NEUR 1520 Neuroscience Study Guide for Exam 2

Sources: the lecture slides and The Mind's Machine, Chapter 4 and Chapter 5 (book only until its lectures are posted). 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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Lecture 13: Development of the Brain

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]

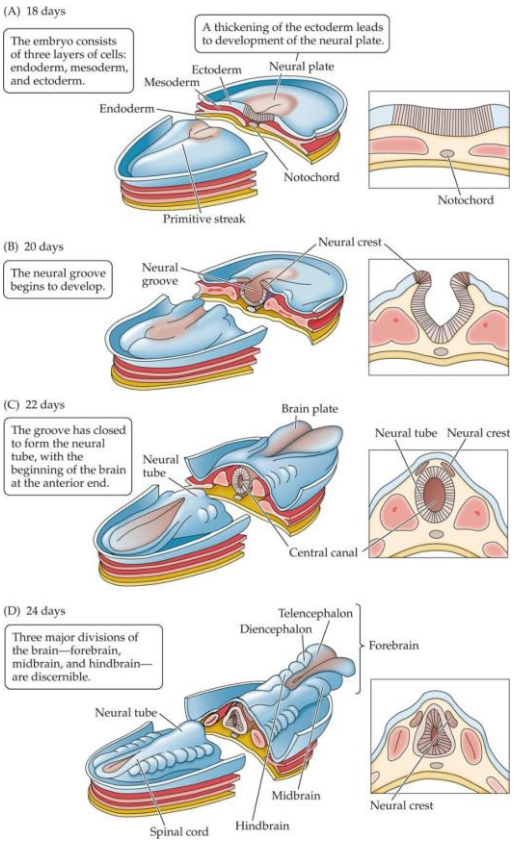
Neural crest: cells on the raised edges of the folding groove. [L13 s06, MM p123]

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]

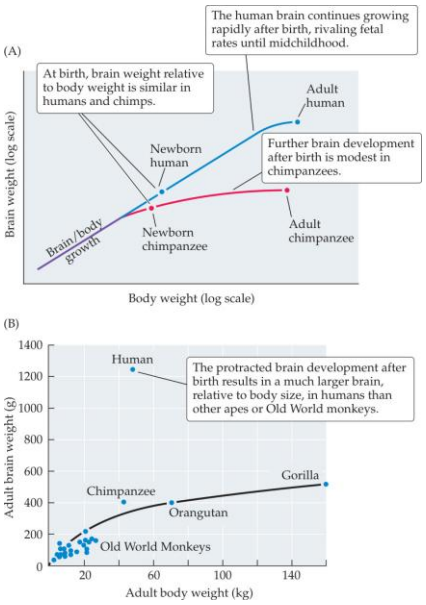
Humans are unique among primates in dramatic brain growth after birth. [MM p123]

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]

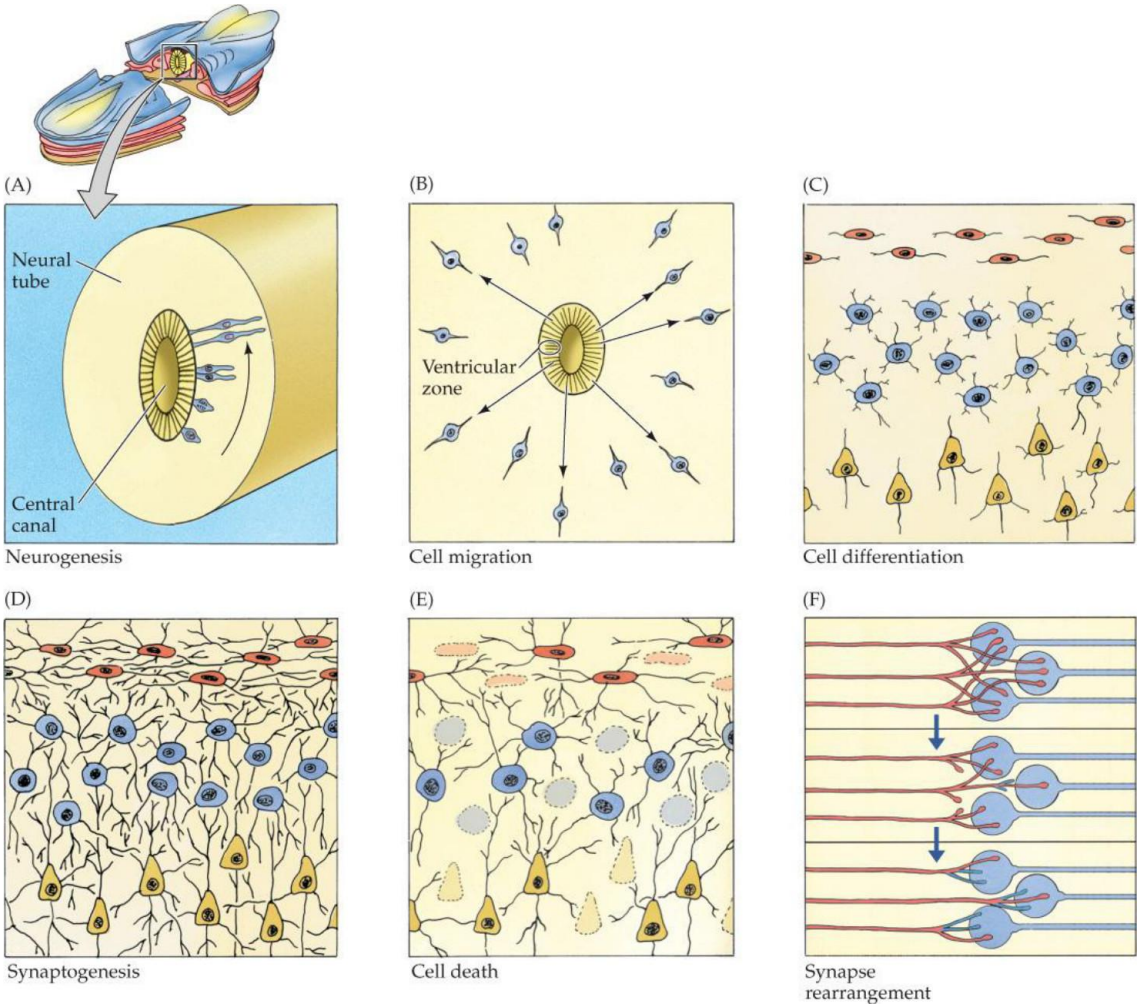
Human brains keep growing fast after birth, rivaling fetal rates until midchildhood; chimps grow modestly. [MM p124]

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]

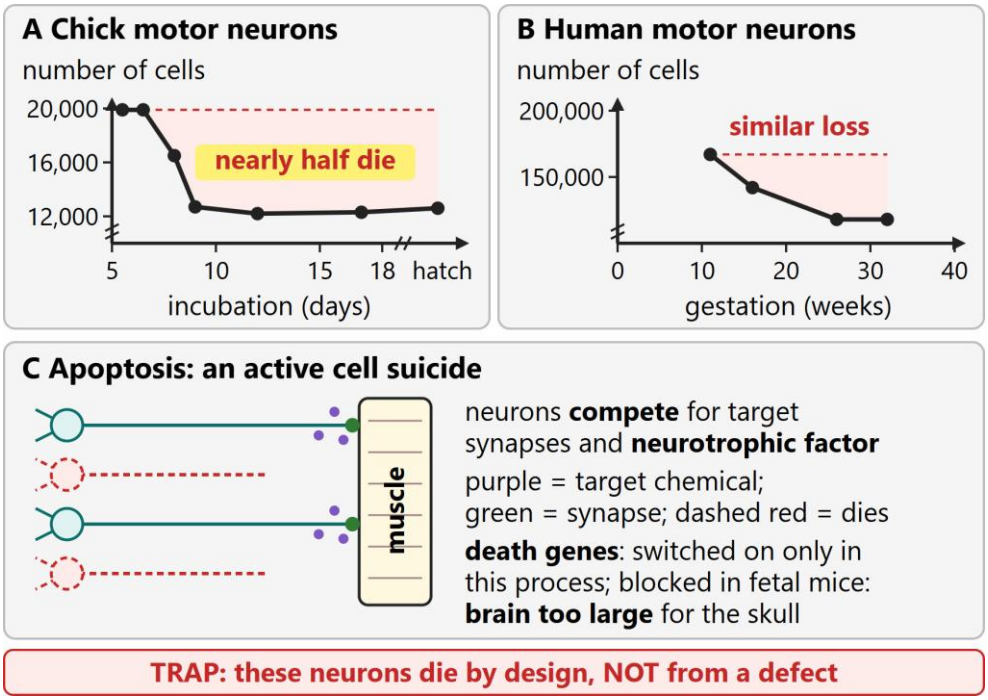
Cell death (**apoptosis** *(programmed cell death)*) is an important, normal part of brain development. [L13 s11, MM p126]

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]

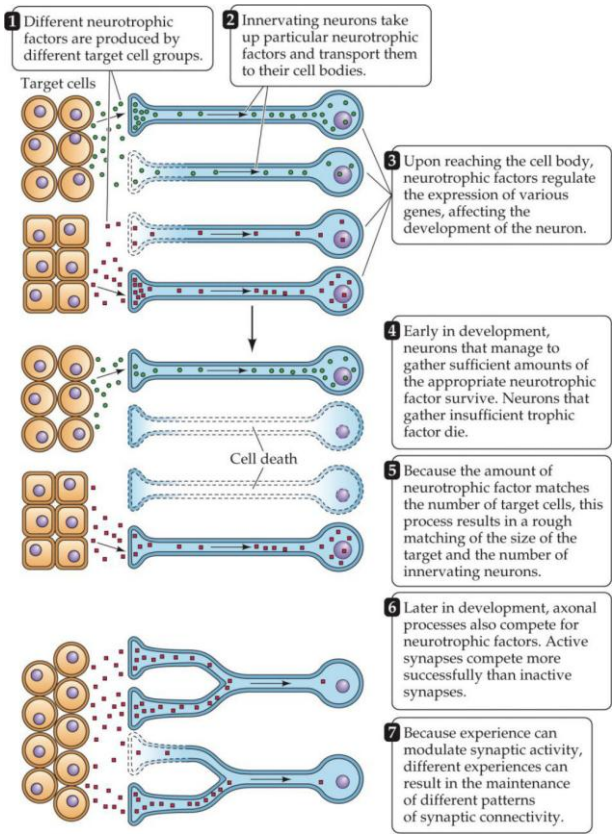
4. Early: neurons gathering enough factor survive; those with too little die. [L13 s12, MM p128]

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**

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

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]

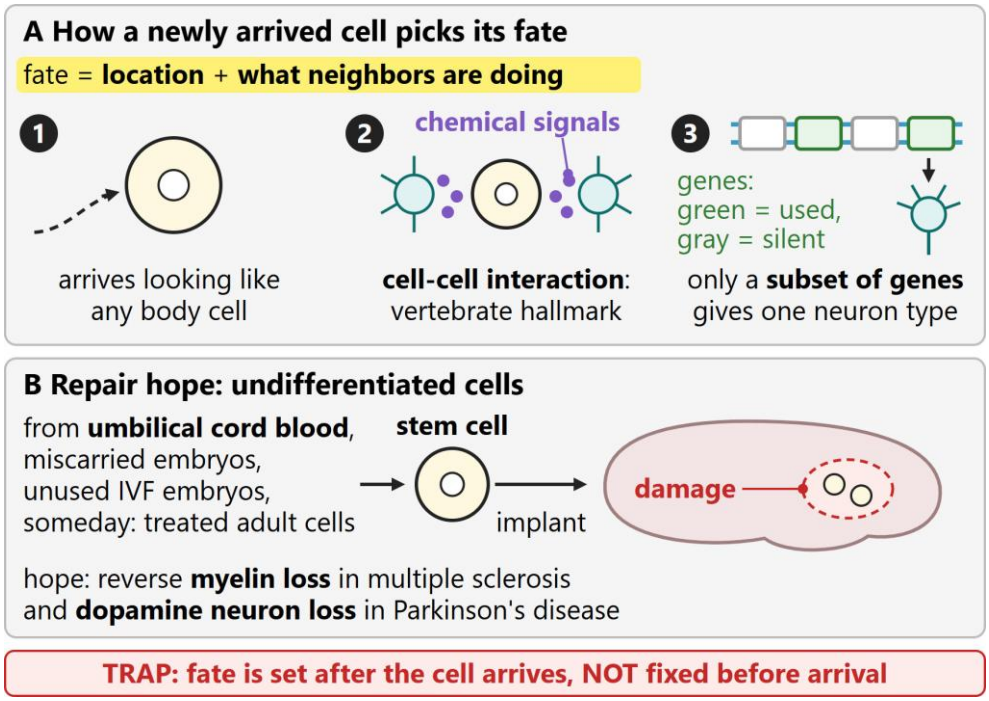
The two loss phases

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]

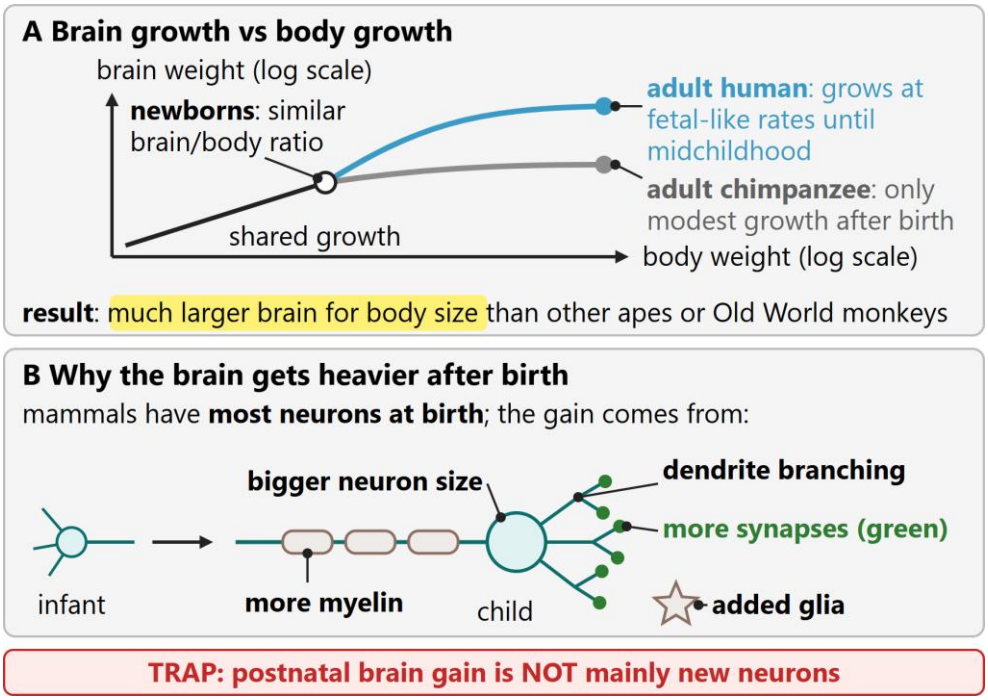
Hope: implanted stem cells replace lost **myelin** (multiple sclerosis) or dopamine neurons (Parkinson's). [MM p126]

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]

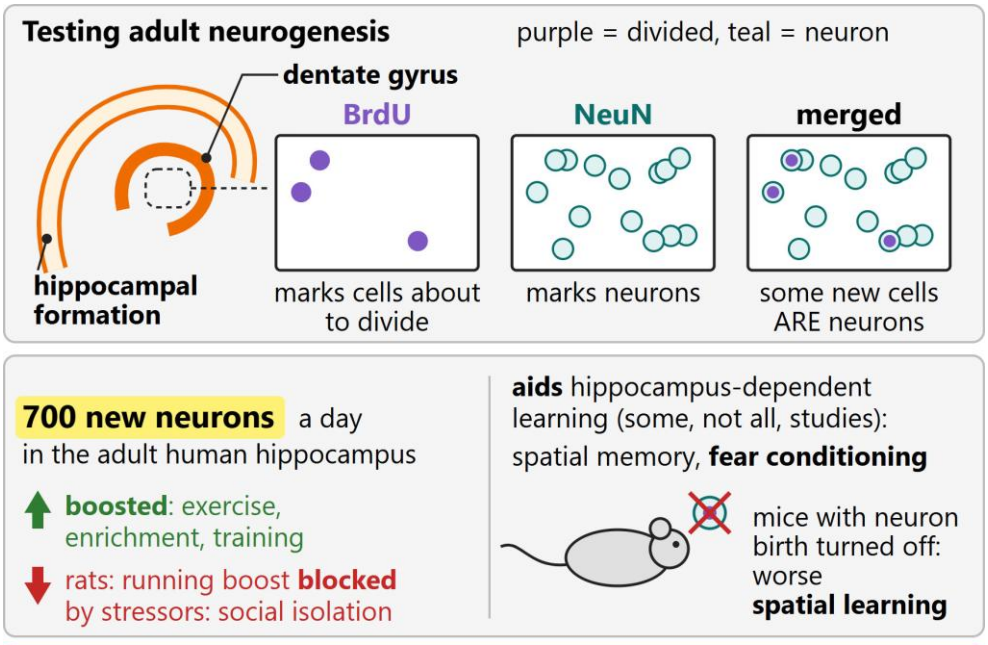
At birth, mammals already have most of the neurons they will ever have. [MM p126]



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]

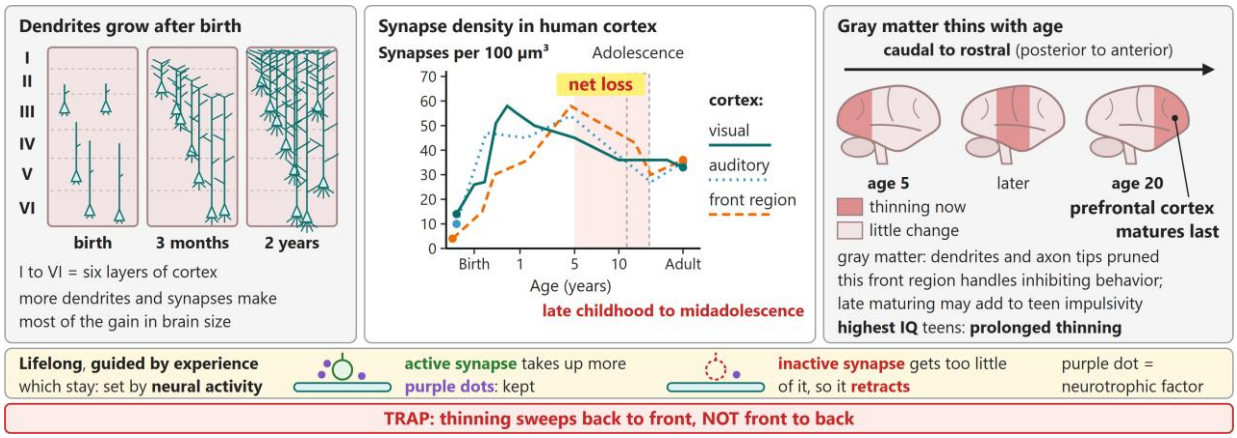
Exercise, environmental enrichment, and training enhance birth or survival of new neurons. [L13 s10, MM p126]
Neurogenesis enhances **hippocampus-dependent learning**: spatial memory and **fear conditioning**. [L13 s10, MM p126]
This learning boost appears in some, but not all, studies. [MM p126]
Mice 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]

Lecture 14: Synapse Formation and Rearrangement

4.2.1 Describe the process of synapse rearrangement, and offer evidence that a net loss of synapses may be adaptive

⚠ **Do not mix up: More synapses is NOT better: fragile X brains keep too many immature spines.** [L14 s08, MM p131]

Review: the six pictured stages are neurogenesis, migration, differentiation, synaptogenesis, cell death, rearrangement. [L14 s02, L14 s03]
Before and after birth, cortical neurons grow longer, more elaborate dendrites jammed with synapses. [MM p129]
This massive **increase** in dendrites and synapses causes most of the brain size **increase** after birth. [MM p129]



Cortex dendrites grow after birth, synapse density rises then falls, gray matter thins back to front [MM p130]

On the figure: six layers · net loss · auditory · gray matter · caudal to rostral · prefrontal cortex · neural activity · neurotrophic factor

Cortex at birth, **3** months, and **2 years** shows dendrites expanding; mature cortex has **six layers**. [MM p129]
Synapse rearrangement (**synaptic remodeling** *(pruning and rebuilding synapses)*): loss of some synapses, development of others. [MM p129]
Synapse rearrangement typically takes place after the period of cell death. [MM p129]
About half of the spinal motor neurons that form later die. [MM p129]
Spinal motor neurons are motor neurons of the **spinal cord** *(CNS tube in the back)*. [MM p129]
Synapse rearrangement continues throughout adulthood, guided by experience. [L14 s05]
After cell death, each motor neuron innervates many muscle fibers; each fiber gets several neurons. [MM p129]
Later, motor neurons retract axon collaterals until each fiber has **only** one motor neuron. [MM p129]
Which synapses stay: competition for trophic factors and/or between **Hebbian synapses** *(synapses strengthened by success)*. [MM p129]
Similar rearrangement occurs in cerebellum, brainstem, visual cortex, and autonomic nervous system. [MM p130]
Human cortex: **net loss** of synapses from late childhood until midadolescence. [L14 s05, MM p130]
Synapse density in visual, **auditory**, **prefrontal cortex** rises after birth, then declines. [L14 s06, MM p130]
Synapse density declines after the first year of life. [L14 s06, MM p130]
Prefrontal cortex synapse density peaks later than visual cortex and keeps falling through adolescence. [L14 s06]

Remodeling shows as thinning of cortical **gray matter** *(surface layer of cortex)* as dendrites and terminals are pruned. [L14 s07, MM p130]

Thinning proceeds **caudal to rostral** *(back to front, posterior to anterior)*, so prefrontal cortex matures last. [L14 s05, L14 s07, MM p130]

Prefrontal cortex is important for inhibiting behavior. [MM p130]

Late prefrontal maturation may contribute to teenagers' impulsivity and relative lack of control. [L14 s05, MM p130]

