with too little die. [L13 s12, MM p128]

5. Factor amount matches target size, so neuron number roughly matches the target. [L13 s12, MM p128]

A bigger target makes more factor, so more innervating neurons survive; a smaller target, fewer. [L13 s12, MM p128]

6. Later: axon branches compete for factors; active synapses beat inactive synapses. [L13 s12, MM p128]

7. Experience changes synaptic activity, so different experiences keep different connection patterns. [L13 s12, MM p128]



Targets release neurotrophic factors; neurons that collect enough survive, later branches compete [L13 s12]

On the figure: neurotrophic factors · cell death · cell bodies

Competition for neurotrophic factors probably also controls later synapse pruning. [MM p127]

Synapse rearrangement (synaptic remodeling): loss of some synapses and development of others. [L13 s08, MM p129]

Synapse rearrangement typically takes place after the period of **cell death**. [MM p129]

Some original synapses are lost, and many new synapses are formed. [MM p129]

Example: by the end of cell death, each surviving motor neuron innervates many muscle fibers. [MM p129]

At that point, each muscle fiber is innervated by several motor neurons. [MM p129]

Later, motor neurons retract many axon collaterals *(side branches)* until each muscle fiber has one motor neuron. [MM p129]

Kept connections depend on competition for trophic factors and/or between Hebbian synapses. [MM p129]

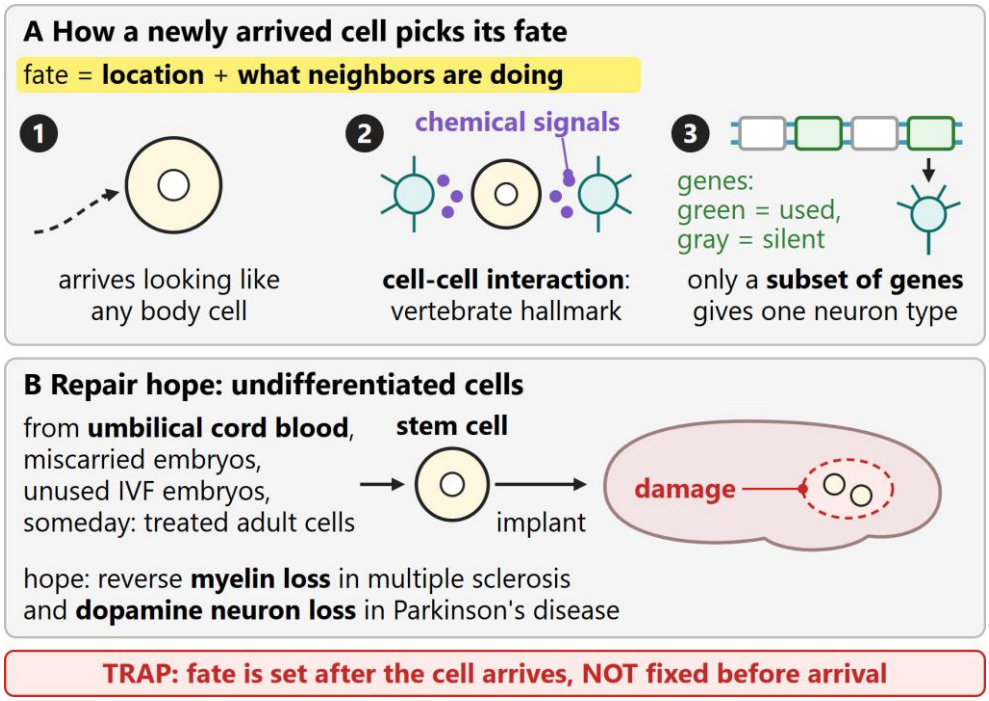
The two loss phases

Loss phase	What is lost	When	Decided by
Cell death (apoptosis)	Many neurons	Stage **5,** early development	Competition for neurotrophic factors
Synapse rearrangement	Some early synapses	Stage **6,** after cell death	Competition; active synapses win

Table source: [L13 s08, L13 s11, MM p127, MM p128, MM p129]