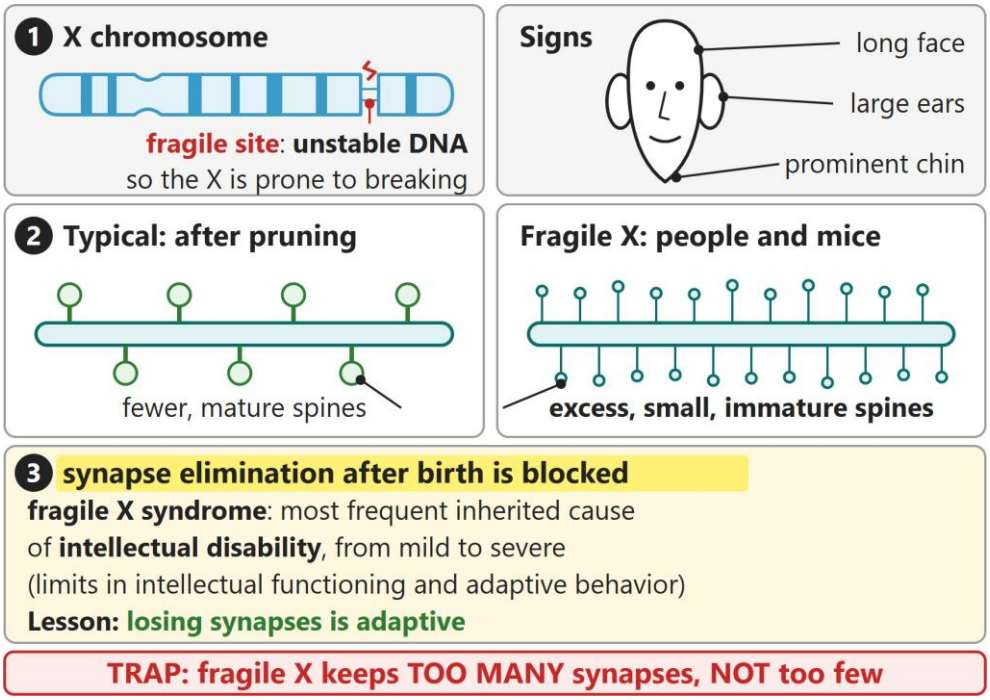
Neural activity is one important influence on which synapses are kept. [MM p130]

Theory: active synapses take up **neurotrophic factor** that keeps them; inactive ones get too little. [MM p130]

Intellectual stimulation probably helps: highest-IQ teenagers show especially prolonged cortical thinning. [MM p130]

Genetic disorders can have a profound effect on the developing brain. [L14 s08]

Intellectual disability: significant limits in intellectual functioning and adaptive behavior. [MM p130]



Fragile X: unstable X site, typical signs, and excess immature spines [MM p131]

On the figure: fragile X syndrome · intellectual disability · fragile site · prominent chin · immature

Fragile X syndrome: most frequent inherited cause of **intellectual disability**, mild to severe. [L14 s08, MM p130, MM p131]

Cause: a **fragile site** *(unstable DNA spot)* makes the X chromosome prone to breaking. [MM p130, MM p131]

Fragile X appearance: elongated face, large prominent ears, **prominent chin**. [MM p131]

Humans and mice with fragile X: cortical neurons have excess small, **immature** **dendritic spines** *(tiny dendrite bumps holding synapses)*. [L14 s08, MM p131]

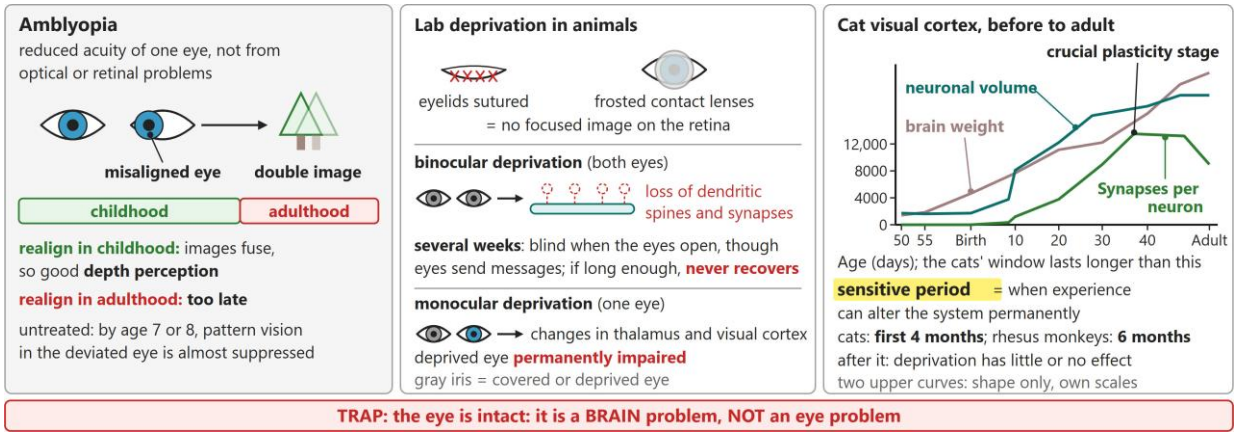
Suggests fragile X blocks the normal elimination of synapses after birth. [L14 s08, MM p131]

Evidence net loss is adaptive: losing synapses helps the brain function better. [MM p130, MM p131]

Touch cortex rearranges synapses throughout life; learning strengthens, weakens, or rearranges synapses. [MM p131]

4.2.2 Describe studies showing that visual experience early in life is required to develop normal vision

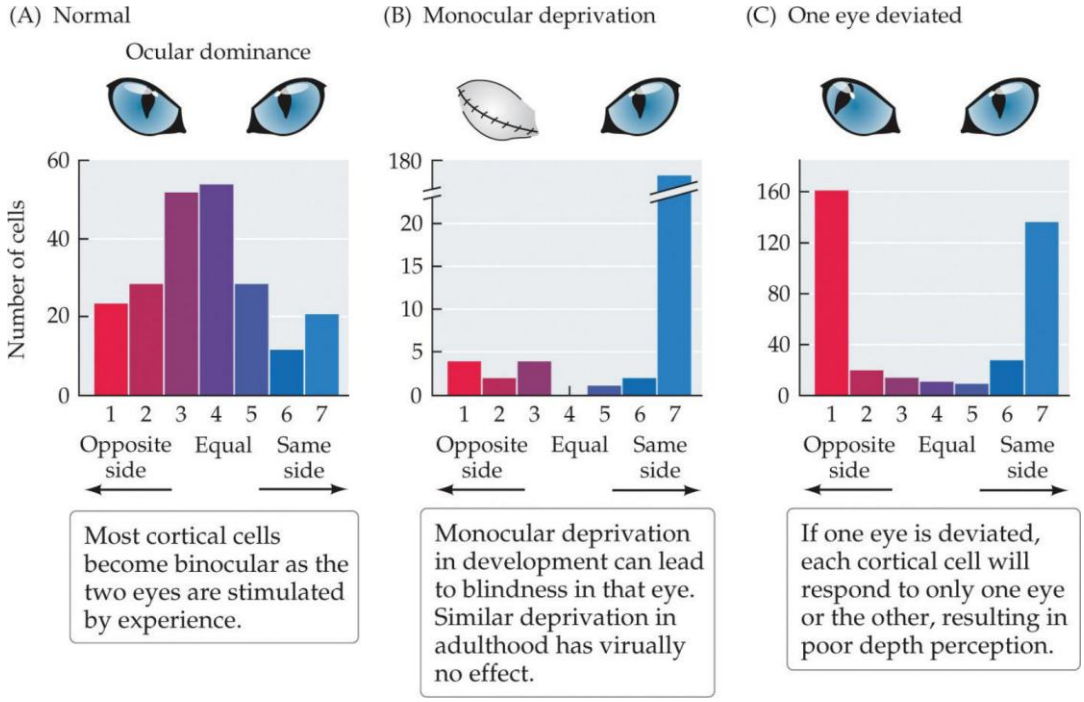
⚠ Do not mix up: Monocular deprivation in adulthood has virtually NO effect: only the sensitive period matters.
[L14 s14, MM p132, MM p133]



Amblyopia, animal deprivation methods, and the cat synapse curve with its sensitive period [MM p131]

On the figure: amblyopia · double image · binocular deprivation · monocular deprivation · sensitive period · synapses per neuron

Amblyopia *(dull vision in one eye)*: reduced acuity in one eye, not from optical or retinal damage. [L14 s09, MM p131]
Amblyopia comes from the Greek amblys, dull, and ops, eye. [L14 s09, MM p131]
Amblyopia: the eye is intact and a sharp image focuses on the retina. [MM p131]
Some people with amblyopia have one eye misaligned: turned inward (cross-eyed) or outward. [L14 s09, MM p131]
Children born misaligned see a **double image**, not a single fused image. [MM p131]
Untreated, by age **7** or **8,** pattern vision in the deviated eye is almost completely suppressed. [MM p131]
Realigned in childhood: the two images fuse and depth perception is good. [MM p131]
Not realigned in childhood: visual acuity in the turned eye cannot be reestablished. [L14 s09, MM p131]
Realignment in adulthood is **too late** to restore acute vision to the turned eye. [MM p131]
Visual deprivation experiments in animals provide the data on amblyopia. [L14 s10, MM p131]
Methods: eyelids reversibly sutured shut, or frosted contact lenses, prevent focused images on the retina. [MM p131]
Binocular deprivation *(blocking sight in both eyes)*: loss of dendritic spines and fewer synapses in visual cortex. [L14 s10, MM p131]
Binocular deprivation for several weeks in development: when eyes open, the animal is blind. [MM p131]
Light enters and the eyes send messages, but the brain seems to ignore them. [MM p131]
If deprivation lasts long enough, sight can never be restored. [L14 s10, MM p131]
Sensitive period *(window when experience causes lasting change)*: when experience or treatment permanently alters the organism. [L14 s10, MM p131]
Effects are biggest during early synapse development in visual cortex; afterward little or none. [MM p131]
Cat visual cortex: **synapses per neuron** climb steeply after birth, peak, then drop by adulthood. [L14 s11, MM p131]
Cat brain weight and neuron volume keep rising while synapses per neuron later fall. [L14 s11, MM p131]
Experience decides which synapses are kept: a crucial stage of **neural plasticity** *(brain change with experience)*. [MM p131]
Monocular deprivation *(blocking light to one eye)*: in the sensitive period, the deprived eye later fails to respond. [L14 s12, MM p132]
Monocular deprivation changes structure and function in the thalamus and visual cortex. [MM p132]



Ocular dominance histograms: normal, one eye covered, and one eye deviated [L14 s14]

On the figure: ocular dominance · number of cells · monocular deprivation · binocular · depth perception

Ocular dominance histogram *(graph of which eye drives each neuron)*: neuron response strength to left versus right eye. [L14 s12, MM p132]

Histogram classes: **1 only** opposite eye, **4** both eyes equally, **7 only** same-side eye. [L14 s14, MM p132]

Ocular dominance histogram axes: x is eye class **1** to **7,** y is **number of cells**. [MM p132]

Normally most cortical neurons, except layer IV, respond equally to either eye. [L14 s12, MM p132]

Normal: most cortical cells become **binocular** as both eyes are stimulated by experience. [L14 s14, MM p132]

Monocular deprivation: most cortical neurons respond **only** to the non-deprived eye. [L14 s13, MM p132, MM p133]

Similar deprivation in adulthood has virtually no effect. [L14 s14, MM p132]

Sensitive period for this effect: cats, first **4** months; rhesus monkeys, to age **6** months. [MM p133]

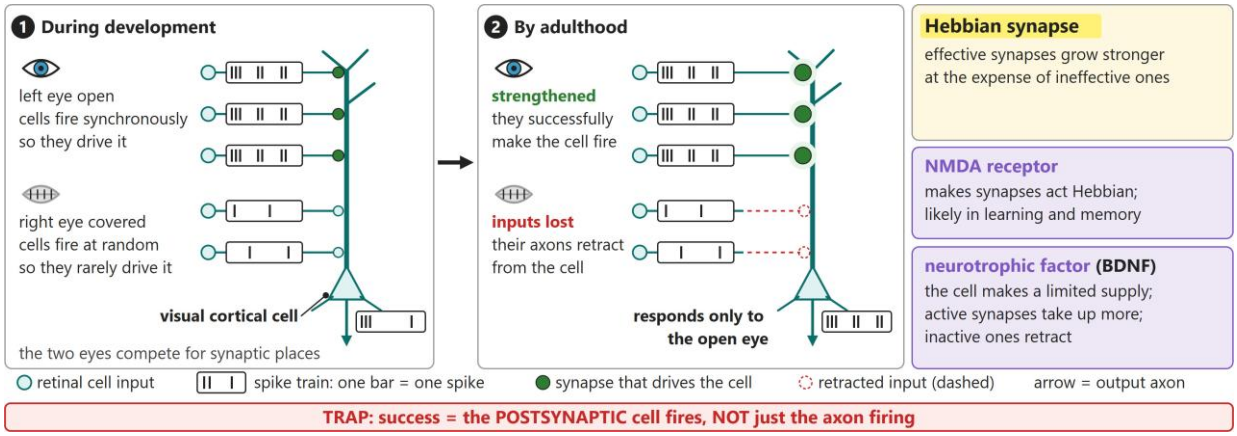
One eye deviated: each cortical cell usually responds to one eye **only**; poor **depth perception**. [L14 s13, L14 s14, MM p132]

Kittens with eyes surgically diverged: normal binocular response of cortical cells greatly reduced. [MM p133]

Why: misaligned eyes no longer give simultaneous, convergent input to visual cortex cells. [MM p133]

Axons from each eye compete for synaptic places *(targets)*; active synapses predominate. [L14 s15, MM p133]

If one eye is silenced, its synapses retract; the other eye's synapses are maintained. [MM p133]



Hebbian synapses: inputs that drive the cell grow stronger, ineffective inputs retract [MM p132]

On the figure: Hebbian synapse · NMDA receptor · neurotrophic factor · BDNF · strengthened

Hebbian synapse *(synapse strengthened by success)*: **strengthened** when it successfully drives the postsynaptic cell. [L14 s15, MM p133]

Hebbian synapses grow stronger or weaker depending on ability to drive the target cell. [L14 s15, MM p133]

Effective synapses grow stronger at the expense of ineffective synapses. [MM p133]

1. Open eye: neighboring retinal cells fire synchronously and drive the postsynaptic neuron. [L14 s16, MM p132]
2. Covered eye: cells fire at random and rarely make the postsynaptic neuron fire. [MM p132]
3. Effective inputs strengthen; ineffective inputs are lost. [L14 s16, MM p132]
4. By adulthood, the cortical cell responds **only** to signals from the open eye. [MM p132]

The **NMDA receptor** *(a glutamate receptor)* makes synapses act Hebbian; likely involved in learning and memory. [MM p133]

Neurotrophic factors may play a role: active synapses take up more of the factor. [L14 s15, MM p133]

Postsynaptic cells make limited factor, so inactive axons may retract for lack of it. [MM p133]

BDNF *(brain-derived neurotrophic factor)* is implicated as the factor competed for in visual cortex. [MM p133]

Babies with **cataracts** *(cloudy lenses)* removed a few months after birth have good vision. [MM p133]

Cataracts removed in adulthood: vision comes slowly and **only** to a limited extent. [MM p133]

Cataracts blocking vision just the first **6** months: face recognition impaired **9 years** later. [MM p133]

Early visual experience is especially crucial for learning to perceive faces. [MM p133]

These effects probably come from synapse rearrangement in visual cortex, as in kittens. [MM p133]

Michael May: blinded at age **3** by chemical explosion; right eye sight restored at **46.** [MM p121]

Images focused properly on the retina, yet vision stayed poor. [MM p121]

Years later, Michael May could not recognize a face, even the wife's, unless the person spoke. [MM p121]

Could not recognize **3**D objects like cubes or spheres unless they were moving. [MM p121]

Skiing: had to close the eyes; seeing was more distracting than helpful. [MM p121]

Had the accident happened in adulthood, surgery would have restored normal vision. [L14 s17, MM p133]

Cause: deprived of form vision from childhood for about **40 years**. [L14 s17, MM p133]

Visual cortex synapses were not strengthened by patterns of light moving across the retina. [L14 s17, MM p133]

Without patterned stimulation, eye-to-brain synapses languished and disappeared. [L14 s17, MM p133]

Normal form vision for the first **3.5 years** may have kept some **residual synapses**, allowing some sight. [MM p133, MM p134]

Soon after surgery, objects recognized under **30%** of the time; no significant gain **10 years** later. [MM p134]

After more than a decade of adult sight, still trouble with **3**D objects and faces. [MM p134]

Other people who first gain sight as adults have similar trouble with objects and faces. [MM p134]

Binocular vs monocular deprivation

	Binocular deprivation	Monocular deprivation
Eyes deprived	Both eyes	One eye
Cortex change	Fewer spines and synapses	Most cells answer **only** the open eye
Vision result	Blind if long enough	Deprived eye permanently impaired

Table source: [L14 s10, L14 s12, L14 s13, MM p131, MM p132]

Ocular dominance histograms

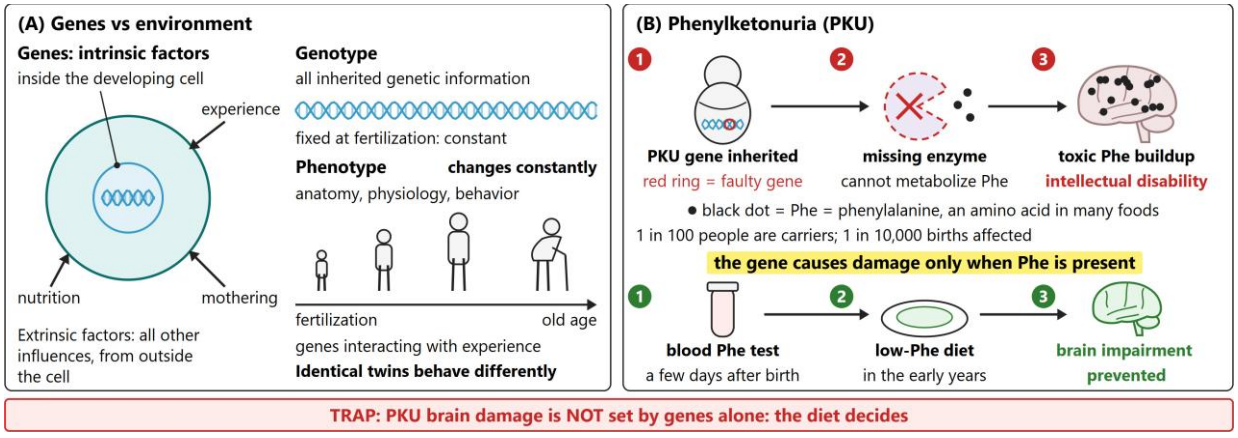
Condition	Histogram	Vision result
Normal	Most cells answer both eyes	Binocular cells
Monocular deprivation	Most cells answer open eye **only**	Deprived eye blind
One eye deviated	Each cell answers one eye	Poor depth perception

Table source: [L14 s12, L14 s13, L14 s14, MM p132, MM p133]

Lecture 15: Experience Can Affect Brain Development by Altering Gene Expression

4.3.1 Describe how the environment can regulate gene expression and how experience and genes interact to affect behavior

⚠ Do not mix up: Genotype does NOT change with experience: phenotype does, through extrinsic effects on genes. [L15 s05, MM p135]



Genes against environment, genotype and phenotype over life, and how PKU damage is prevented [MM p134]

On the figure: genotype · phenotype · intrinsic factors · extrinsic factors · identical twins · phenylalanine · intellectual disability · low-Phe diet

Genotype: sum of all the intrinsic, genetic information an individual has; constant. [L15 s05, MM p135]
Genotype is all the genetic information one individual has inherited. [MM p135]
Genotype is set at the moment of **fertilization** *(sperm joins egg)* and stays the same for life. [MM p135]
Phenotype: sum of an individual's physical characteristics at one particular time. [L15 s05, MM p135]
Phenotype includes anatomical, physiological, and behavioral characteristics. [MM p135]
Phenotype changes constantly, based on extrinsic effects on genes, as we grow up and grow old. [L15 s05, MM p135]
Phenotype changes even in a tiny way with each breath. [L15 s05, MM p135]
Phenotype is set by genotype interacting with **extrinsic factors**, including experience. [MM p135]
Intrinsic factors: genes, which originate within the developing cell itself. [L15 s05, MM p134]
Extrinsic factors: all other influences, which originate outside the developing cell. [L15 s05, MM p134]
Genes direct the production of every protein a cell can make. [MM p134]
An altered gene makes an altered protein, affecting every cell that uses that protein. [MM p134]
So every neural structure, and every behavior, can be altered by changes in genes. [MM p134]
Identical twins: same genotype, but differences in neural phenotypes produce different behaviors. [L15 s05, MM p135]
Identical genotypes do not give identical phenotypes, because extrinsic influences are never identical. [MM p135]
Hundreds of genetic disorders of protein, carbohydrate, or lipid **metabolism** *(body chemistry processing)* harm the developing brain. [MM p135]

Typical defect: a missing **enzyme** *(protein that runs a reaction)* for a key step making or breaking down a body product. [MM p135]

Phenylketonuria (PKU) *(inherited protein metabolism disorder)*: an important example of genes and environment interacting. [L15 s05, MM p135]

PKU defect: no enzyme to metabolize **phenylalanine** (Phe) *(amino acid in many foods)*. [MM p135]

Phenylalanine builds up to toxic levels, damaging the brain and causing **intellectual disability**. [MM p135]

About **1** in **100** people is a PKU carrier; **1** in **10,000** births is affected. [MM p135]

PKU was the first inherited error of metabolism linked to intellectual disability. [MM p135]

Blood phenylalanine is measured in children a few days after birth, for early detection. [MM p135]

Low-Phe diet *(reducing phenylalanine in food)* prevents brain impairment; most critical in early years. [MM p135]

Low-Phe meal example: fruit and protein-free rice and pasta, without cheese. [MM p135]

Gene plus environment: the faulty gene causes intellectual disability **only** when phenylalanine is present. [MM p135, MM p141]

So genotype alone cannot predict brain development: you must also know the child's diet. [MM p135]

Second reason genes are not the whole story: experience changes the activity of genes. [MM p135]

Adult human intelligence comes from inherited genes plus experience deciding where and when genes are expressed. [MM p137]

The large brain growth after birth is molded by experience and social guidance. [MM p137]

Review: new adult neurons grown with exercise, socializing, and mental stimulation is brain **neurogenesis**. [L15 s02, L15 s03]

Review: synapses that strengthen or weaken by effectiveness driving the target cell are **Hebbian synapses**. [L15 s02, L15 s03]

Genotype vs phenotype

	Genotype	Phenotype
What it is	All intrinsic, genetic information	Physical characteristics at one time
Includes	Genes	Anatomy, physiology, behavior
Over life	Constant, fixed at fertilization	Changes constantly
Set by	Genes inherited	Genotype plus extrinsic factors, experience

Table source: [L15 s05, MM p135]

Intrinsic vs extrinsic factors

	Intrinsic factors	Extrinsic factors
What	Genes	All other influences
Origin	Within the developing cell	Outside the developing cell
Examples	Inherited gene, altered gene	Diet (nutrition), experience, mothering

Table source: [L15 s05, MM p134, MM p135]

4.3.2 Define epigenetic changes, and explain how they might play a role in the interaction of genes and the environment

⚠ **Do not mix up: Epigenetic changes alter gene EXPRESSION, NOT the nucleotide sequence of the gene.** [L15 s06, MM p135]

Clones: asexually produced organisms that are genetically identical. [L15 s06, MM p135]

Cloned pigs vary in behavior and temperament as much as normal siblings do. [MM p135]

Genetically identical mice raised in different laboratories behave very differently on many tests. [MM p135]

Nearly every cell has the full genotype but uses **only** a small subset of genes at once. [MM p135]

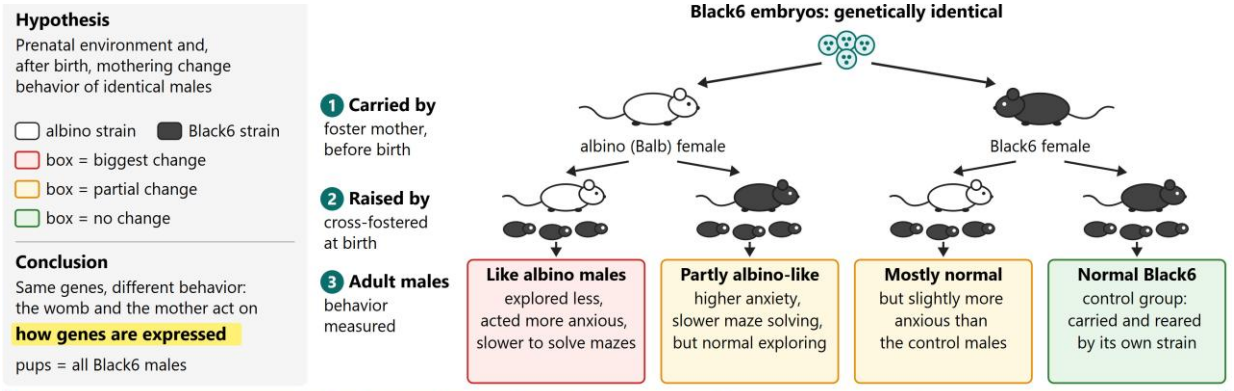
Gene expression: a cell uses a particular gene to make that gene's protein. [MM p135]

Epigenetics: study of factors that change gene expression without changing the gene sequence. [L15 s06, MM p135]

The same protein is made, but the amount varies a lot, so brain development varies. [MM p135]

Genetically identical mice raised by different mothers show different behaviors. [L15 s06, MM p136]

Hypothesis: prenatal environment and/or mothering after birth can change behavior of genetically identical male mice. [L15 s07, MM p136]



Identical Black6 embryos carried and raised by different mothers grow into males who behave differently [L15 s07]

On the figure: Black6 · Balb · cross-fostered · albino · genetically identical

1. **Genetically identical Black6** embryos are implanted into a Black6 or **albino** (**Balb**) mother before birth. [L15 s07, MM p136]

2. At birth, males are **cross-fostered** *(switched to another mother)* to a Black6 or albino mother. [L15 s07, MM p136]

3. Adult male behavior is measured on maze running and anxiety, where the strains normally differ. [L15 s07, MM p136]

Conclusion: same genes, so differences come from prenatal environment and mothering altering gene expression. [L15 s07, MM p136]

Genetically identical individuals may behave very differently because of different epigenetic influences. [MM p141]

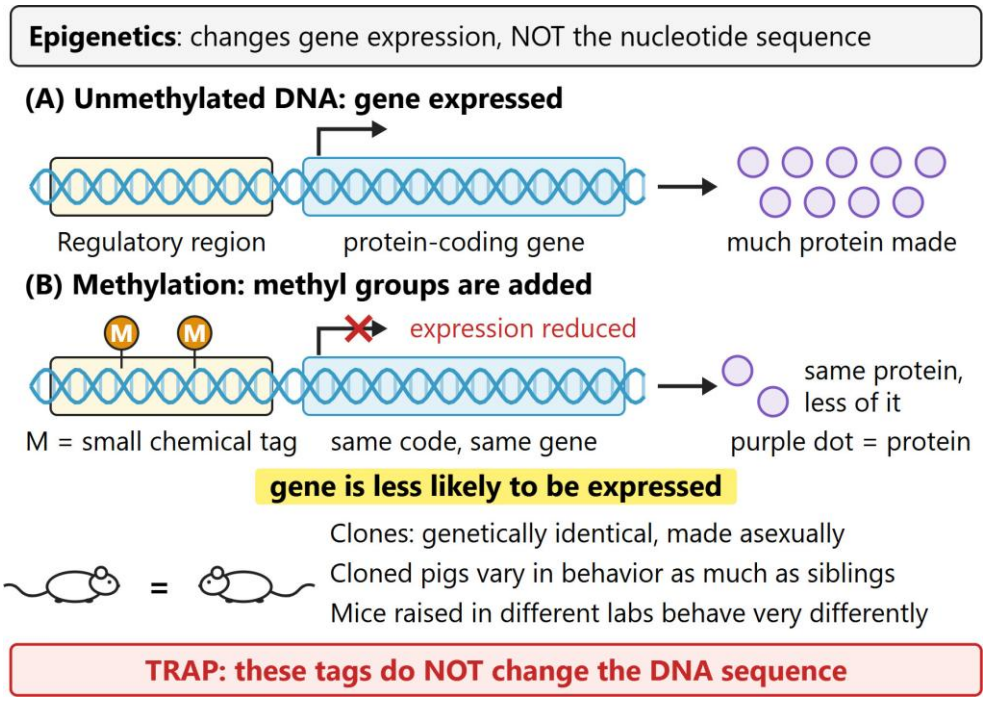
Cross-fostered Black6 mice

Carried by	Raised by	Adult male behavior
Black6	Black6	Normal Black6, as expected
Black6	Albino	Mostly normal Black6, slightly more anxious
Albino	Black6	Partly albino-like: anxious, slow mazes, explores normally
Albino	Albino	Like albino: explore less, anxious, slow mazes

Table source: [L15 s07, MM p136]

4.3.3 Describe the mechanism by which rodent dams can alter their offspring's lifelong stress response

⚠ **Do not mix up: Poor mothering means MORE methylation, FEWER stress hormone receptors, but HIGHER stress hormone levels.** [L15 s09, MM p137]



Unmethylated gene makes much protein; methyl groups on the regulatory region reduce expression [MM p135]

On the figure: unmethylated DNA · methylation · methyl groups · regulatory region · protein-coding gene

Methylation: chemical change to DNA; same nucleotide sequence, but gene is less likely to be expressed. [L15 s08, MM p136]

Unmethylated DNA: no **methyl groups**, so the gene is expressed and much protein is made. [L15 s09, MM p137]

Methylation: same code, same gene, expression reduced; same protein, less of it. [L15 s08, MM p135, MM p136]

A **protein-coding gene** *(DNA stretch that makes a protein)* sits next to its **regulatory region**. [L15 s09, MM p134, MM p137]

Methyl groups attach at the gene's **regulatory region** *(stretch that controls the gene)*. [L15 s09, MM p137]

Pups with inattentive mothers, or interrupted maternal care, secrete more **glucocorticoids** *(stress hormones)* under stress as adults. [MM p136]

Poor maternal care induces methylation of the **glucocorticoid receptor gene** *(stress hormone receptor gene)* in the brain. [L15 s08, MM p136]

Result: rodent pups become hyperresponsive to stress for the rest of their lives. [L15 s08, MM p136]

1. Mother gives **low licking and grooming** to pups. [L15 s09, MM p137]
2. **Methyl groups** are added to the **stress hormone receptor gene**'s **regulatory region**. [L15 s09, MM p137]
3. **Gene expression** is reduced, so fewer hormone receptors are expressed in the brain. [L15 s09, MM p137]
4. Adult has high **stress hormone levels** and high anxiety. [L15 s09, MM p137]
5. Adult daughter gives low licking and grooming to its own pups. [L15 s09, MM p137]

Attentive mothers prevent methylation, so their daughters grow up to be attentive mothers too. [L15 s09, MM p137]

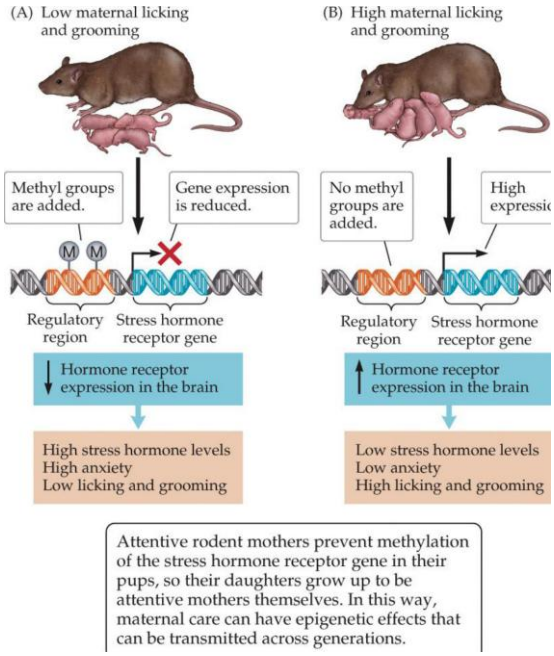
So maternal care has epigenetic effects that can be transmitted across generations. [L15 s09, MM p137]

In humans, the same gene is methylated in people who suffered childhood abuse. [L15 s08, MM p136]

The gene is more often methylated in postmortem brains of suicide victims abused as children. [MM p136]

Suicide victims not abused as children were no more likely than controls to have it methylated. [MM p136]

Suggests methylation in abused children may make them hyperresponsive to stress as adults. [MM p136]



Low licking adds methyl groups and lowers receptors; high licking does the opposite [L15 s09]

On the figure: **methyl groups** · **regulatory region** · **stress hormone receptor gene** · **stress hormone levels** · **low licking and grooming** · **high licking and grooming** · **gene expression**

Mothering is an environmental factor that can affect gene expression. [MM p141]

Low vs high licking mothers

	Low licking and grooming	High licking and grooming
Methyl groups	Added	Not added
Receptor gene expression	Reduced	High
Brain hormone receptors	Decreased	Increased
Stress hormone levels	High	Low
Anxiety	High	Low
Daughters as mothers	Low licking and grooming	High licking and grooming

Table source: [L15 s09, MM p137]

Lecture 16: The Brain Continues to Change as We Grow Older

4.4.1 Describe the current model of processes underlying the degeneration seen in Alzheimer's disease

⚠ **Do not mix up: Tangle NUMBER tracks how bad cognitive impairment is; tangles are probably SECONDARY to plaques.** [MM p140]

Review, low licking and grooming: methyl groups are added and gene expression is reduced. [L16 s02, L16 s03]

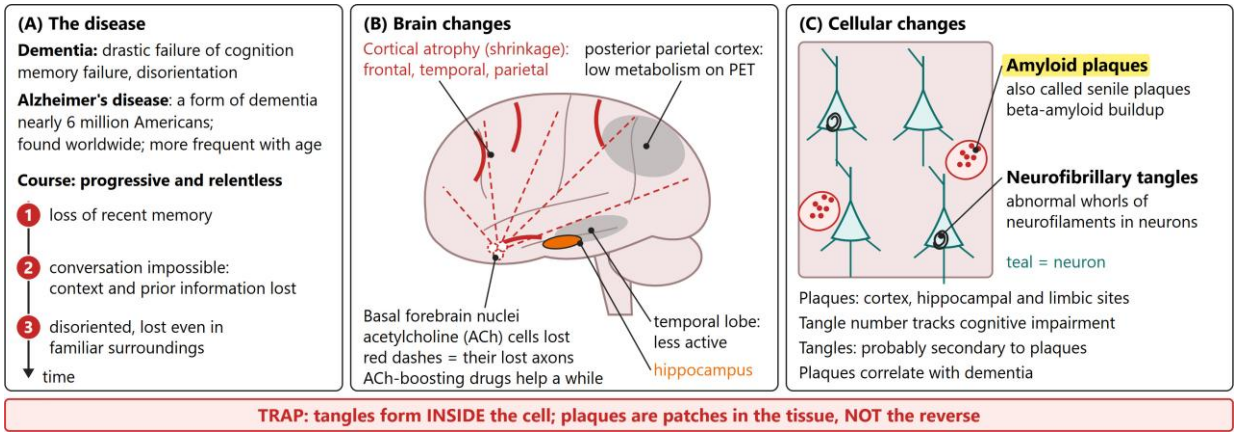
Review, high licking and grooming: no methyl groups are added and gene expression is high. [L16 s02, L16 s03]

Slower responses seem inevitable with aging, but many cognitive abilities change little until advanced age. [MM p138]

Most people reaching an advanced age lead happy, productive lives, at a slower pace. [MM p138]

PET scans: cerebral metabolism normally stays almost constant as we age. [MM p138]

Alzheimer's disease instead shows a dramatic decline in brain activity. [MM p138]



Alzheimer's disease course, brain changes, and the cell changes in plaques and tangles [MM p139]

On the figure: dementia · Alzheimer's disease · cortical atrophy · posterior parietal cortex · amyloid plaques · senile plaques · neurofibrillary tangles · basal forebrain

Dementia: drastic failure of cognitive ability, including memory failure and disorientation. [L16 s05, MM p139]

Alzheimer's disease: a form of dementia; may appear in middle age, more frequent in the aged. [L16 s05, MM p139]

Nearly **6** million Americans have Alzheimer's, a number that will keep growing as the population ages. [MM p139]

Alzheimer's is found worldwide with almost no geographic differences. [MM p139]

Alzheimer's frequency **increases** with aging up to age **85** to **90.** [MM p139]

People reaching that age symptom-free become less and less likely to ever develop them. [MM p139]

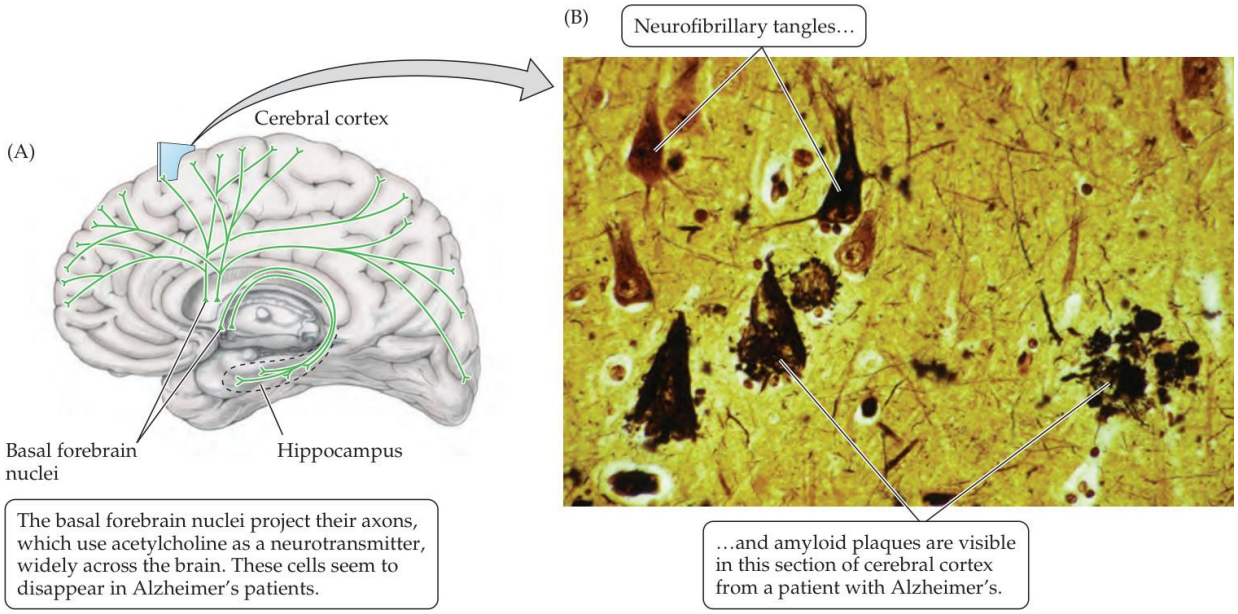
So Alzheimer's is a disease, not simply wear and tear in the brain. [MM p139]

Staying physically and mentally active reduces risk, also refuting the idea that brains simply wear out. [MM p139]

1. Begins as memory loss of recent events. [L16 s05, MM p139]
2. Memory loss grows so extensive that conversation is impossible: context and prior information are lost. [L16 s05, MM p139]
3. Cannot answer simple questions, such as what year it is or where they are. [MM p139]
4. Becomes disoriented, easily lost even in familiar surroundings; decline is progressive and relentless. [MM p139]

Brain shows striking **cortical atrophy** *(shrinking of the cortex)*, especially frontal, temporal, and parietal areas. [L16 s05, MM p139]

PET: marked reduction of metabolism in **posterior parietal cortex** and parts of the temporal lobe. [L16 s05, MM p139]



Basal forebrain acetylcholine axons across the cortex, with tangles and plaques in cortex tissue [MM p139]

On the figure: basal forebrain · hippocampus · neurofibrillary tangles · amyloid plaques · acetylcholine

Amyloid plaques (also **senile plaques**): patches formed by buildup of **beta-amyloid** *(protein that piles up)*. [L16 s08, MM p139]

Amyloid plaques appear in cortex, **hippocampus**, and associated limbic system sites. [MM p139]

Amyloid plaque: small brain area with abnormal cellular and chemical patterns; plaques correlate with dementia. [MM p139]

Beta-amyloid: a protein that accumulates in amyloid plaques in Alzheimer's disease. [L16 s08, MM p139]

Neurofibrillary tangles: abnormal whorls of **neurofilaments** *(threads inside nerve cells)* tangled inside the cell. [L16 s08, MM p140]

The number of tangles is directly related to the size of cognitive impairment. [MM p140]

Neurons in the **basal forebrain** that make **acetylcholine (ACh)** *(a neurotransmitter)* are gradually lost. [L16 s08, MM p140]

Basal forebrain nuclei send ACh axons widely across the brain; these cells seem to disappear. [L16 s09, MM p139]

Drugs that boost ACh signaling may reduce some symptoms for a time. [MM p140]

1. Beta-amyloid builds up. [L16 s08, MM p139]
2. Amyloid plaques form in cortex, hippocampus, and limbic sites. [L16 s08, MM p139]
3. Neurofibrillary tangles form, probably as a secondary response to plaques. [MM p140]
4. More tangles go with more cognitive impairment. [MM p140]

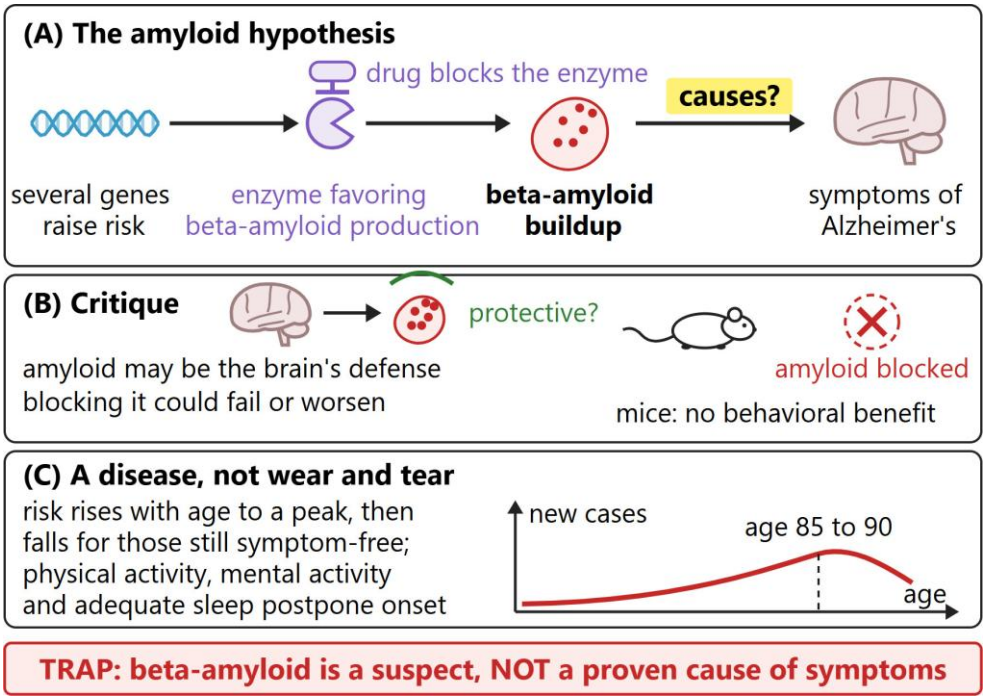
Three cellular changes in Alzheimer's

Change	What it is	Key point
Amyloid plaques	Patches of beta-amyloid buildup	In cortex, hippocampus, limbic sites
Neurofibrillary tangles	Whorls of neurofilaments inside cells	Number tracks cognitive impairment
ACh neuron loss	Basal forebrain neurons die	ACh drugs ease symptoms briefly

Table source: [L16 s08, MM p139, MM p140]

4.4.2 Critique the amyloid hypothesis of Alzheimer's

⚠ **Do not mix up: Beta-amyloid is a suspect, NOT a proven cause: it may be the brain's response.** [MM p140]



The amyloid hypothesis, its critique, and risk with age [MM p141]

On the figure: amyloid hypothesis · beta-amyloid · buildup · mice · physical activity · mental activity

The **amyloid hypothesis** *(beta-amyloid buildup causes the symptoms)*: skepticism is growing. [MM p140]

Beta-amyloid is a suspected cause because amyloid plaques correlate with dementia. [MM p139, MM p141]

Several genes affect beta-amyloid **buildup** in plaques and **increase** Alzheimer's risk. [MM p141]

Amyloid levels on PiB imaging correlated with who would develop Alzheimer's. [MM p140]