4.1.3 Identify the basic mechanism that directs each developing neuron to take on the appropriate structure and function

⚠ **Do not mix up: Cell fate is NOT fixed before migration: location and neighbors decide it.** [MM p124]



How a new cell picks its fate, and stem cells for repair [MM p125]

On the figure: cell-cell interaction · subset of genes · stem cell · umbilical cord blood · myelin

Basic mechanism: **cell-cell interactions** *(cells signaling their neighbors)* direct each neuron's structure and function. [L13 s08, MM p124, MM p125]

Cell-cell interaction: one cell affects the differentiation of other, usually neighboring, cells. [MM p125]

A differentiating cell's fate depends on where it is and what neighbors are doing. [MM p124]

Developing brain cells constantly send chemical signals, each shaping the others' development. [MM p124]

Hallmark of vertebrate development: cells sort themselves out by cell-cell interactions. [MM p124, MM p125]

Each cell expresses a particular **subset of genes** to make the proteins its type needs. [MM p124, MM p125]

Neurotrophic factors from targets also regulate gene expression in the neuron. [L13 s12, MM p128]

Stem cell *(undifferentiated cell)*: can take on the fate of any cell the donor makes. [MM p125]

Because of cell-cell interactions, stem cells placed in a region differentiate and integrate properly. [MM p125]

Stem cell sources: **umbilical cord blood**, miscarried embryos, unused in vitro fertilization embryos. [MM p125]

Adult cells might someday be treated in a dish to become stem cells. [MM p125, MM p126]

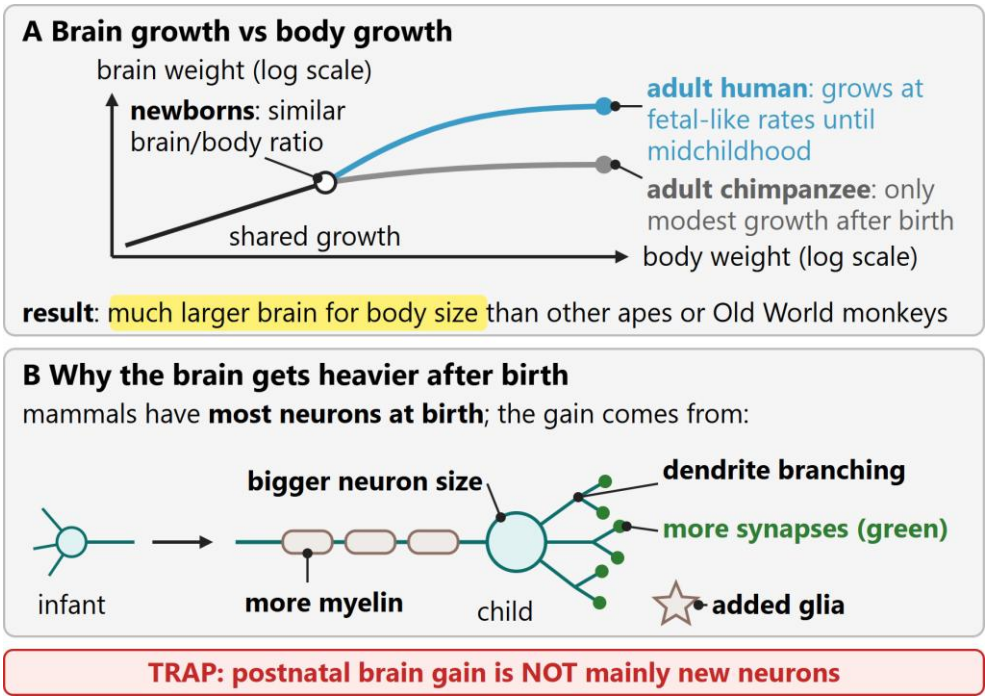
Hope: implanted stem cells replace lost **myelin** (multiple sclerosis) or dopamine neurons (Parkinson's). [MM p126]

Stem cells could be placed in brain areas of **degeneration** *(damage)* to fill in. [MM p126]

4.1.4 Discuss the significance of generating new neurons in adulthood

⚠ **Do not mix up: Most neurons exist by birth, yet adults DO make some new neurons.** [MM p126]