Treatment strategy: drugs that interfere with enzymes favoring beta-amyloid production. [MM p140]

Growing skepticism: does beta-amyloid actually cause the symptoms of Alzheimer's? [MM p140, MM p141]

Alternative: amyloid may be the brain's defense, something the brain does to avoid symptoms. [MM p140]

If so, blocking amyloid production would not help and might even worsen the disease. [MM p140]

Support for the doubt: several manipulations in **mice** blocked amyloid but gave no behavioral benefit. [MM p140]

Genes and experience interact: **physical activity**, **mental activity**, and adequate sleep can postpone onset of Alzheimer's. [MM p140, MM p141]

Best current way to avoid Alzheimer's: remain physically and mentally active. [MM p140]

Critique of the amyloid hypothesis

For amyloid as cause	Against amyloid as cause
Plaques correlate with dementia	Blocking amyloid in mice: no behavior benefit
Genes raising amyloid raise risk	Amyloid may be a protective response
PiB amyloid predicts who develops it	Blocking amyloid might worsen disease

Table source: [MM p139, MM p140, MM p141]

4.4.3 Discuss how brain imaging may help us understand the mechanism(s) of Alzheimer's

⚠ **Do not mix up: Only HIPPOCAMPAL formation size, NOT general brain shrinkage, correlated with memory decline in aging.** [L16 s06, MM p138]

Question: is mild memory impairment tied to shrinking of specific regions, or general brain shrinkage? [L16 s06, MM p138]

Participants: healthy, cognitively normal people aged **55** to **87.** [L16 s06, MM p138]

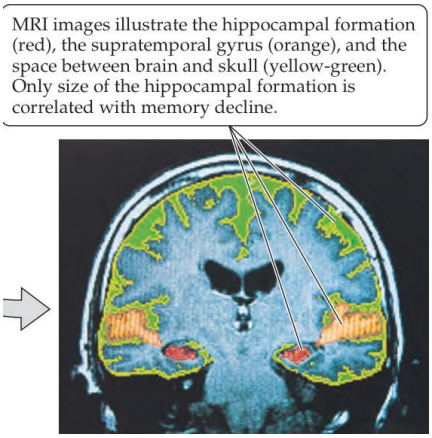
Methods: memory tests, plus brains measured from **MRI** *(scan of brain structure)* images. [L16 s06, MM p138]

Effects of sex, age, IQ, and overall brain atrophy were removed statistically. [MM p138]

Result: **only hippocampal formation** volume correlated with memory decline. [L16 s06, L16 s07, MM p138]

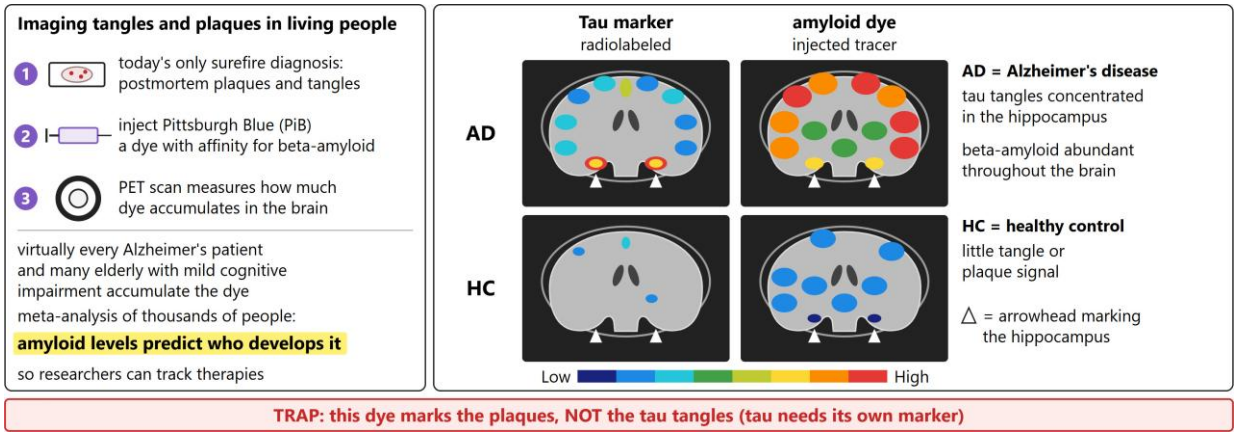
MRI colors: hippocampal formation red, **supratemporal gyrus** orange, space between brain and skull yellow-green. [L16 s07, MM p138]

Only hippocampal size correlated: supratemporal gyrus and skull space (general shrinkage) did not. [L16 s06, L16 s07, MM p138]



Coronal MRI showing the hippocampal formation, supratemporal gyrus, and skull space [MM p138]

On the figure: MRI · hippocampal formation · supratemporal gyrus



Imaging plaques and tangles: Pittsburgh Blue PET and tau marker in Alzheimer's brains and healthy controls [MM p140]

On the figure: Pittsburgh Blue · affinity · PET scan · meta-analysis · tau tangles · healthy control

Only surefire diagnosis now: postmortem brain exam showing amyloid plaques and neurofibrillary tangles. [MM p140]

Pittsburgh Blue (PiB): injected dye with an **affinity** *(tendency to bind)* for beta-amyloid. [L16 s10, MM p140]

A **PET scan** *(brain scan of an injected tracer)* then shows how much dye accumulates in the brain. [MM p140]

Virtually every brain of a person with Alzheimer's accumulates PiB. [MM p140]

So do brains of many elderly people with mild cognitive impairment. [MM p140]

Meta-analysis of thousands: PiB amyloid levels correlated with who would develop Alzheimer's. [MM p140]

Implication: easier to track how well therapies for Alzheimer's work. [MM p140]

Injected **radiolabeled markers** *(radioactive tags that show on scans)* can image **tau tangles**. [L16 s10, MM p140]

PiB marks beta-amyloid plaques, **NOT** tau tangles; tau needs its own radiolabeled marker. [L16 s10, MM p140]

Alzheimer's brain: tau tangles concentrated in the hippocampus, compared with a **healthy control**. [L16 s10, MM p140]

Alzheimer's brain: beta-amyloid abundant throughout the brain; healthy control shows low amyloid. [L16 s10, MM p140]

PET also shows reduced metabolism in posterior parietal and temporal cortex in Alzheimer's. [L16 s05, MM p139]

Imaging tangles vs plaques

Scan target	Marker	Alzheimer's brain (AD)	Healthy control (HC)
Tau tangles	Radiolabeled marker	Concentrated in hippocampus	Little signal
Beta-amyloid	Pittsburgh Blue (PiB)	Abundant throughout brain	Low

Table source: [L16 s10, MM p140]

Book 5.1: Sensory Processing and the Somatosensory System

5.1.1 Understand the concepts of labeled lines and sensory transduction

⚠ **Do not mix up: All senses use the SAME action potentials: the separate line, not the signal, tells the sense.** [MM p144]

Case: a man lost light touch below the neck after a viral infection at age **19.** [MM p143]

The infection hit a very specific set of nerves sending body information to the brain. [MM p143]

Still felt: pain, deep pressure, and warm and cool surfaces on the skin. [MM p143]

Lost: all information about muscle activity and body position, though all muscles still move. [MM p143]

Result: could not walk across a room without falling, nor walk up or down stairs. [MM p143]

The few others with this loss spent the rest of their lives in wheelchairs. [MM p143]

Fix: the man learned to walk by watching the moving body, using **vision** as feedback. [MM p143]

Lights out: the man collapses and must lie still until the lights return. [MM p143]

Pointing repeatedly to one spot in the air, the man beats control participants in accuracy. [MM p143]

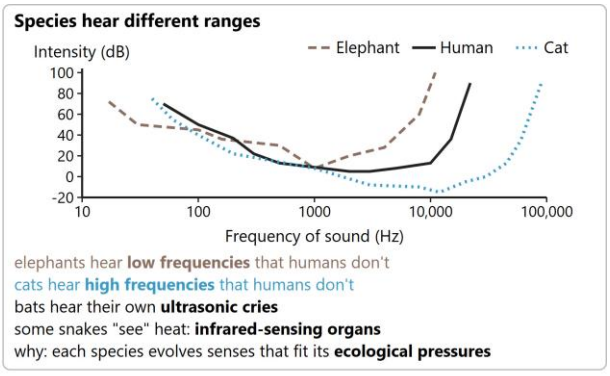
Cost: constantly watching the body is a mental drain; in bed, covers tether the limbs. [MM p143]

Shows: losing body sense is devastating, though it is not one of the familiar five senses. [MM p143]

Air molecules are sensed as odors; air vibrations as sounds; reflected light builds vision. [MM p143]

Species differ in what they must sense, so evolution gave each its own capabilities. [MM p144]

System type	Modality	What it senses
Mechanical	Touch	Contact with body surface
	Pain	Tissue damage
	Hearing	Sound vibrations in air or water
	Vestibular	Head movement and orientation
	Joint	Position and movement
	Muscle	Tension
Light	Vision	Photons, from a source or reflected
Thermal	Cold	Decrease in skin temperature
	Warmth	Increase in skin temperature
Chemical	Smell	Odorant molecules in air
	Taste	Substances in contact with the tongue
	Vomeronasal	Pheromones in air or water
Electrical	Electroreception	Differences in current density
Magnetic	Magnetoreception	Magnetic fields for orientation



receptor cells sense some forms of energy (**stimuli**), not others: they act as **filters** and convert the key ones into **electrical signals**

TRAP: each receptor responds to only SOME kinds of energy, NOT every form

Sensory systems and what they detect, and species hearing ranges [MM p144]

On the figure: elephants · cats · ultrasonic · infrared · receptor cells · filters · ecological · stimuli

Bats detect their own **ultrasonic** *(too high-pitched for humans)* cries, which humans cannot hear. [MM p144]

Some **snakes** have **infrared** *(heat radiation)* sensing organs in the face to "see" heat sources in the dark. [MM p144]

Receptor cell: specialized cell that converts a particular energy or substance into a membrane potential change. [MM p144]

Stimulus: a physical event that triggers a sensory response. [MM p144]

Receptor cells sense some forms of energy but not others, so they act as **filters**. [MM p144]

Receptor cells ignore the background and convert key **stimuli** into electrical signals, the nervous system's language. [MM p144]

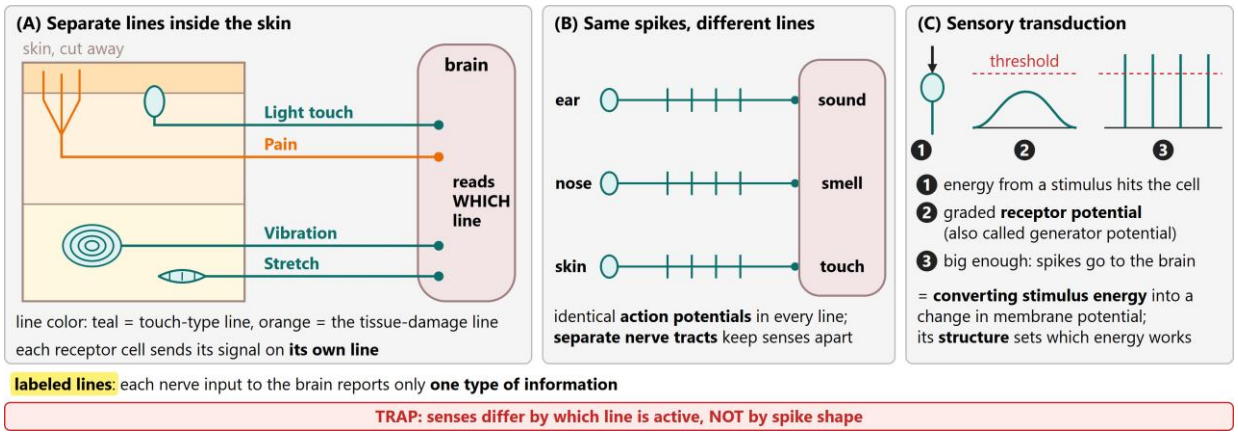
Different energies need different sensory organs, just as a photo needs a camera, not a microphone. [MM p144]

The eye alone comes in a dazzling array of sizes, shapes, and forms across animals. [MM p144]

Each species' auditory abilities reflect its unique **ecological** pressures. [MM p144, MM p145]

Elephants hear low sound frequencies that humans do not hear. [MM p145]

Cats hear high sound frequencies that humans do not hear. [MM p145]



Separate lines for each touch type, identical spikes, and transduction steps [MM p145]

On the figure: labeled lines · separate nerve tracts · light touch · vibration · stretch · pain · receptor potential · generator potential

Labeled lines: each nerve input to the brain reports **only** one particular type of information. [MM p144]

The end product of every sensory receptor, the action potential, is the same for all modalities. [MM p144]

The brain tells modalities apart because each sense travels in **separate nerve tracts**. [MM p144]

Lines are labeled right from the outset: one signals a sound, another a smell, others touch. [MM p144]

Labeled lines also exist within touch: separate lines for **light touch**, **vibration**, and skin **stretch**. [MM p144, MM p145]

Each skin receptor signals on its own line, so the brain knows which touch happened. [MM p145]

Separate labeled lines run from hand skin to brain for **pain**, touch, vibration, and stretch. [MM p145]

A receptor cell's **structure** determines which energy or chemical it responds to. [MM p145]

Mechanisms vary, but the outcome is always the same: an electrical change in the receptor. [MM p145]

Receptor potential *(local voltage change in a receptor)*: also called **generator potential**; may start an action potential. [MM p145]

A receptor potential is a local, stimulus-caused change in a receptor cell's resting potential. [MM p145]

A receptor potential resembles an **excitatory postsynaptic potential** *(small excitatory voltage bump)*. [MM p145, MM p146]

Sensory transduction: a receptor cell converts stimulus energy into a change in membrane potential. [MM p146]

Transduction converts environmental stimuli into action potentials the brain can understand. [MM p146]

Review: species ecology shapes sensory abilities; species sense mainly stimuli important to them. [MM p144, MM p147, MM p174]

Review: labeled lines each transmit one type of information, such as sound, smell, or touch type. [MM p144, MM p147]

Review: transduction turns a stimulus into a receptor potential, which can trigger action potentials. [MM p146, MM p147, MM p174]

Summary: receptor cells give the brain **only** selected information; skin has several specialized touch receptors. [MM p174]

Classification of sensory systems

System type	Modality	Sensed stimuli
Mechanical	Touch	Contact with body surface
Mechanical	Pain	Tissue damage
Mechanical	Hearing	Sound vibrations in air or water
Mechanical	Vestibular	Head movement and orientation
Mechanical	Joint	Position and movement
Mechanical	Muscle	Tension
Light	Vision	Photons, from light sources or reflections
Thermal	Cold	Decrease in skin temperature
Thermal	Warmth	Increase in skin temperature
Chemical	Smell	Odorant chemicals in air
Chemical	Taste	Substances contacting tongue or taste receptors
Chemical	Vomeronasal	Pheromones in air or water
Electrical	Electroreception	Differences in electrical current density
Magnetic	Magnetoreception	Magnetic fields for orientation

Table source: [MM p144]

5.1.2 Describe several different types of receptors in the skin and the stimuli they detect

⚠ **Do not mix up: Pacinian corpuscles sense vibration and texture; Merkel's discs and Meissner's corpuscles sense object form.** [MM p146]

Touch is not just touch: pressure, vibration, tickle, "pins and needles", smoothness, and wetness. [MM p146]

Each is recorded by skin receptors, then sent along **separate axons** to the brain. [MM p146]

Skin layers from outside in: **epidermis**, **dermis**, **hypodermis** *(deepest skin layer)*. [MM p146]

Pacinian corpuscle: also called **lamellated corpuscle**; a skin receptor detecting vibration and pressure. [MM p146]

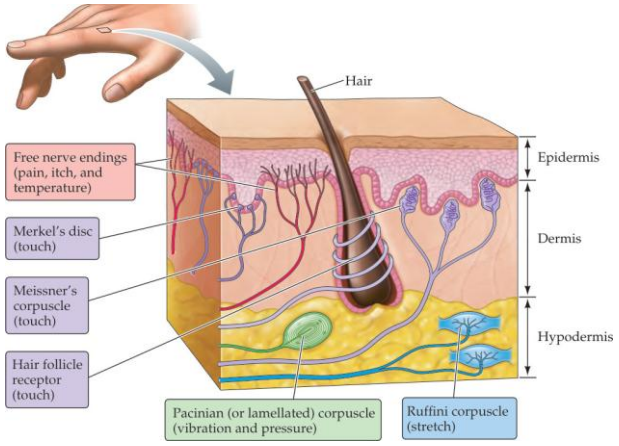
A Pacinian corpuscle is a tiny onion-like structure embedded in the innermost layer of skin. [MM p146]

Its onion-like **layered capsule** wraps the nerve ending. [MM p146]

As a filter, **only** vibrations above about **200 cycles per second** stimulate its nerve ending. [MM p146]

Vibrations above about **200** cycles per second are created when we feel a **texture** against skin. [MM p146]

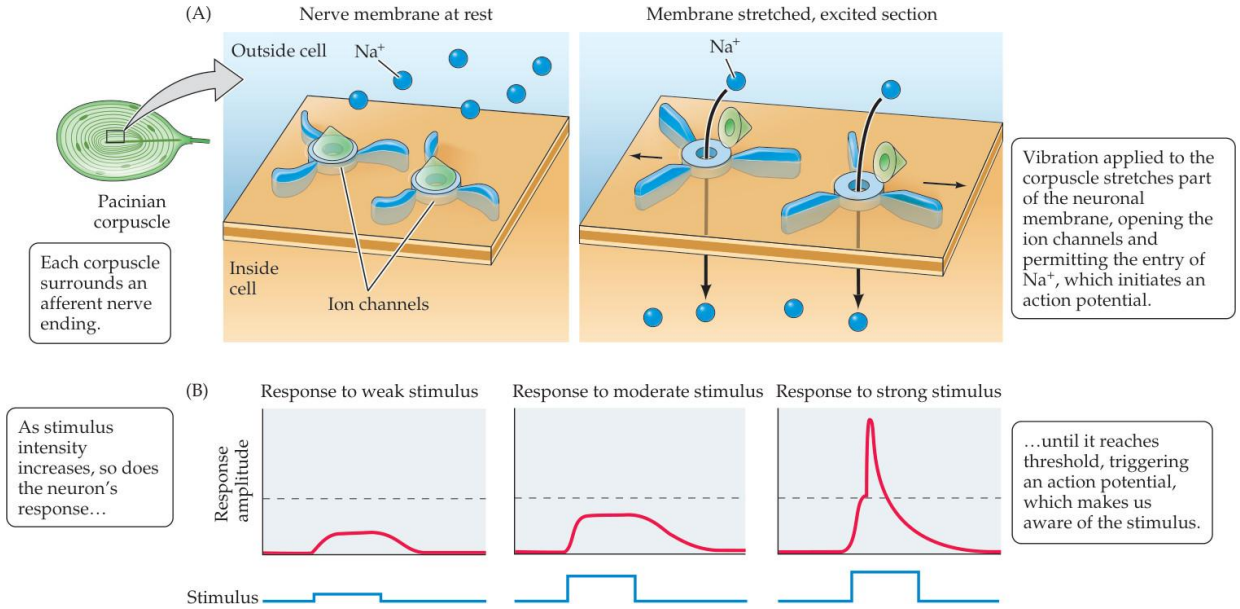
At rest, before any stimulus: the nerve membrane keeps its ion channels **closed**. [MM p147]



Skin layers with the touch, stretch, and pain receptors in each [MM p146]

On the figure: epidermis · dermis · hypodermis · Pacinian corpuscle · Meissner's corpuscle · Merkel's disc · Ruffini corpuscle · hair follicle receptor

With the channels closed, Na+ stays outside the cell. [MM p147]



Pacinian corpuscle: stretch opens sodium channels, receptor potential grows until threshold [MM p147]

On the figure: Pacinian corpuscle · afferent · Na+ · threshold

1. Each corpuscle surrounds an **afferent** *(carrying signals toward the CNS)* nerve ending. [MM p147]
2. Vibration or pressure stretches part of the nerve ending's membrane. [MM p146, MM p147]
3. Stretch pops open **mechanically gated sodium channels**; **Na+** enters the cell. [MM p146, MM p147]
4. A **graded receptor potential** forms; its amplitude is directly proportional to stimulus strength. [MM p146]
5. If it exceeds **threshold**, action potentials travel via sensory nerves to the spinal cord. [MM p146]

Threshold: here, the stimulus intensity just adequate to trigger an action potential in a sensory cell. [MM p146]

Weak and moderate stimuli: generator potential grows with intensity but stays below threshold, no action potential. [MM p147]

A strong stimulus reaches threshold, triggering an action potential that makes us aware of the stimulus. [MM p147]

Meissner's corpuscle: also called **tactile corpuscle**; light touch, especially **changes** in stimuli. [MM p146]

Meissner's corpuscles are more numerous and detect localized movement between skin and a surface. [MM p146]

Merkel's disc: light touch, especially **edges** and isolated **points** on a surface. [MM p146]

Meissner's corpuscles and Merkel's discs mediate most of our ability to perceive object **forms**. [MM p146]

Ruffini corpuscle: detects **stretching** of the skin; **only** sparsely distributed. [MM p146]

Ruffini corpuscles detect stretch of skin patches when we move fingers or limbs. [MM p146, MM p147]

Hair follicle receptor: wraps the hair root and signals touch. [MM p146]

Free nerve ending: an axon ending in the skin with no specialized cell attached. [MM p147]

Free nerve endings detect **pain, itch, heat, and cold** (changes in temperature). [MM p146, MM p147]

All these receptors are most concentrated where touch is finest: **fingertips, tongue, and lips**. [MM p147]

Review: Pacinian senses vibration, Meissner's changes, Merkel's edges and points, Ruffini stretch. [MM p146, MM p147]

Receptors in the skin

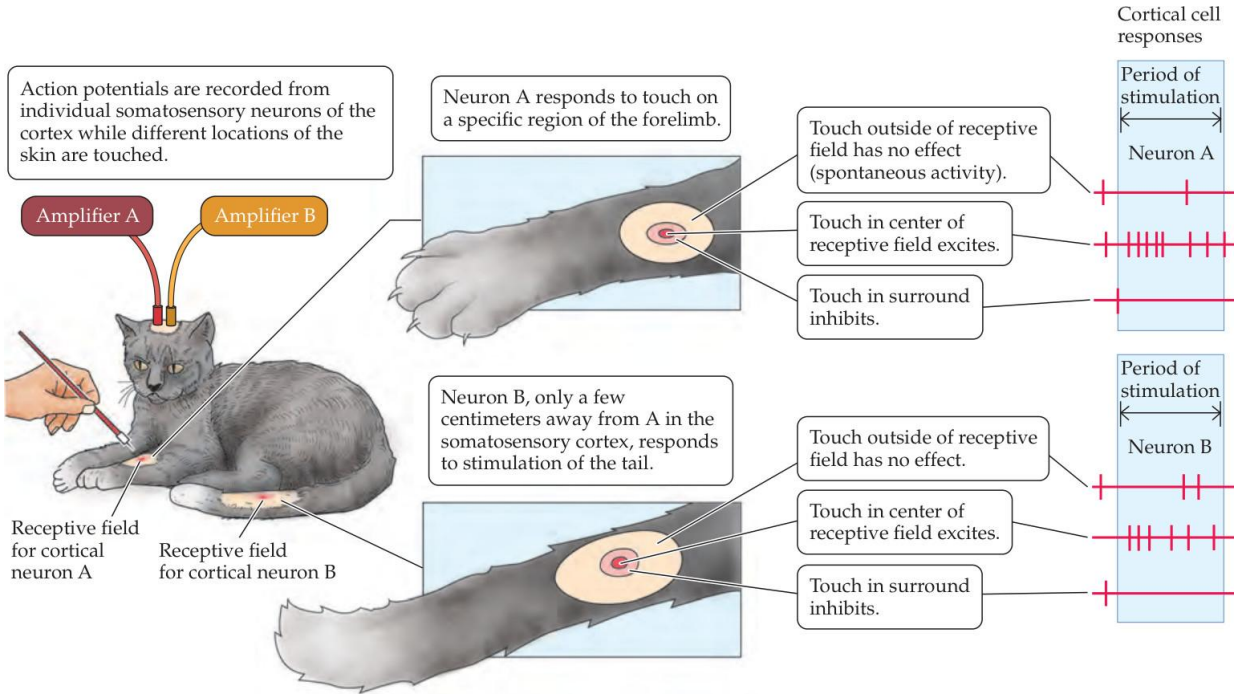
Receptor	Location in skin	Detects	Note
Free nerve endings	Reach into epidermis	Pain, itch, temperature	Bare axon, no specialized cell
Merkel's disc	Base of epidermis	Light touch	Edges and isolated points
Meissner's corpuscle	Top of dermis	Light touch	Changes; skin moving on surface
Hair follicle receptor	Around hair root	Touch	Touch at the hair
Pacinian corpuscle	Innermost layer (hypodermis)	Vibration and pressure	Texture; above about **200** cycles per second
Ruffini corpuscle	Deepest layer (hypodermis)	Skin stretch	Finger and limb movement; sparse

Table source: [MM p146, MM p147]

5.1.3 Relate the concepts of receptive fields and sensory adaptation

⚠ Do not mix up: PHASIC receptors adapt fast; TONIC receptors keep firing and signal duration, like many pain sensors. [MM p149]

Senses are **NOT** an accurate snapshot: they send limited, even distorted, information to the brain. [MM p147]
Much **selection and analysis** happens along sensory pathways before information reaches the brain. [MM p147]
The brain gets a filtered picture: survival-critical stimuli emphasized over less important ones. [MM p147]
Filtering appears in stimulus coding, receptive fields, adaptation, and active suppression by the brain. [MM p147]
Labeled lines code stimulus **type**; intensity and location need other coding. [MM p147]
A sensory neuron's action potentials always have the same size and duration. [MM p147, MM p148]
So **intensity** is coded in the number and frequency of action potentials and their rhythm. [MM p148]
Neurons fire up to maybe **1,200 action potentials per second**, probably less in most. [MM p148]
So frequency in one neuron could represent **only** a very limited range of intensities. [MM p148]
Fix: multiple receptor cells, each specializing in one part of the intensity range. [MM p148]
Stronger stimuli **recruit** extra neurons sensitive to higher intensities. [MM p148]
Intensity is then represented by the number and thresholds of activated cells. [MM p148]
Somatosensory system *(body sensation system)*: receptors and neural mechanisms for body sensations like touch and pain. [MM p148]
Somatosensory **location** is coded by the position of the stimulated receptors on the sensory surface. [MM p148]
Labeled lines carry location: we know which skin patch a mosquito bites, to aim the slap. [MM p148]
Vision: an object's location determines which receptors in the eye are stimulated. [MM p148]
Bilateral systems (two eyes, ears, nostrils) code left versus right differences as location cues. [MM p148]
In visual and touch pathways, neurons at all levels, receptors to cortex, form orderly **maplike** arrangements. [MM p148]
Maps are not exact but reflect both spatial position and **receptor density**. [MM p148]
Sensitive, densely innervated sites like the lips get more cells than the skin of the back. [MM p148]
Each cell in a sensory map responds best to one stimulus type in one place. [MM p148]
Receptive field: the stimulus region and features that affect a sensory cell's activity. [MM p148]
A neuron's receptive field is the region of space where a stimulus alters its firing rate. [MM p148]
Receptive fields are found by recording responses to many stimuli: which ones change the resting rate? [MM p148]
Somatosensory receptive fields are **doughnut-shaped**: a center and a surround. [MM p148]
Either an excitatory center with inhibitory surround, or an inhibitory center with excitatory surround. [MM p148]
The center and surround shape makes **edges** on the objects we feel easier to detect. [MM p148]
Fields differ in size, shape, and the quality of stimulation that activates them. [MM p148]
Some neurons prefer light touch, others fire most to painful stimuli, others to cooling. [MM p148]
Neurons at every level of the pathway have their own receptive field. [MM p148]
Receptive fields change considerably at each successive level as neurons add processing. [MM p148, MM p174]



Cat cortex neurons A and B: center touch excites, surround inhibits, outside does nothing [MM p149]

On the figure: receptive field · Neuron A · Neuron B · forelimb · tail · center · surround · spontaneous activity

Cat experiment: record single somatosensory cortex neurons while touching different skin locations. [MM p149]

Neuron A responds to touch on a specific region of the **forelimb**. [MM p149]

Neuron B, **only** a few centimeters away in cortex, responds to touch on the **tail**. [MM p149]

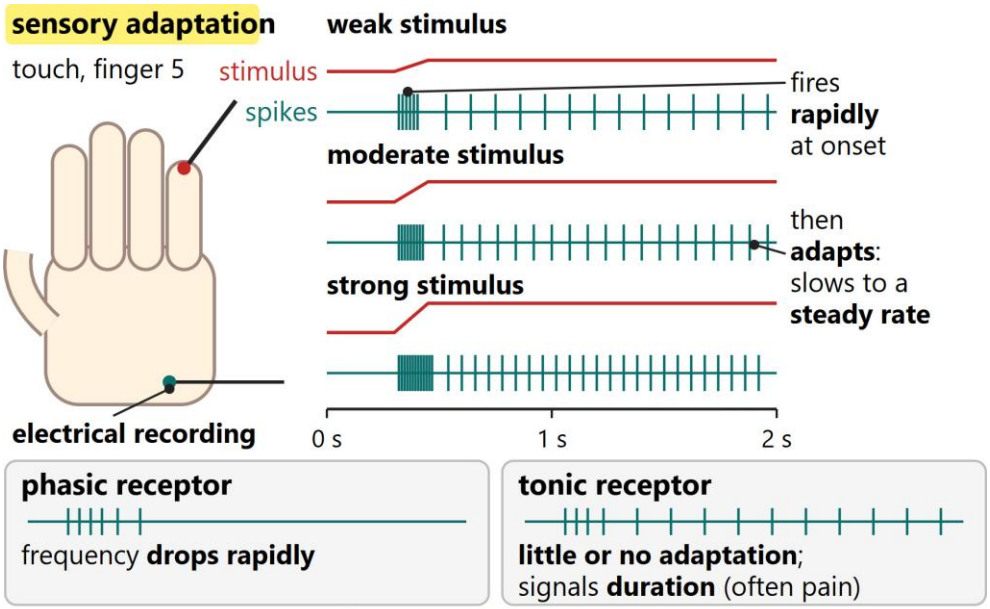
Touch in the **center** excites; touch in the **surround** inhibits. [MM p149]

Touch outside the **receptive field** has no effect: **only** **spontaneous activity** continues. [MM p149]

Sensory adaptation: progressive loss of receptor response as stimulation is maintained. [MM p148]

Adaptation lets us ignore unchanging stimuli: clothes on our skin, the buzz of overhead lights. [MM p148]

Adaptation helps senses avoid overload and stay vigilant for critical events. [MM p148, MM p149]



Sensory adaptation: phasic receptors drop fast, tonic receptors keep firing [MM p148]

On the figure: sensory adaptation · phasic receptor · tonic receptor · electrical recording · duration · adapts

Phasic receptor: action potential frequency drops **rapidly** as stimulation is maintained. [MM p149]

Tonic receptor: frequency declines slowly or not at all; can signal stimulus **duration**. [MM p149]

Pain sensors are often tonic: sustained high activity helps us avoid further injury. [MM p149]

Fifth-finger touch: the neuron fires rapidly at onset, whether the stimulus is weak, moderate, or strong. [MM p149]

An **electrical recording** of the fifth-finger neuron shows its action potentials over time. [MM p149]

Then the fifth-finger neuron **adapts**, slowing to a steady rate. [MM p149]

Adaptation shows senses shift **away from accurate portrayal** of the external world. [MM p149]

Pacinian corpuscle adaptation comes from the **elasticity** of the corpuscle itself. [MM p149, MM p150]

Remove the corpuscle (a separate accessory structure): the bare fiber does **NOT** adapt, firing on. [MM p150]

Survival depends more on sensitivity to important **changes** than on exact reporting of stimuli. [MM p150]

Three ways to quiet senses: adaptation, physically blocking stimuli, and neural suppression. [MM p150]

Blocking stimuli: closing eyelids; tiny **middle-ear muscles** reduce sound reaching the inner ear. [MM p150]

Neural: reciprocal connections descend from the brain to lower levels, inhibiting ascending sensory axons. [MM p150]

Central modulation of sensory information: higher centers like cortex and thalamus suppress some inputs, amplify others. [MM p150]

Central modulation is a feature of many sensory and pain pathways. [MM p150]

Central modulation helps the brain attend to some stimuli more than others. [MM p150]

Review: intensity is coded by action potential number, frequency, rhythm, and recruitment of cells. [MM p148, MM p150]

Review: cells for strong stimuli extend the range, since one neuron can fire **only** so fast. [MM p148, MM p150]

Review: receptive fields are found by recording a cell while stimulating many skin spots. [MM p148, MM p149, MM p150]

Review: adaptation and central modulation both change a sensory neuron's response to stimuli. [MM p148, MM p150]

Phasic vs tonic receptors

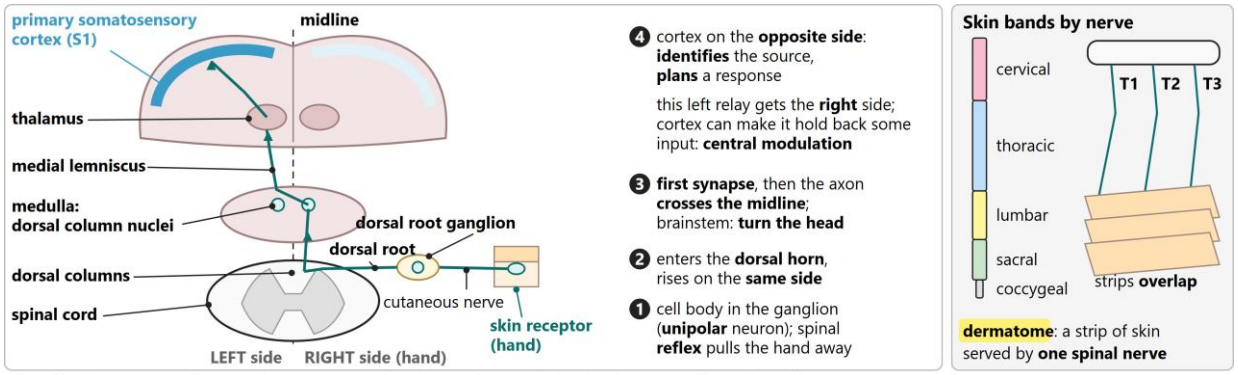
Feature	Phasic receptor	Tonic receptor
Adaptation	Yes, rapid	Little or none
Firing with steady stimulus	Drops rapidly	Declines slowly or not at all
Signals	Changes, onset	Stimulus duration
Example	Pacinian corpuscle (adapts)	Pain sensors (often)

Table source: [MM p149, MM p150]

5.1.4 Describe the neural pathway for the system reporting touch information from the body

⚠ Do not mix up: Touch crosses the midline in the MEDULLA; pain, temperature, and itch cross in the spinal cord. [MM p151, MM p174]

Pain, temperature, and itch use a separate route: the **anterolateral system** (spinothalamic system). [MM p151, MM p174]
Each sensory system has its own pathway from the periphery to successively higher levels. [MM p150]
Touch receptor axons are bundled into sensory nerves running to the **dorsal** *(rear)* spinal cord. [MM p150]
Dorsal column system: carries most touch to the brain in dorsal columns of spinal white matter. [MM p150]
Dorsal columns: a large wedge of white matter in the dorsal spinal cord. [MM p150]



Touch pathway from skin to cortex, and skin strips served by each spinal nerve [MM p151]

On the figure: primary somatosensory cortex · thalamus · medial lemniscus · dorsal column nuclei · dorsal columns · medulla · cutaneous · dorsal root

1. Skin touch receptors fire; action potentials travel along a **cutaneous** *(skin)* nerve. [MM p151]
2. The axon's **unipolar neuron** has its cell body in the **dorsal root ganglion**. [MM p151]
3. The axon enters the spinal cord through the **dorsal root**, into the dorsal horn. [MM p151]
4. It joins the **dorsal column** and ascends to the brainstem with no synapse yet. [MM p150, MM p151]
5. In the **medulla**, first synapse onto a neuron of the **dorsal column nuclei**. [MM p151]
6. The medullary neuron's axon **crosses the midline** and rises in the **medial lemniscus**. [MM p150, MM p151]
7. It reaches the **thalamus**: the left thalamus now receives right-side body information. [MM p151]
8. The thalamus sends it to **primary somatosensory cortex** (S1). [MM p150, MM p151]

At all levels, inputs follow a somatosensory map dividing the body surface into discrete bands. [MM p150]
Dermatome *(skin strip of one nerve)*: strip of skin innervated by a particular spinal nerve. [MM p150]
From Greek derma, "skin", and tome, "part" or "segment". [MM p150]
Spinal segments in order: cervical, thoracic, lumbar, sacral, coccygeal. [MM p151]
Body bands map to cervical, thoracic, lumbar, and sacral segments in an orderly sequence. [MM p151]
Cervical bands cover the neck and arms; thoracic bands the trunk; lumbar and sacral bands the legs. [MM p151]
Each dorsal root (T1, T2, T3) serves its own skin strip; adjacent dermatomes overlap somewhat. [MM p151]
Maplike organization also appears in vision and hearing. [MM p150]
Each station in a sensory pathway does a basic part of information processing. [MM p150]
Spinal cord: a painful finger triggers reflexive hand withdrawal before we even feel pain. [MM p150]
Brainstem: circuits turn the head toward the source of pain. [MM p150]
Cortex: most complex processing, such as identifying the source (a sliver) and planning a response. [MM p150]
Thalamus: regions at the top of the brainstem that trade information with the cortex. [MM p150]
For most senses, information reaches the thalamus before being relayed to cortex. [MM p150, MM p152]
Each sensory modality is sent to a separate division of the thalamus. [MM p152]
Cortex can direct the thalamus to emphasize some sensory information and suppress other information. [MM p152]

1. Sensory information enters the CNS via spinal cord (peripheral nerves) or brainstem (cranial nerves). [MM p152]
2. It travels to the thalamus. [MM p152]

3. The thalamus shares it with cortex; cortex directs the thalamus to suppress some sensations. [MM p152]

4. Primary sensory cortex swaps information with nonprimary sensory cortex. [MM p152]

Primary sensory cortex: region receiving most of a modality's information from the thalamus. [MM p152]

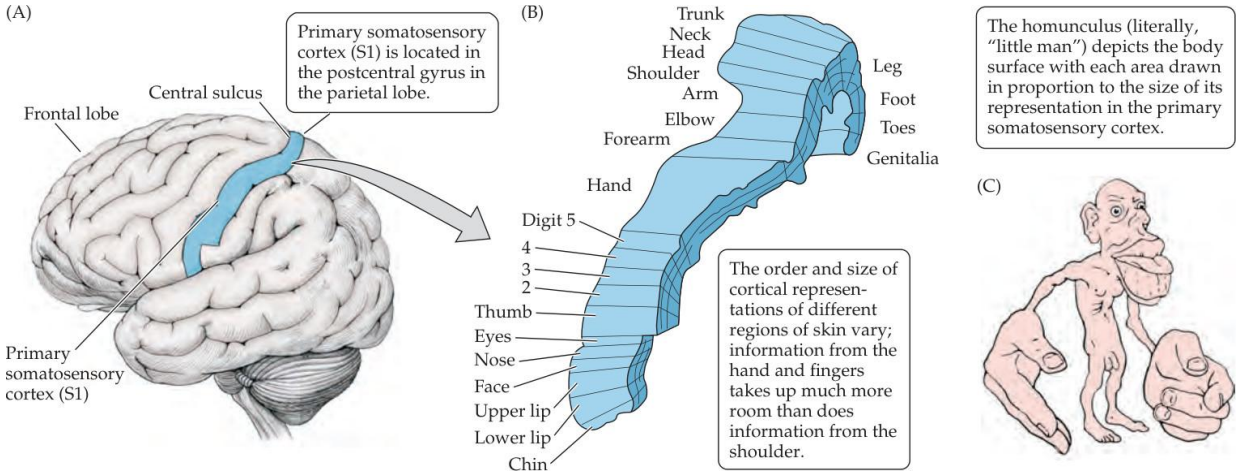
Exception: in **olfaction** *(smell)*, primary cortex gets input directly from secondary sensory neurons. [MM p152]

Primary sensory cortex is generally the first cortical destination of sensory inputs. [MM p152]

Nonprimary sensory cortex: also called secondary sensory cortex; gets direct projections from primary cortex. [MM p152]

Nonprimary areas often process the same information in collaboration with primary cortex. [MM p152]

Each cortical sensory region processes different aspects of our perceptual experiences. [MM p152]



Primary somatosensory cortex strip and the body map ordered along it [MM p153]

On the figure: central sulcus · postcentral gyrus · homunculus · genitalia · thumb · chin · elbow · trunk

Primary somatosensory cortex (S1) *(first body touch area)*: the **postcentral gyrus** of the parietal lobe. [MM p152, MM p153]

Postcentral gyrus lies just posterior to the **central sulcus**, which divides parietal from frontal lobe. [MM p152]

S1 of each hemisphere receives touch from the **opposite** (contralateral) side of the body. [MM p152, MM p174]

S1 is a distorted body map: region size is proportional to skin receptor density. [MM p152]

Hand and fingers get large S1 areas; the less sensitive shoulder gets a small one. [MM p152, MM p153]

Sensory homunculus *("little man")*: each body part drawn in proportion to its share of S1. [MM p152, MM p153]

S1 body map order, from the midline outward: **genitalia**, toes, foot, leg, **trunk**, neck, head, shoulder. [MM p153]

S1 next: arm, **elbow**, forearm, hand, digits **5** to **2, thumb**, eyes, nose, face, lips, **chin**. [MM p153]

Using one sense can influence perception from another sense. [MM p152]

Humans detect a visual signal more accurately when a sound comes from the same place. [MM p152]

Association areas: sensory areas that process a mixture of inputs from different modalities. [MM p153]

Some "visual" cells also respond to auditory or touch stimuli. [MM p153]

Polymodal neuron: a neuron on which information from more than one sensory system converges. [MM p153]

Convergence on polymodal neurons lets different sensory systems interact. [MM p153]

Synesthesia: a stimulus in one modality evokes an involuntary extra sensation in another modality. [MM p153]

Synesthesia examples: seeing a number evokes a color; each music note has a sound and flavor. [MM p153]

Synesthesia occurs in **only** a few people. [MM p153]

Old view: sensory cortex fixed early in life. Now: cortical maps are highly **plastic**. [MM p153]

Cortical maps change considerably as a result of experience. [MM p153]

Two artists born without arms, using their toes extensively, had distinct maps of each toe. [MM p153]

Control participants did not have distinct maps of each toe. [MM p153]

String musicians have expanded cortical maps of the **left fingers**, which press the strings. [MM p153]

Losing a **hand** in adulthood: brain imaging shows cortical reorganization. [MM p153]

Normally, S1's hand region lies between the upper **arm** and **face** regions. [MM p153]

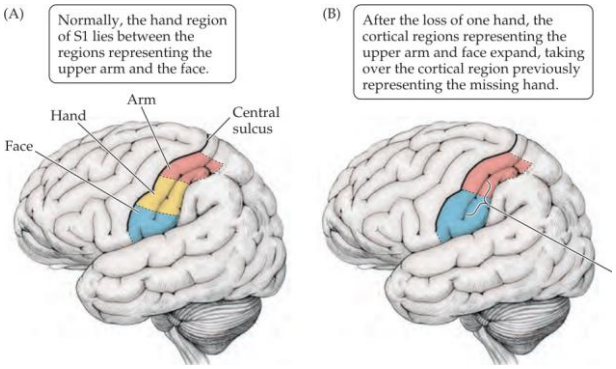
After losing one hand, the arm and face regions expand into the former hand region. [MM p153]

The former hand region now responds to touch on the face or arm. [MM p153]

A man got a transplanted hand **35 years** after losing the original hand. [MM p153, MM p154]

Within a few months, S1 reorganized to receive the new hand's sensation in the right place. [MM p154]

Some map changes follow weeks or months of use or disuse. [MM p154]



Hand region of S1 before and after hand loss: arm and face take over [MM p153]

On the figure: **hand** · **arm** · **face** · **central sulcus**

Map changes may come from growth of new synapses and dendrites, or loss of others. [MM p154]

Review: the main touch pathway is the **dorsal column system**. [MM p150, MM p154]

Review: dorsal column parts: dorsal root ganglion, **dorsal columns**, dorsal column nuclei, medial lemniscus, thalamus, S1. [MM p151, MM p154]