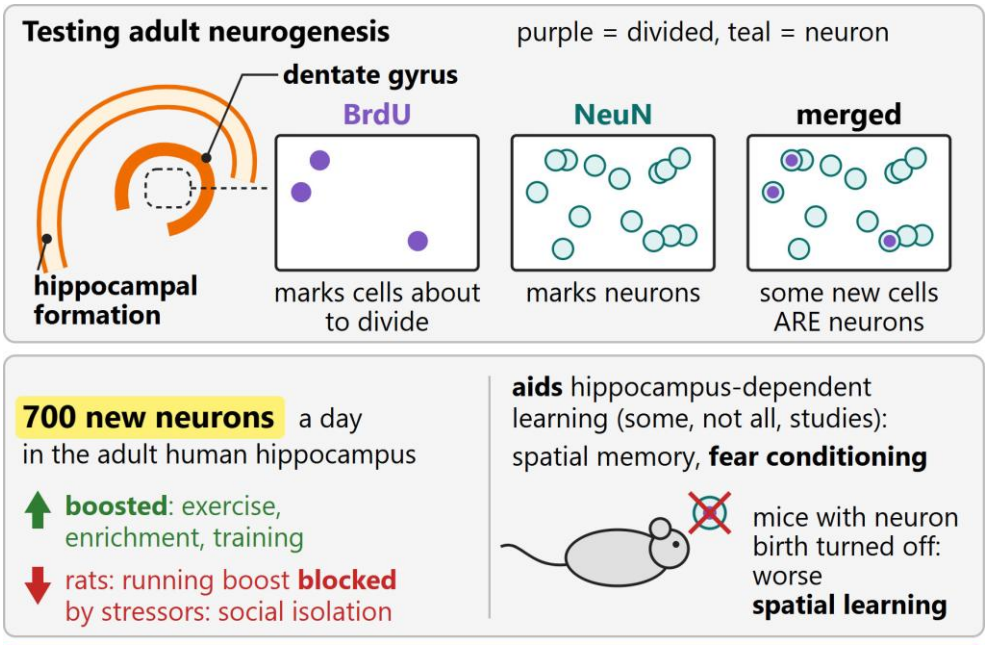
At birth, mammals already have most of the neurons they will ever have. [MM p126]



Why the brain gets heavier after birth: myelin, dendrites, synapses, glia [MM p124]

On the figure: dendrite branching · more synapses · more myelin · added glia

> Brain growth after birth: bigger neurons, **dendrite branching**, **more synapses**, **more myelin**, **added glia**. [MM p126]
> More dendrites and synapses cause most of the brain size **increase** after birth. [MM p129]



Testing adult neurogenesis in the dentate gyrus with BrdU and NeuN [MM p126]

On the figure: adult neurogenesis · dentate gyrus · BrdU · NeuN · 700 new neurons · fear conditioning

> **Adult neurogenesis**: new neurons made in adulthood, especially in the **dentate gyrus** *(part of the hippocampal formation)*. [L13 s10, MM p126]
> One estimate: **700 new neurons** every day in the adult human hippocampus. [MM p126]
> New adult neurons are a tiny minority, but there is reason to think they matter. [MM p126]

Exercise, environmental enrichment, and training enhance birth or survival of new neurons. [L13 s10, MM p126]

Neurogenesis enhances **hippocampus-dependent learning**: spatial memory and **fear conditioning**. [L13 s10, MM p126]

This learning boost appears in some, but not all, studies. [MM p126]

Mice with adult neurogenesis genetically turned off: marked spatial learning impairment, little else. [MM p126]

Training, such as studying, improves neurogenesis. [L13 s10, MM p126]

Rats: physical exercise boosts neurogenesis; stressors such as social isolation block this effect. [L13 s10, MM p126]

BrdU *(marker for newly made DNA)*: label taken into the DNA of cells about to divide. [MM p126]

NeuN *(neuron marker)*: labels neurons, separating them from nearby glial cells. [MM p126]

Merging BrdU and NeuN images shows some newly born dentate gyrus cells are neurons. [MM p126]