Review: S1 sits in the postcentral gyrus, mapping the contralateral body by receptor density. [MM p152, MM p154]

Review: senses interact; a sound from the same place improves visual detection. [MM p152, MM p154]

Summary: successive pathway levels allow increasingly elaborate processing. [MM p174]

Summary: the cortex holds multiple body maps; S1 overrepresents highly sensitive body regions. [MM p174]

Touch pathway stations

Station	What happens
Skin receptor	Touch transduced to action potentials
Dorsal root ganglion	Cell body of the unipolar sensory neuron
Dorsal column (spinal cord)	Axon ascends to medulla, no synapse yet
Dorsal column nuclei (medulla)	First synapse; next axon crosses midline
Medial lemniscus	Crossed axons rise to thalamus
Thalamus	Relays opposite-side body touch to cortex
S1 (postcentral gyrus)	Distorted contralateral body map

Table source: [MM p150, MM p151, MM p152]

Book 5.2: Pain, the Body's Emergency Signaling System

5.2.1 List and describe the three separate components of pain experience

⚠ Do not mix up: Motivational-affective = emotional words (sickening, fearful); cognitive-evaluative = overall rating (mild, excruciating). [MM p154]

Pain: an unpleasant sensory and emotional experience tied to actual or potential tissue damage. [MM p154]

Glossary definition of **pain**: the discomfort normally associated with tissue damage. [MM p154]

Pain is at best a mixed blessing: unpleasant but adaptive. [MM p154]

Pain forcefully guides behavior in ways that minimize risk to the body. [MM p154]

Immediate, short-term pain: we withdraw from the source, often reflexively, preventing further damage. [MM p154]

Longer-lasting pain: encourages sleep, inactivity, grooming, feeding, and drinking, which promote **recuperation** *(recovery)*. [MM p154]

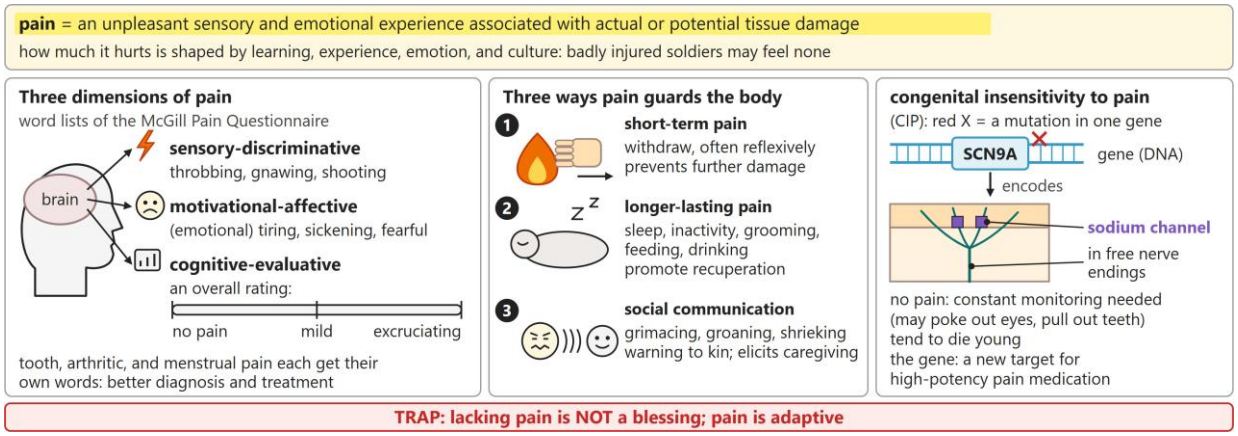
Pain-related **social communication** (grimacing, groaning, shrieking) warns kin. [MM p154]

These signals also draw caregiving from kin: grooming, defending, and feeding. [MM p154]

Learning, experience, emotion, and culture all strongly affect how we perceive pain. [MM p154]

Example: badly injured soldiers and athletes may show an apparent absence of pain. [MM p154]

Opposite example: a child may be anguished by a paper cut. [MM p154]



Pain dimensions in the McGill Pain Questionnaire, uses of pain, and CIP [MM p154]

On the figure: McGill Pain Questionnaire · sensory-discriminative · motivational-affective · cognitive-evaluative · recuperation · social communication · congenital insensitivity to pain

McGill Pain Questionnaire: widely used pain measure; people pick words tapping three pain dimensions. [MM p154]

1. Sensory-discriminative dimension *(what the pain feels like)*: throbbing, gnawing, shooting. [MM p154]
2. Motivational-affective dimension *(the emotional side)*: tiring, sickening, fearful. [MM p154]
3. Overall cognitive-evaluative dimension *(judging how bad overall)*: no pain, mild, excruciating. [MM p154]

Different pains get different descriptor sets: tooth, arthritic, and menstrual pain are described differently. [MM p154, MM p155]

This detailed analysis gives better information for diagnosing and treating illness. [MM p155]

Congenital insensitivity to pain *(born unable to feel pain)*: people tend to die young from repeated injuries. [MM p154]

Review, why pain is a positive adaptation: it drives withdrawal, recuperation, and caregiving, limiting damage. [MM p154]

5.2.2 Describe the neuronal receptor cells that detect painful stimuli and the molecular receptor proteins they use

⚠ **Do not mix up: First sharp pain is NOT from C fibers: it is fast A delta via TRPM3.** [MM p156]

Most tissues of the body, but not all, contain receptors for painful stimuli. [MM p155]

These pain receptors are best studied in the skin. [MM p155]

Nociceptor *(pain receptor)*: receptor responding to stimuli that damage tissue or threaten damage. [MM p155]

Nociceptors sit on **free nerve endings** *(bare nerve tips)* specialized to detect damage. [MM p155]

Free nerve ending: an axon ending in the skin with no specialized cell attached. [MM p147]

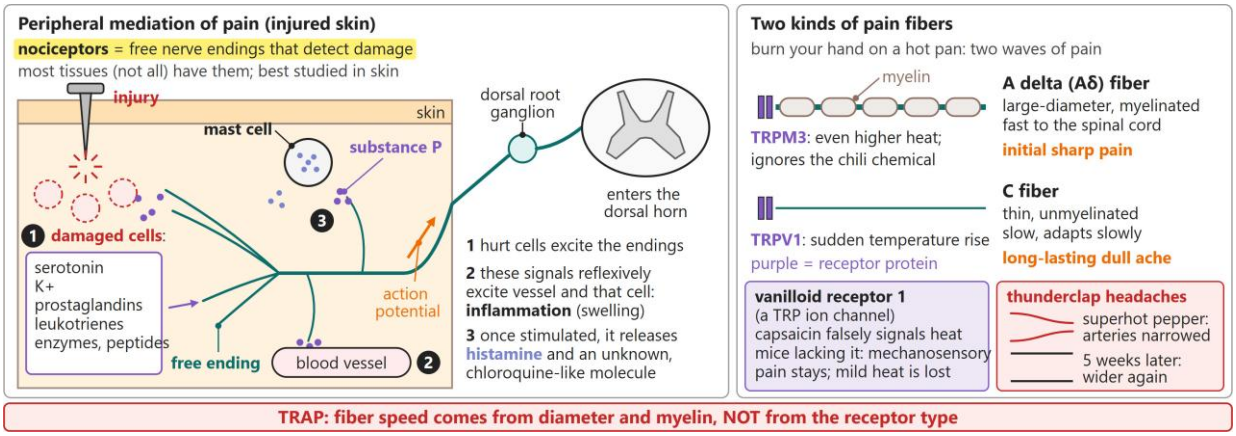
Free nerve endings in the skin detect pain, itch, heat, and cold. [MM p146, MM p147]

Injured cells release chemicals that activate nearby nociceptors. [MM p155]

The same chemicals also cause **inflammation** *(injury swelling)*. [MM p155]

Nociceptor stimulants in injured tissue include serotonin, histamine, and various enzymes and peptides. [MM p155]

Different nociceptors respond to different stimuli, such as pain and/or temperature changes. [MM p155]



Injury chemicals excite nociceptors, then pain fibers A delta and C with TRPM3 and TRPV1 [MM p155]

On the figure: nociceptors · mast cells · substance P · dorsal root ganglion · A delta · C fiber · TRPM3 · TRPV1

1. Damaged cells release substances (serotonin, K+, **prostaglandins** *(chemical injury signals)*, leukotrienes) exciting nociceptor endings. [MM p155]

2. Action potentials from the periphery reflexively excite blood vessels and **mast cells** *(cells that release histamine)*: inflammation. [MM p155]

3. Stimulated mast cells release histamine and an unknown, chloroquine-like molecule. [MM p155]

Nerve endings release **substance P** onto mast cells and blood vessels, promoting swelling. [MM p155]

4. Signal passes the **dorsal root ganglion**, enters the dorsal root, synapses in the dorsal horn. [MM p155]

5. Pain fibers release **glutamate** (transmitter) and **substance P** (neuromodulator) in the spinal cord. [MM p155]

6. Dorsal horn cells send the signal across the midline and up to the thalamus. [MM p155]

Congenital insensitivity to pain (CIP) *(born unable to feel pain)*: linked to a mutation in the gene **SCN9A**. [MM p155]

Clue case: a boy who could feel no pain died performing dangerous pranks. [MM p155]

Studying the boy's family helped identify the nociceptor that detects physical damage. [MM p155]

Children with CIP need constant monitoring so they do not poke out eyes or pull teeth. [MM p155]

SCN9A encodes a **sodium channel** *(gate letting sodium in)* expressed in nociceptor free nerve endings. [MM p155]

The SCN9A sodium channel offers a new target for high-potency pain medication. [MM p155]

Some free nerve endings detect temperature changes. [MM p155]

Capsaicin: the chemical that makes chili peppers spicy hot. [MM p155]

Capsaicin studies revealed the receptor signaling sudden temperature **increases**; why spicy food seems to burn. [MM p155]

TRPV1 (transient receptor potential vanilloid type **1,** or vanilloid receptor **1**): reports a temperature rise. [MM p156]

TRPV1 belongs to the **transient receptor potential (TRP)** family of **ion channels** *(gates letting ions cross)*. [MM p156]

Mice lacking the TRPV1 gene: still respond to mechanical pain, but not mild heat or capsaicin. [MM p156]

TRPV1 normally warns of danger from rising temperature. [MM p156]

Chili peppers evolved capsaicin to ward off mammal predators by falsely signaling burning heat. [MM p156]

TRPM3 (transient receptor potential type M3): free nerve ending receptor; channel opens as temperature rises. [MM p156]

TRPM3 detects even higher temperatures than TRPV1 but does **NOT** respond to capsaicin. [MM p156]

TRPM3 sits on **A delta fibers**; TRPV1 sits on **C fibers**. [MM p156]

A delta (Aδ) fiber: moderately large, **myelinated** *(fat-insulated)*, fast-conducting axon usually carrying pain. [MM p156]

Large diameter plus myelination let A delta action potentials reach the spinal cord very quickly. [MM p156]

C fiber: small, **unmyelinated** *(no insulating fat)* axon that conducts pain slowly and adapts slowly. [MM p156]

Hand burned on a hot pan: initial sharp pain = fat A delta fibers via TRPM3. [MM p156]

The long-lasting dull ache that follows comes from slower C fibers via TRPV1. [MM p156]

C fibers adapt slowly. [MM p156]

Other TRP receptors detect coolness and spices such as oregano, cloves, garlic, and wasabi. [MM p156]

How those other TRP receptors relate to pain receptors is still unknown. [MM p156]

Overstimulating TRPV1 can be hazardous to health. [MM p156]

Case: a **34**-year-old professional eater ate a whole Carolina Reaper pepper. [MM p156]

Result: dry heaves, neck pain, then a series of **thunderclap headaches**. [MM p156]

Thunderclap headache: excruciating, sudden-onset headache peaking in a minute, subsiding, then returning. [MM p156]

MRI of the brain: no abnormalities. [MM p156]

CAT scan of blood vessels: several arteries supplying the brain had narrowed remarkably. [MM p156]

The narrowed arteries may have caused the headaches; more seconds-long headaches followed over days. [MM p156]

Five weeks later, headaches gone: brain arteries had expanded to a more normal size. [MM p156]

Superhot chili peppers have caused severe, even fatal, heart attacks. [MM p156]

Review, how pain receptors work: injury chemicals or heat activate receptor proteins on free nerve endings. [MM p155, MM p156]

Review, pain vs touch receptors: pain uses free nerve endings with no specialized cell. [MM p146, MM p155]

Touch uses specialized receptors: the onion-like **Pacinian corpuscle** (vibration and pressure), **Meissner's corpuscles**. [MM p146, MM p155]

Other touch receptors: **Merkel's discs** (edges and points) and **Ruffini corpuscles** (skin stretch). [MM p146, MM p155]

Summary: free nerve endings detect damage or temperature through specialized receptor proteins. [MM p174]

A delta vs C fibers

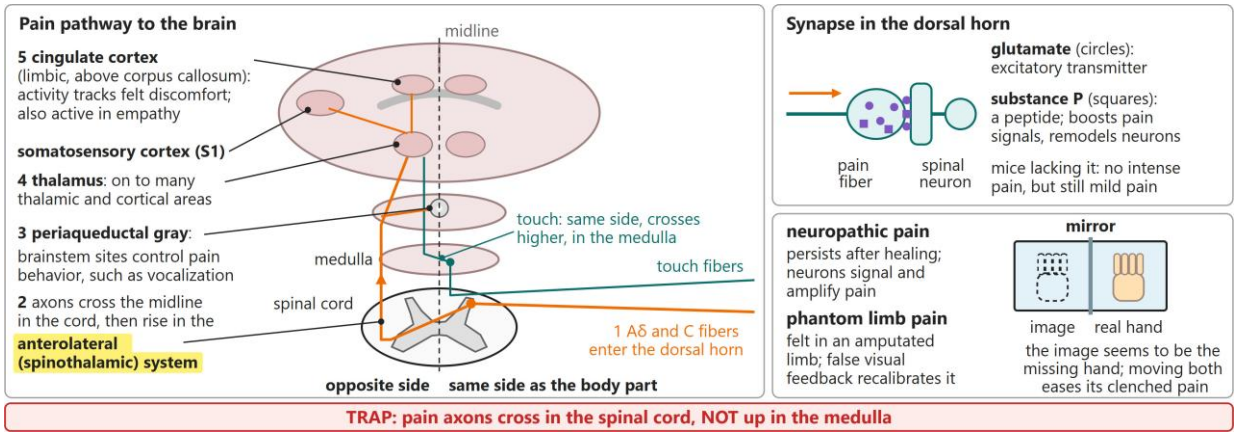
Feature	A delta (Aδ) fiber	C fiber
Size	large diameter	small, thin
Myelin	myelinated	unmyelinated
Speed	fast	slow
Heat receptor	TRPM3 (higher heat, no capsaicin)	TRPV1 (heat and capsaicin)
Pain felt	initial sharp pain	long-lasting dull ache

Table source: [MM p156]

5.2.3 Trace the neuronal pathway that transmits pain information from the periphery to the brain, as well as the neuronal pathway by which the brain can modulate pain

⚠ **Do not mix up: Pain pathway crosses the midline in the SPINAL CORD; touch (dorsal column) crosses in the MEDULLA.** [MM p157, MM p151]

Anterolateral system (also **spinothalamic system**): carries most pain information from body to brain. [MM p157]



Pain pathway crossing in the spinal cord, substance P synapse, and mirror box [MM p157]

On the figure: cingulate cortex · periaqueductal gray · anterolateral · midline · substance P · glutamate · neuropathic pain · phantom limb pain

1. Pain travels on fast myelinated A delta fibers and slow unmyelinated C fibers. [MM p157]
2. Pain and temperature fibers enter the **dorsal horns** *(back gray matter of cord)* of the spinal cord. [MM p157]
3. They synapse onto spinal neurons there. [MM p157]
4. Dorsal horn neuron axons cross the **midline** to the opposite side in the spinal cord. [MM p157]
5. They ascend the cord in the **anterolateral quadrant** *(front side part of cord)*. [MM p157]

6. Brainstem sites receive pain information and control pain behavior such as vocalization. [MM p157]
7. Reaches **thalamic nuclei**; pain is distributed to many thalamic and cortical areas, including S1. [MM p157]
8. **Cingulate cortex** is especially activated; pain information is eventually integrated there. [MM p157]

The anterolateral system is distinct from the touch **dorsal column system**. [MM p157]

Like touch, each hemisphere receives pain inputs from the **contralateral** *(opposite)* body side. [MM p157]

In the spinal cord, pain fibers release excitatory **glutamate** plus the peptide **substance P**. [MM p157]

Substance P: a peptide transmitter involved in pain transmission. [MM p157]

Substance P selectively boosts pain signals and remodels pain pathway neurons. [MM p157]

Mice lacking substance P cannot feel intense pain but still feel mild pain. [MM p157]

Cingulate cortex (also **cingulum**): medial cortex dorsal to the **corpus callosum** *(band joining the hemispheres)*; limbic system. [MM p157]

Same mildly painful stimulus: more cingulate and S1 activation goes with more reported discomfort. [MM p157]

Different cingulate subregions seem to handle emotional versus sensory aspects of pain. [MM p157, MM p158]

One cingulate part activates even when we just empathize with a loved one in pain. [MM p158]

Descending control, one possibility the book gives: [MM p159]

1. Opiates or endorphins bind opioid receptors in the brainstem **periaqueductal gray** *(midbrain gray area)*. [MM p159, MM p157]
2. The periaqueductal gray brainstem system sends descending projections to the spinal cord. [MM p159]
3. The projections activate the spinal cord pain-gating mechanism. [MM p159]
4. Gates close: transmission of pain signals to the brain is blocked. [MM p159, MM p158]

Central modulation: descending brain connections inhibit ascending sensory and pain axons at lower levels. [MM p150]

Neuropathic pain: pain persisting long after the injury that started it has healed. [MM p158]

Neuropathic pain is a disagreeable example of **neuroplasticity** *(nervous system change)*. [MM p158]

Neurons keep signaling, even amplifying, pain with no tissue damage at all. [MM p158]

Phantom limb pain: neuropathic pain that seems to come from an amputated limb. [MM p158]

Phantom limb pain is notoriously difficult to treat. [MM p158]

Mirror box: the mirror makes both limbs look intact. [MM p158]

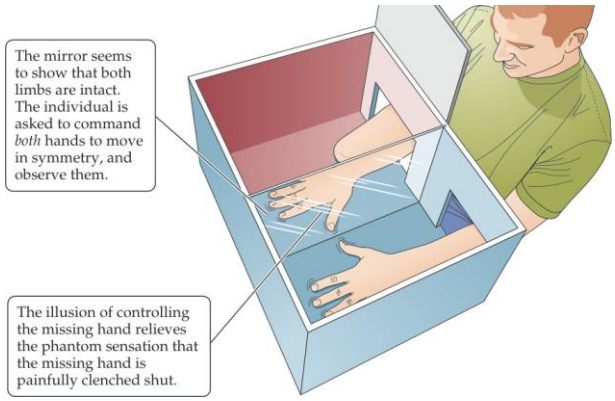
The person commands **both hands** to move in symmetry and watches them. [MM p158]

Illusion of controlling the **missing hand** relieves the feeling it is painfully clenched shut. [MM p158]

Visual feedback, even false, apparently lets the brain recalibrate the pain signal. [MM p158]

Review, sketch: fibers, dorsal horn, cross midline, anterolateral cord, brainstem, thalamus, S1 and cingulate. [MM p157]

Summary: pain, temperature, and itch enter the cord, cross, and ascend the anterolateral system. [MM p174]



Mirror box: seeing both hands move relieves phantom limb pain [MM p158]

On the figure: mirror · both hands · missing hand · phantom

Touch pathway vs pain pathway

Feature	Touch	Pain
System	dorsal column system	anterolateral (spinothalamic) system
Receptors	specialized skin receptors	free nerve endings (nociceptors)
First synapse	dorsal column nuclei, medulla	dorsal horn, spinal cord
Crosses midline in	medulla	spinal cord
Ascends in	dorsal columns	anterolateral quadrant
Relay	thalamus	brainstem sites, thalamus
Cortex	somatosensory cortex	S1 and cingulate cortex
Body side served	contralateral	contralateral

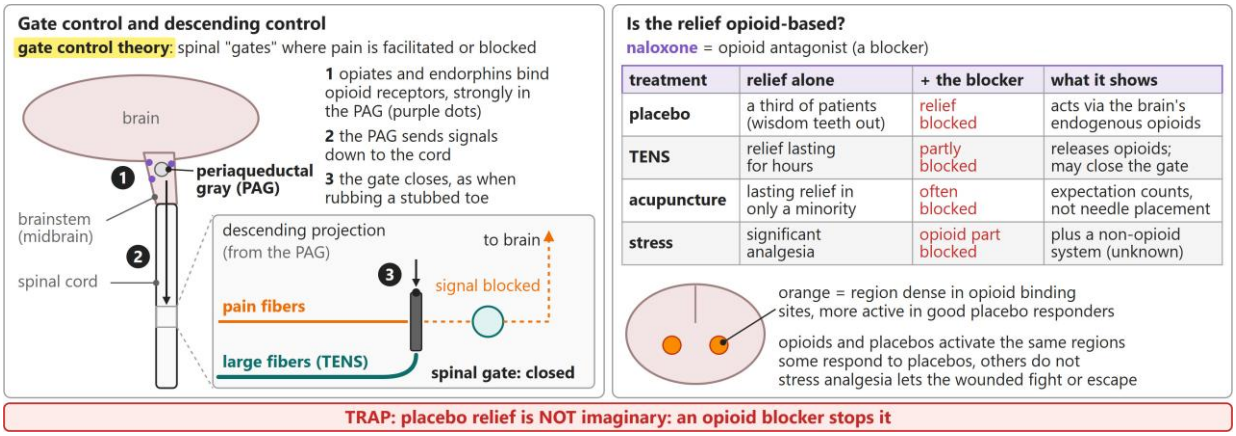
Table source: [MM p146, MM p150, MM p151, MM p155, MM p157]

5.2.4 Discuss the various methods for controlling pain, including advantages and disadvantages of each

⚠ Do not mix up: Naloxone does NOT relieve pain: it BLOCKS opioid-based relief (opiates, placebo, acupuncture). [MM p159, MM p160]

Pain control is hard: even cutting nerves may give **only** temporary relief. [MM p158]

The pain system eventually finds a way to restore its signal to the brain. [MM p158]



treatment	relief alone	+ the blocker	what it shows
placebo	a third of patients (wisdom teeth out)	relief blocked	acts via the brain's endogenous opioids
TENS	relief lasting for hours	partly blocked	releases opioids; may close the gate
acupuncture	lasting relief in only a minority	often blocked	expectation counts, not needle placement
stress	significant analgesia	opioid part blocked	plus a non-opioid system (unknown)

TRAP: placebo relief is NOT imaginary: an opioid blocker stops it

Gate control and descending control, and which reliefs a naloxone blocker stops [MM p159]

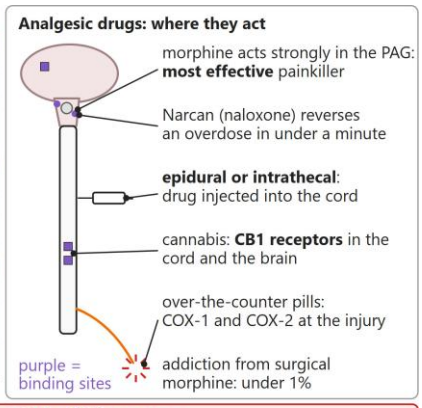
On the figure: gate control theory · periaqueductal gray · naloxone · placebo · TENS · acupuncture · endogenous opioids · stress

Gate control theory: spinal gates, where pain is facilitated or blocked, control signals reaching the brain. [MM p158]

If the theory is right, effective relief may depend on keeping the gates closed. [MM p158]

Analgesia: absence of or reduction in pain (Greek an, not; algesis, feeling of pain). [MM p158]

Type	Mechanism
PSYCHOGENIC	
Placebo	May activate endorphin-mediated pain control system
Hypnosis	Alters brain's perception of pain
Stress	Uses both opioid and non-opioid mechanisms
Cognitive (learning, coping strategies)	May activate endorphin-mediated pain control system
PHARMACOLOGICAL	
Opiates	Bind to opioid receptors in periaqueductal gray and spinal cord
Spinal block	Blocks pain signals in spinal cord
Anti-inflammatory drugs	Block chemical inflammatory signals at the site of injury
Cannabinoids	Act in nociceptor endings, spinal cord, and brain
STIMULATION	
TENS/mechanical	On large fibers, blocks or alters pain signal to brain
Acupuncture	Activates endogenous opioids and/or placebo-like effect, possibly modulating effect on activity of peripheral pain pathways
Central gray	Electrically activates endorphin-mediated pain control systems, blocking pain signal in spinal cord



TRAP: aspirin and acetaminophen do NOT work like morphine; they act via COX enzymes

Types of pain relief and where analgesic drugs act [MM p160]

On the figure: opiates · naloxone · epidural · intrathecal · CB1 · COX-1 · TENS · acupuncture

Four categories: analgesic drugs, electrical stimulation, placebos, and activating **endogenous opioids**. [MM p158, MM p159, MM p160]

Opiates (opium-related drugs, like morphine): known for centuries to relieve pain. [MM p159]

Opiates and **endogenous opioids** *(the body's own painkillers)* bind specific brain receptors to reduce pain. [MM p159]

Endorphin: one of three kinds of endogenous opioids. [MM p159]

Opiate action is especially strong in the brainstem **periaqueductal gray** *(midbrain gray area)*. [MM p159]

Epidural or **intrathecal injection**: opiates injected carefully, directly into the spinal cord. [MM p159]

Advantage: opiates are the most effective painkillers; no other drug matches them. [MM p159]

People using painkillers for severe pain usually do not become addicted. [MM p159]

Addiction risk from morphine for surgical pain is vastly exaggerated: estimated under **1%**. [MM p159]

Disadvantage: the few who become addicted face a very real danger of overdose death. [MM p159]

Extremely potent opioids (OxyContin, fentanyl) worsened the opioid epidemic, causing more deaths. [MM p159]

Naloxone (Narcan): potent opiate **antagonist** *(blocker)*, often given after drug overdoses. [MM p159]

Given in time, naloxone saves lives; more public safety officers now carry it. [MM p159]
Naloxone, the Lazarus drug, can revive people dying of narcotic overdose in under a minute. [MM p159]
Aspirin and **acetaminophen** (Tylenol): over-the-counter, non-opiate; reduce pain and inflammation. [MM p159]
They act especially through **cyclooxygenase** *(pain and inflammation enzymes)* enzymes **COX-1** and **COX-2**. [MM p159]
Disadvantage: non-opiate drugs are less effective than opiates. [MM p159]
Cannabis: reduces pain by stimulating endogenous **CB1 cannabinoid receptors** in spinal cord and brain. [MM p159]
TENS (transcutaneous electrical nerve stimulation): mild electrical stimulation of nerves around injury sites. [MM p159]
TENS skin electrodes excite nerves supplying the region where pain is **referred** *(felt)*. [MM p159]
Exact mechanism unclear; one possibility is that TENS closes the spinal pain gate. [MM p159]
Everyday version: rubbing a stubbed toe brings a little relief. [MM p159]
TENS stimulates the nerves near the injury more efficiently than rubbing does. [MM p159]
Advantage: TENS may bring dramatic relief lasting for hours. [MM p159]
Naloxone partially blocks TENS: TENS works at least partly by releasing endogenous opioids. [MM p159]
Placebo effect: symptom relief after a treatment known to be ineffective or inert. [MM p159]
In some people, simply believing they get a proven treatment relieves pain. [MM p159]
Wisdom teeth patients given morphine or placebo: fully a third on placebo felt relief. [MM p159]
Placebo given with naloxone (opioid receptor blocker): the placebo benefit disappeared. [MM p159]
Conclusion: placebos likely work by activating the brain's endogenous opioid system. [MM p159]
Brain imaging: opioids and placebos activate the same brain regions. [MM p159]
Disadvantage: for unknown reasons, some people consistently respond to placebos and others do not. [MM p159]
Acupuncture: inserting needles at designated skin points to relieve pain or neurological malfunction. [MM p160]
Acupuncture is ancient and very popular. [MM p160]
Disadvantage: **only** a minority of users get lasting relief from chronic pain. [MM p160]
When it works, endorphin release may be key: naloxone often blocks acupuncture. [MM p160]
So acupuncture resembles placebos. [MM p160]
Needle placement has little to do with the pain effect, despite many placement rules. [MM p160]
Expectation of relief seems to be the key, presumably releasing endogenous opioids. [MM p160]
Stressful events can produce significant analgesia: gravely wounded soldiers may feel no pain for a time. [MM p160]
Animal research: **stress** activates an opioid-dependent analgesia that naloxone blocks. [MM p160]
Stress also activates an uncharacterized non-opioid system, possibly using **endocannabinoids** *(body's own cannabis-like chemicals)*. [MM p160]
These built-in analgesic systems let a wounded individual fight or escape instead of being overwhelmed. [MM p160]
Chronic back pain: the prefrontal cortex shrinks much faster than normal, like rapid aging. [MM p160]
The wide range of relief strategies shows how elusive pain is. [MM p160]
Acupuncture may also modulate activity of peripheral pain pathways. [MM p160]
Review, most effective drugs: opiates; bind opioid receptors, especially periaqueductal gray, and spinal cord. [MM p159, MM p160]
Review, TENS: may close the spinal pain gate; partly releases endogenous opioids. [MM p159]
Review, placebo and acupuncture: naloxone blocks both, so both likely use endogenous opioids. [MM p159, MM p160]
Review, shared factor: expectation of relief; acupuncture needle placement barely matters. [MM p159, MM p160]
Summary: brain and spinal regions using endogenous opioids such as endorphins modulate pain. [MM p174]
Summary: opioid systems are also active in the placebo effect and acupuncture. [MM p174]

Types of pain relief

Type	Group	Mechanism
Placebo	Psychogenic	May activate endorphin pain control system
Hypnosis	Psychogenic	Alters brain perception of pain
Stress	Psychogenic	Uses opioid and non-opioid mechanisms
Cognitive (learning, coping strategies)	Psychogenic	May activate endorphin pain control system
Opiates	Pharmacological	Bind opioid receptors in periaqueductal gray, spinal cord
Spinal block	Pharmacological	Blocks pain signals in spinal cord
Anti-inflammatory drugs	Pharmacological	Block chemical inflammatory signals at injury site
Cannabinoids	Pharmacological	Act in nociceptor endings, spinal cord, brain
TENS/mechanical	Stimulation	On large fibers, blocks or alters pain signal
Acupuncture	Stimulation	Endogenous opioids and/or placebo-like effect
Central gray	Stimulation	Electrically activates endorphin system; blocks spinal pain signal

Table source: [MM p160]

Pain control: pros and cons

Method	Advantage	Disadvantage
Cutting nerves	may relieve pain	relief may be **only** temporary
Opiates	most effective painkillers	overdose death risk if addicted
Aspirin, acetaminophen	reduce pain and inflammation	less effective than opiates
TENS	dramatic relief lasting hours	exact mechanism unclear
Placebo	relieves a third in study	works in some people, not all
Acupuncture	very popular; may release endorphins	lasting relief **only** in a minority

Table source: [MM p158, MM p159, MM p160]

Book 5.3: Movement and the Motor System

5.3.1 Discuss the importance of motor planning and sensory feedback in controlling behavior

⚠ **Do not mix up: Acts are NOT chains of reflexes: a motor plan is set BEFORE the act begins.** [MM p161]

All behavior involves movements: muscle contractions are our sole means of interacting with the world. [MM p161]

Movement: a single relocation of a body part, usually from a brief muscle contraction. [MM p161]

Reflex: a simple, highly stereotyped, unlearned response to a particular stimulus. [MM p161]

Reflex example: an eye blink in response to a puff of air. [MM p161]

Act: complex behavior, as distinct from a simple movement (getting dressed, walking, speaking). [MM p161]

Old idea: reflexes are the basic units; acts are reflexes chained, each sensation triggering the next. [MM p161]

Flaw: units fit a larger plan and are not always produced in the same order. [MM p161]

Motor plan (also **motor program**): a set of muscle commands established BEFORE the act occurs. [MM p161]

Feedback from movements informs and fine-tunes the motor program while it unfolds. [MM p161]

But the basic sequence of movements is planned ahead. [MM p161]

Motor plan examples range from skilled piano playing to simple escape behaviors of crayfish. [MM p161]

Electromyography (EMG) *(recording electrical activity of muscles)*: electrical recording of muscle activity. [MM p161]

EMG plus body positions lets researchers track the simple movements that make up an act. [MM p161]

EMG experiment: after an auditory signal, a person pulls up on a **lever**. [MM p161]

Calf muscle (**gastrocnemius**) fires BEFORE the **biceps**: legs steady the body before the arm pulls. [MM p161]

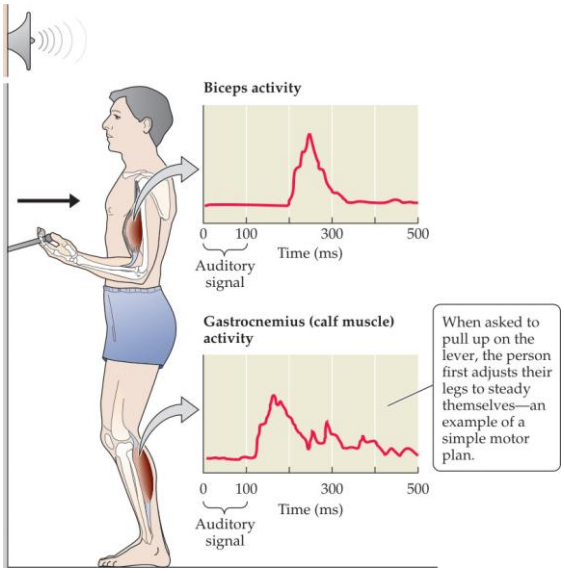
Adjusting the legs before moving the arm is an example of a simple **motor plan**. [MM p161, MM p162]

Motor plans resemble engineering: two goals, accuracy (minimize error) and speed (finish quickly). [MM p162]

Speed and accuracy trade-off: improving one goal usually costs the other, in machines and nervous systems. [MM p162]

Neuromuscular system: muscles plus brain mechanisms and nerves that prepare and execute motor plans. [MM p162]

The neuromuscular system also gets sensory feedback for use in error correction. [MM p162]



Muscle activity recorded while a person pulls a lever: calf before biceps [MM p161]

On the figure: **gastrocnemius** · **biceps** · **calf muscle** · **lever** · **motor plan**

The six levels of the motor control hierarchy, as the book numbers them: [MM p162]

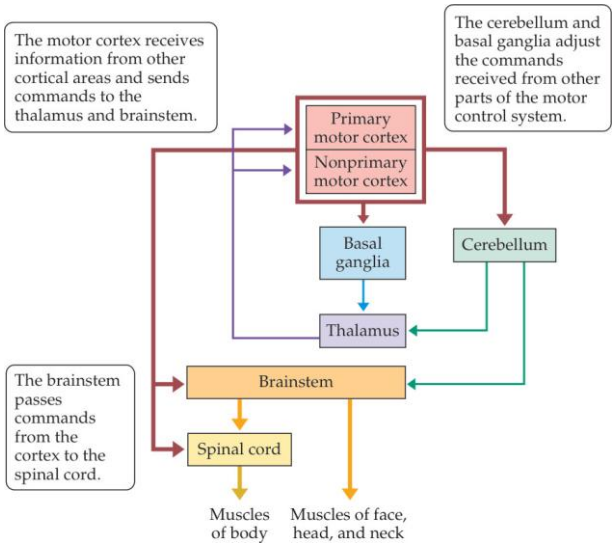
> **1. Skeletal system** and attached muscles: determine which movements are possible. [MM p162]
>
> **2. Spinal cord**: controls skeletal muscles on brain commands, or directly from sensory input in reflexes. [MM p162]
>
> **3. Brainstem**: integrates motor commands from higher brain levels and sends them to the spinal cord. [MM p162]

Brainstem also relays body sensory information from spinal cord to forebrain. [MM p162]

> **4. Primary motor cortex**: initiates some of the main commands for action. [MM p162]
>
> **5. Nonprimary motor cortex** *(motor areas next to M1)*: extra commands, via M1 and directly to lower levels. [MM p162]

Very top of the hierarchy: **prefrontal cortex**, crucial for formulating behavioral plans. [MM p162]

> **6. Cerebellum** and **basal ganglia**, via the **thalamus**: modulate other parts of the control system. [MM p162]



Hierarchy of movement control from cortex to muscles [MM p162]

On the figure: **primary motor cortex** · **nonprimary motor cortex** · **basal ganglia** · **cerebellum** · **thalamus** · **brainstem** · **spinal cord**

> Motor cortex gets information from other cortical areas; sends commands to thalamus and brainstem. [MM p162]
>
> Cerebellum and basal ganglia adjust commands received from other parts of the motor control system. [MM p162]
>
> Basal ganglia and cerebellum send output to the thalamus; the thalamus feeds the motor cortex. [MM p162]
>
> Brainstem passes commands from cortex to spinal cord. [MM p162]
>
> Spinal cord drives muscles of the body; brainstem drives muscles of face, head, neck. [MM p162]
>
> Visual Summary: hierarchy = skeleton and muscles, spinal cord, brainstem, M1, nonprimary cortex, cerebellum, basal ganglia. [MM p174]
>
> Review, reflex vs movement vs act: unlearned stereotyped response; single body part relocation; complex behavior. [MM p161, MM p162]
>
> Review, sensory feedback: informs and fine-tunes the motor plan and allows error correction. [MM p161, MM p162]
>
> Review, speed vs accuracy: improving one usually comes at a cost to the other. [MM p162]
>
> Review, motor plan: commands to muscles set up in the nervous system before the act. [MM p161]

Reflex vs movement vs act

Term	What it is	Example
Reflex	Simple, unvarying, unlearned response to stimulus	Eye blink to puff of air
Movement	Single relocation of a body part	An arm movement or leg movement
Act	Complex behavior built from many movements	Dressing, walking, speaking a sentence

Table source: [MM p161]

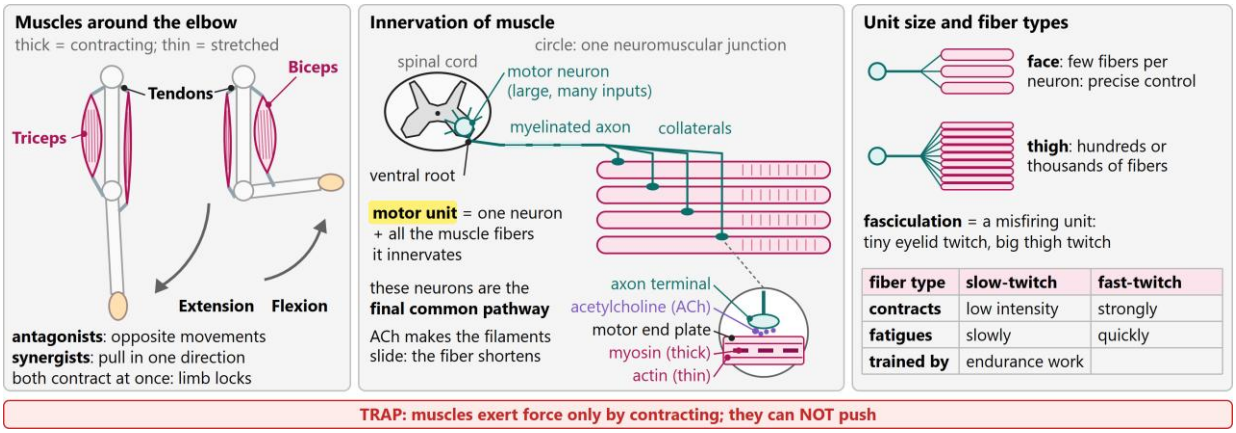
5.3.2 Trace the pathways by which the brain sends commands to individual muscles

⚠ **Do not mix up: Pyramidal tracts CROSS in the medulla: the LEFT motor cortex controls the RIGHT body side.** [MM p167]

Joints vary in planes of movement: universal joints (hip, shoulder) vs hinge joints (elbow, knee). [MM p162]

Hinge joints move mostly in one direction. [MM p162]

Tendons *(cords tying muscle to bone)* connect muscles to bones. [MM p162]



Muscles around the elbow, motor unit and neuromuscular junction, fiber types [MM p163]

On the figure: antagonist · synergist · tendons · triceps · biceps · motor unit · neuromuscular junction · fasciculation

Muscles around a joint are reciprocal: one group contracting stretches the other group. [MM p162]

Antagonist: a muscle that counteracts the effect of another muscle. [MM p162]

Synergist: a muscle that acts together with another muscle, moving a limb one direction. [MM p162]

Limb movement depends on degree and rate of contraction in some muscles, relaxation in others. [MM p162, MM p163]

Contracting opposing muscles at the same time locks a limb in position. [MM p163]

Muscles exert force **only** by contracting, so muscle attachments determine the resulting movement. [MM p163]

Elbow: **triceps** extends the arm; **biceps** flexes it; so they are antagonists. [MM p163]

Skeletal muscles move the skeleton; they are **striate muscle** *(striped looking muscle)*. [MM p163]

Stripes come from overlapping layers of contractile proteins **myosin** and **actin**. [MM p163]

Smooth muscle: in visceral organs and blood vessels; not generally involved in voluntary behavior. [MM p163]

Contraction: actin and myosin filaments slide past each other, overlap **increases**, the fiber shortens. [MM p163]

Most muscles mix two fiber types: slow-twitch and fast-twitch. [MM p163]

Endurance athletes enhance the slow-twitch properties of their muscles through training. [MM p163]

Motor neuron (also **motoneuron**): neuron that transmits neural messages to muscles (or glands). [MM p163]

Motor neurons of the spinal cord and brainstem make muscles contract. [MM p163]

Neuromuscular junction: where the motor neuron terminal meets its target muscle fiber. [MM p163]

The neuromuscular junction is where the nerve transmits its message to the muscle fiber. [MM p163]

A motor neuron action potential releases **acetylcholine (ACh)** at ALL of its axon terminals. [MM p163, MM p164]

ACh: neurotransmitter released by the autonomic nervous system, motor neurons, and neurons throughout the brain. [MM p163]

Muscle fibers respond to ACh with molecular events making actin and myosin contract. [MM p164]

Motor unit: one motor neuron plus all the muscle fibers it innervates. [MM p164]

Fasciculation *(small involuntary muscle twitch)*: a misfiring motor unit. [MM p164]

Example: eyelid "jumping nerves" when fatigued is a misfiring facial motor unit. [MM p164]

Spinal motor neurons have large cell bodies and very widespread dendritic fields. [MM p164]

Why: they integrate sensory inputs plus descending brain signals through thousands of synapses. [MM p164]

Virtually all motor neuron axons are myelinated, so action potentials reach muscles quickly. [MM p164]

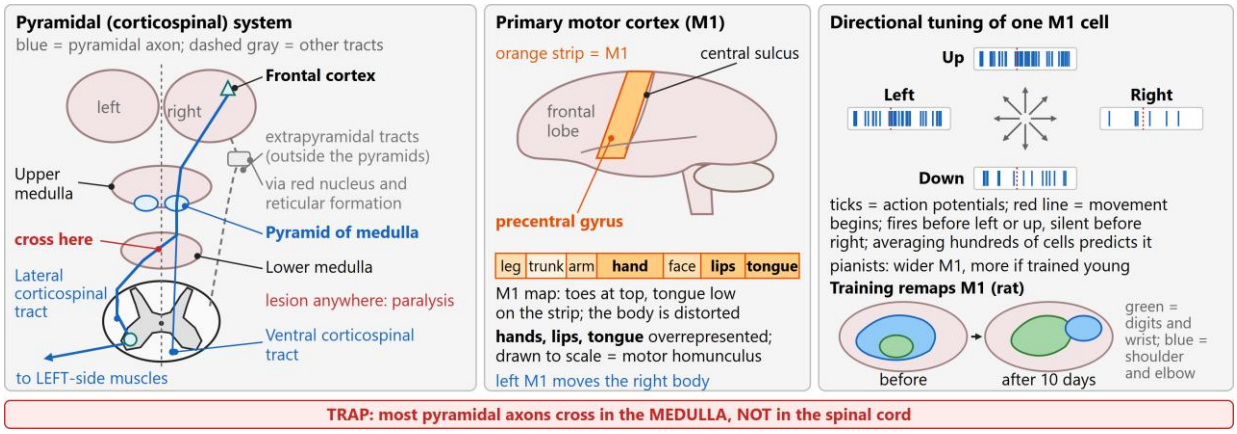
Final common pathway: motor neurons, the sole route by which spinal cord and brain control muscles. [MM p164]

Head muscles are controlled directly by the brain via **cranial nerves**. [MM p167]

Rest of the body: commands from brain and spinal cord via the **somatic nerves**. [MM p167]

The brain sends commands through two major pathways: **pyramidal** and **extrapyramidal** systems. [MM p167]

Pyramidal system (also **corticospinal system**): frontal cortex neurons whose axons form the pyramidal tract. [MM p166, MM p167]



Pyramidal tract crossing in the medulla, M1 strip, and directional tuning [MM p167]

On the figure: pyramid · lower medulla · upper medulla · precentral gyrus · central sulcus · corticospinal tracts · extrapyramidal · directional tuning

Pyramidal tract, path from brain to muscle: [MM p167]

1. Cell bodies in frontal cortex; many in **primary motor cortex (M1)**, the **precentral gyrus**. [MM p167]
2. Axons pass through the brainstem. [MM p167]
3. In the medulla they form the **pyramid**, a wedge-shaped anterior bulge each side of midline. [MM p167]
4. Fibers cross to the opposite side in the medulla. [MM p167]

In cross sections, the pyramids sit in the **upper medulla**; fibers cross in the **lower medulla**. [MM p167]

5. They descend in the lateral and ventral **corticospinal tracts** of the spinal cord. [MM p167]
6. They reach spinal motor neurons or interneurons in the spinal cord. [MM p174]
7. Spinal motor neurons send axons out the **ventral roots** to the periphery. [MM p163]
8. Near the muscle each axon splits into **collaterals** *(axon branches)*, each innervating a separate fiber. [MM p163]
9. At each neuromuscular junction, ACh is released onto the motor end plate; the fiber contracts. [MM p163, MM p164]

Crossing means the right cortex controls the left body side, and left controls right. [MM p167]

Lesions anywhere in the pyramidal tract cause paralysis of muscles controlled by the damaged neurons. [MM p167]

Extrapyramidal system: motor tracts from forebrain to brainstem and spinal cord OUTSIDE the medulla pyramids. [MM p167]

The extrapyramidal system includes the basal ganglia and some closely related brainstem structures. [MM p167]

Many extrapyramidal projections pass through the **reticular formation** and **red nucleus** of midbrain and brainstem. [MM p167]

The basal ganglia are an important point of origin for extrapyramidal projections. [MM p167]

Extrapyramidal lesions do **NOT** prevent moving individual joints and limbs. [MM p167]

But they interfere with spinal reflexes, usually exaggerating them, and with motor fine-tuning. [MM p167]

Spinal cord injuries come from vehicle accidents, violence, falls, and sports injuries. [MM p167]

Complete severing of the cord: immediate and permanent paralysis below the injury level. [MM p168]

Spinal reflexes may or may not be lost, depending on destruction below the injury site. [MM p168]

Reflexes may even become STRONGER from loss of descending inhibition from the brain. [MM p168]

Over **250,000** people in the United States have spinal cord injuries. [MM p168]

Thousands more occur each year, mostly in young people. [MM p168]

Reconnecting the injured spinal cord no longer seems far-fetched. [MM p168]

Primary motor cortex (M1): apparent executive region for initiating movement; a major pyramidal tract source. [MM p168]

Precentral gyrus: frontal strip just in front of the **central sulcus**, crucial for motor control. [MM p168]

M1 is mainly the precentral gyrus, so M1 is part of the frontal lobe. [MM p167, MM p168]

Like S1, M1 occupies one large gyrus and maps the CONTRALATERAL *(opposite side)* body. [MM p168]

Stimulating a discrete region of left M1 moves the matching region on the right body side. [MM p168]

The M1 map is distorted: precisely controlled hands, lips, tongue are overrepresented. [MM p168]

Motor homunculus: a figure drawn with body proportions as represented in M1. [MM p168]

M1 strip order, one end: genitalia, toes, feet, ankle, knee, leg, hip, trunk, neck, shoulder. [MM p167]

M1 strip continues: elbow, wrist, a very large hand area, brow, eyelids, eyeballs, face. [MM p167]

M1 strip other end: lips (large area), jaw, tongue, throat, chewing, salivation. [MM p167]

Homunculus body parts are proportional to the amount of motor cortex for their muscles. [MM p167]

The M1 map is an oversimplification: body regions intermingle because body parts coordinate across M1. [MM p167, MM p168]

Monkey M1 recordings: many cells change firing rate with movement direction. [MM p169]

Each M1 cell fires most for one particular direction (**directional tuning**). [MM p168, MM p169]

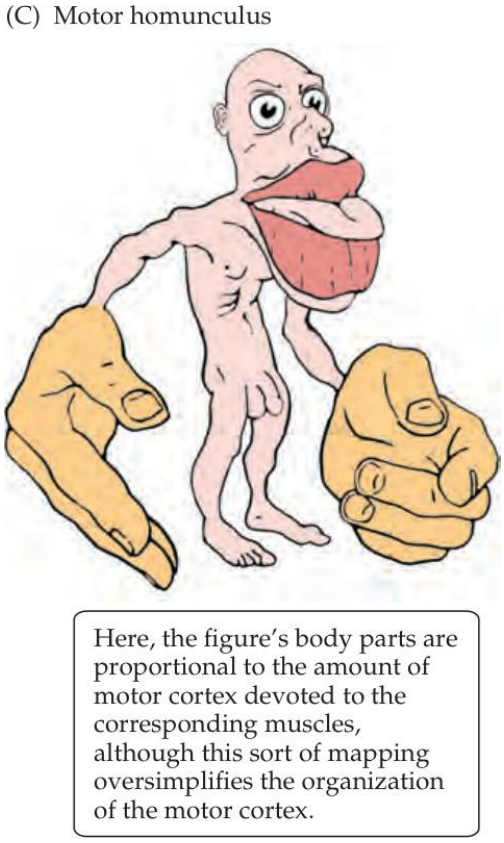
Example cell: silent before arm moves right, fires vigorously before moves left or straight up. [MM p168]

Averaging hundreds of M1 neurons predicts arm movement direction with reasonable accuracy. [MM p169]

Millions of M1 neurons exist, so larger sampling would predict more accurately. [MM p169]

M1 representations are not static: they change with training. [MM p169]

Piano players: M1 is wider than in nonmusicians, especially the hand area. [MM p169]



Motor homunculus with body parts sized by motor cortex [MM p167]

On the figure: motor homunculus

The younger the training started, the larger the gyrus in adulthood: experience expands M1. [MM p169]

TMS *(magnetic stimulation through the skull)*: movements from an M1 patch change with use or learning. [MM p169]

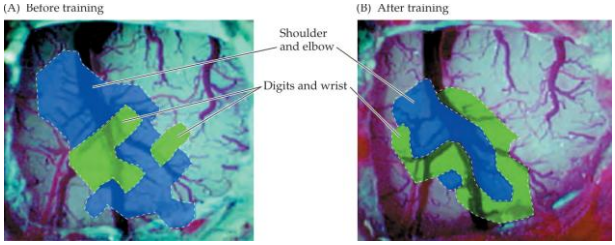
Rats trained **10** days on precise reaching and grasping: motor cortex remapped. [MM p169]

Digit and **wrist** area expanded into areas previously for **shoulder and elbow**. [MM p169]

Premotor cortex: just anterior to M1; actually a mosaic of subareas with distinct properties. [MM p169]

Visual Summary: muscles work in pairs; antagonists oppose, synergists work together. [MM p174]

Visual Summary: action potentials travel along motor neuron axons to the neuromuscular junction, releasing ACh. [MM p174]



Rat motor cortex before and after reach training: digit and wrist area grows [MM p169]

On the figure: wrist · shoulder and elbow

Visual Summary: pyramidal fibers start mainly in M1 and adjacent regions; run directly to spinal cord. [MM p174]

Visual Summary: disproportionate M1 amounts in the precentral gyrus serve finely controlled muscles. [MM p174]

Review, muscles and joints: antagonist and synergist muscles around joints, attached to bones by **tendons**. [MM p162, MM p170]

Review, motor unit: one motor neuron, its axon collaterals, and all fibers it innervates. [MM p164, MM p170]

Review, path: M1, brainstem, medulla crossing, corticospinal tract, motor neuron, ventral root, muscle. [MM p167, MM p170]

Review, M1: precentral gyrus, maps contralateral body, overrepresents precise parts like hands and lips. [MM p168, MM p170]

Review, pyramidal vs extrapyramidal: through the medulla pyramids vs outside them. [MM p167, MM p170]

Review, nonprimary motor cortex: extra motor commands directly and via M1; SMA and premotor. [MM p169, MM p170]

Slow-twitch vs fast-twitch fibers

Fiber type	Contraction	Fatigue
Slow-twitch	Relatively low intensity	Fatigues slowly
Fast-twitch	Contracts strongly	Fatigues quickly

Table source: [MM p163]

Large vs small motor units

Motor unit	Example muscle	Fibers per motor neuron	Fasciculation
Large	Thigh	Hundreds or thousands	Much larger twitch
Small	Face (precise control)	Only a few	Tiny eyelid twitch

Table source: [MM p164]

Pyramidal vs extrapyramidal system

Feature	Pyramidal	Extrapyramidal
Other name	Corticospinal system	None given
Origin	Frontal cortex, mostly M1	Basal ganglia, cerebellum, brainstem nuclei
Route	Through medulla pyramids, crosses there	Outside the medulla pyramids
Relay stations	Direct to spinal cord	Reticular formation, red nucleus
Lesion effect	Paralysis of affected muscles	Exaggerated reflexes, poor fine-tuning

Table source: [MM p167, MM p172, MM p174]

5.3.3 Distinguish between the two main types of sensory feedback from muscles to the nervous system

⚠ **Do not mix up: Muscle spindle senses LENGTH (stretch); Golgi tendon organ senses TENSION (force), not length.** [MM p165]

Brain and spinal cord continually monitor muscles, limb positions, and motor instructions being issued. [MM p164]

Proprioception *(body position sense)*: information about the position and movement of the body. [MM p164]

From Latin proprius, "own," and recipere, "to receive"; called a "sixth sense." [MM p164]

A man whose proprioceptive axons were killed by a virus can still move every muscle. [MM p164]

The man lost information about muscle activity and body position, and light touch below the neck. [MM p164]

Two **proprioceptors** *(body position sensors)*: muscle spindles (length) and Golgi tendon organs (tension). [MM p165]

Muscle spindle: receptor lying parallel to a muscle; fires to the CNS when muscle lengthens. [MM p165]

The spindle is a capsule buried among **muscle fibers**, holding **intrafusal fibers**. [MM p165]

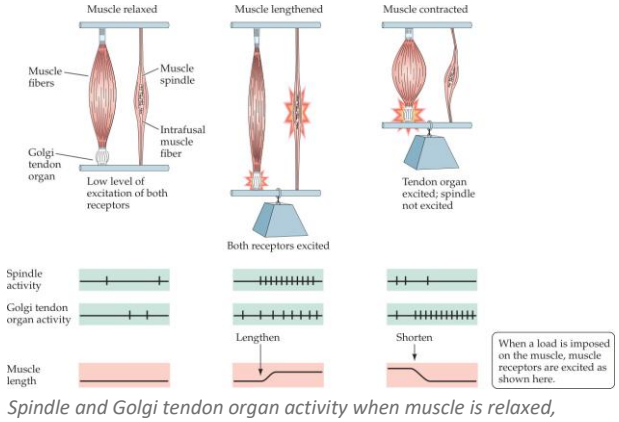
Intrafusal fiber: any small muscle fiber inside a muscle spindle (Latin intra "within," fusus "spindle"). [MM p165]

Muscle stretched beyond **relaxed** state: spindle sensory endings fire action potentials in sensory nerves. [MM p165]

Example: a heavy book handed to you bends the arm down, lengthening the biceps. [MM p165]

Spindle signal tells extent and rate of change in muscle length, so the imposed **load**. [MM p164, MM p165]

A special motor neuron sets intrafusal fiber length to match movements the brain plans. [MM p165]

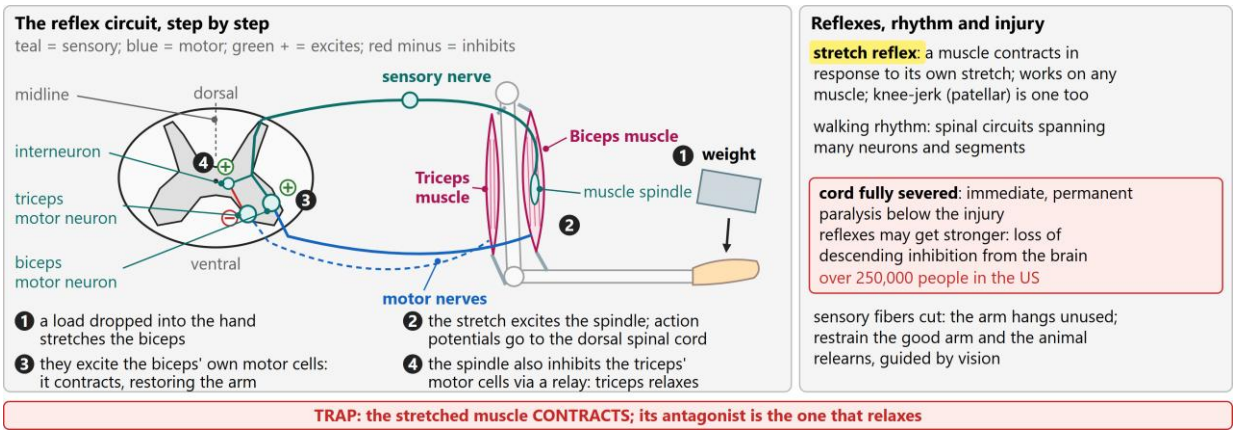


Spindle and Golgi tendon organ activity when muscle is relaxed, lengthened, or contracted [MM p165]

On the figure: **muscle spindle** · **Golgi tendon organ** · **muscle fibers** · **load** · **relaxed**

Setting intrafusal length calibrates the spindle to the EXPECTED limb position. [MM p165]

Muscle spindle wiring: sensory fibers carry length signals out; a motor fiber sets intrafusal length. [MM p164, MM p165]
Golgi tendon organ: receptor in tendons; fires to the CNS when a muscle contracts. [MM p165]
Golgi tendon organs are especially sensitive to muscle TENSION as the muscle shortens. [MM p165]
Its nerve endings weave through the tendon; strong loads that stretch the tendon excite them. [MM p165]
Main function: monitor force of muscle contractions, a second source of muscle information. [MM p165]
Golgi tendon organs detect overloads that threaten to tear muscles and tendons. [MM p165]
Golgi tendon organs cause reflexive relaxation of the muscle, protecting it (you drop the book). [MM p165]
Another familiar stretch reflex: the knee-jerk, or **patellar reflex**. [MM p165]
Severing sensory fibers from a monkey's arm muscles: monkey stops using that arm. [MM p165, MM p166]
This happens even though motor neuron connections to the muscles are preserved; the arm dangles. [MM p166]
If the good arm is restrained, the monkey learns to use the affected arm, becoming dexterous. [MM p166]
The monkey guides the arm with visual feedback, as the man without proprioception does. [MM p166]
In the dark the man collapses, yet still points to a spot more accurately than controls. [MM p166]
Everyone supplements proprioception with feedback from other senses, like vision. [MM p166]
Spinal cord: lowest hierarchy level; simple circuits produce reflexive responses to sensory stimuli. [MM p166]
Stretch reflex: contraction of a muscle in response to stretch of that same muscle. [MM p166]
A stretch reflex can be elicited by stretching any muscle. [MM p166]



Stretch reflex circuit step by step in the spinal cord [MM p166]
On the figure: stretch reflex · muscle spindle · biceps · triceps · weight

Stretch reflex circuit, in order: [MM p166]

1. A **weight** dropped into the outstretched hand suddenly stretches the **biceps**. [MM p166]
2. Stretch excites the **muscle spindle**, which sends action potentials to the dorsal spinal cord. [MM p166]
3. Spindle action potentials synapse onto biceps motor neurons; biceps contracts, restoring arm position. [MM p166]
4. Spindle also excites interneurons that inhibit **triceps** motor neurons, so the triceps relaxes. [MM p166]

Result: a compensatory movement returns hand and arm to their intended position. [MM p166]
Not all spinal circuits are simple: rhythmic walking uses many neurons across multiple spinal segments. [MM p166]
Visual Summary: spindles (muscles) and tendon organs (tendons) send crucial muscle information to the CNS. [MM p174]
Visual Summary: **efferent** *(outgoing from the CNS)* impulses adjust spindle sensitivity by controlling spindle length. [MM p174]
Review, proprioception: body sense; spindles report length, tendon organs report tension. [MM p164, MM p165, MM p170]

Muscle spindle vs Golgi tendon organ

Feature	Muscle spindle	Golgi tendon organ
Location	Within muscle, parallel to fibers	Woven through the tendon
Senses	Length and rate of change	Tension, force of contraction
Fires when	Muscle is lengthened	Muscle contracts or strong load
Special part	Intrafusal fiber, length set by motor neuron	Nerve endings in tendon
Reflex result	Stretch reflex: same muscle contracts	Overload: reflexive relaxation of muscle

Table source: [MM p164, MM p165, MM p166]

Receptor activity by muscle state

Muscle state	Spindle	Golgi tendon organ
Relaxed	Low excitation	Low excitation
Lengthened by load	Excited	Excited
Contracted (shortened)	Not excited	Excited

Table source: [MM p165]

5.3.4 Discuss the interaction of various cortical and subcortical brain regions in regulating behavior

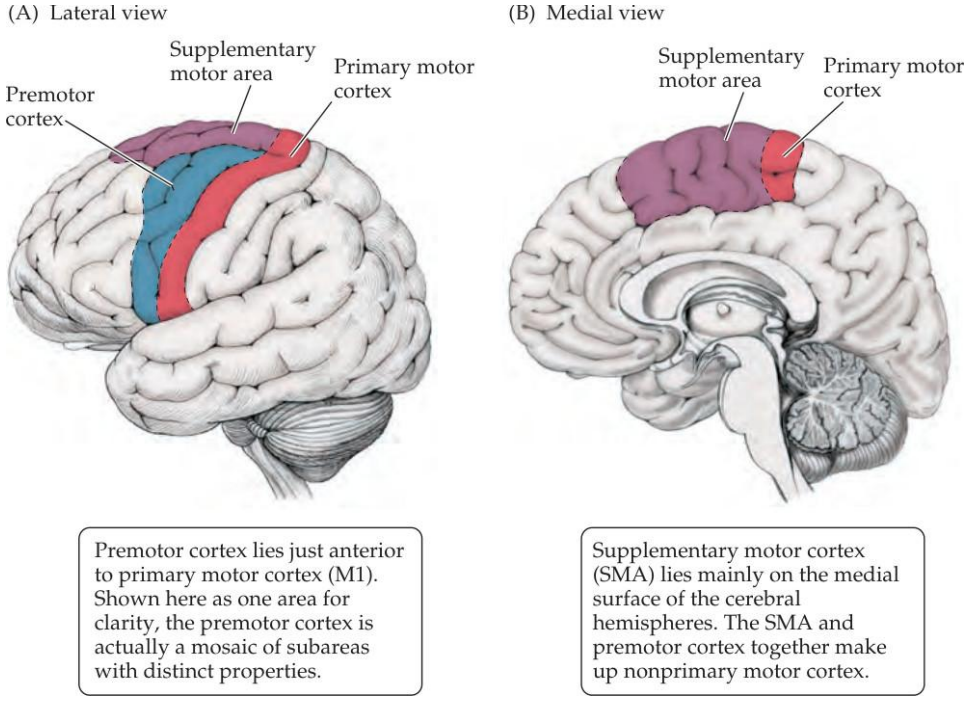
⚠ **Do not mix up: SMA runs INTERNAL preprogrammed sequences; premotor cortex runs sequences guided by EXTERNAL events.** [MM p170]

Nonprimary motor cortex: frontal regions just anterior to M1 that modulate M1 activity. [MM p169]

Nonprimary motor cortex acts directly on brainstem and spinal cord, and indirectly through M1. [MM p169]

Two main nonprimary regions: **supplementary motor area (SMA)** and **premotor cortex**. [MM p169]

SMA: mainly on the medial hemisphere surface; gets basal ganglia input; modulates M1. [MM p169]



Premotor cortex, supplementary motor area and primary motor cortex, lateral and medial views [MM p169]

On the figure: SMA · premotor cortex · M1

SMA: important for INITIATING movement sequences, especially from an internal preprogrammed plan. [MM p170]

Premotor cortex: activated when motor sequences are guided by external events. [MM p170]

Premotor cortex is a mosaic of units controlling behavior categories: defensive movements, feeding behavior. [MM p170]

So premotor areas mostly map BEHAVIORS, rather than specific MOVEMENTS as in **M1**. [MM p170]

Damage to motor cortex (stroke, injury) causes plegia or paresis, usually contralateral. [MM p170]

Plegia: paralysis, the loss of the ability to move. [MM p170]

Paresis: muscular weakness, often from damage to motor cortex. [MM p170]

One-sided forms: **hemiplegia** *(paralysis of one side)* or **hemiparesis** *(weakness of one side)*. [MM p170]

Apraxia *(cannot perform planned complex movements)*: inability to carry out complex movements, though not paralyzed. [MM p170]

In apraxia, weakness is absent, and language comprehension and motivation are intact. [MM p170]

Apraxia comes from damage to nonmotor zones: parietal or frontal association cortex. [MM p170]

From Greek a, "not," and praxis, "action"; several subtypes exist. [MM p170]

Apraxia is a high-level motor-programming problem: cannot work out the needed movement sequence. [MM p170]

Mirror neuron: active when an individual makes a movement AND sees another make it. [MM p170]

Found in premotor subregion **F5**, in ventral premotor cortex of monkeys. [MM p170, MM p171]

Hypothesis tested: F5 neurons encode specific detailed movements rather than muscle contractions. [MM p171]

Experiment: single F5 neurons recorded while a monkey made reaching movements. [MM p171]

F5 neurons fire shortly before a particular hand and arm movement reaching for an object. [MM p170, MM p171]

Different neurons fire during different reaching movements, so they seem to trigger specific movements. [MM p170]

Surprise: they also fire when the monkey watches another monkey or a human do it. [MM p170, MM p171]

Mirror neurons fire as though the monkey were imagining doing the same action. [MM p170, MM p171]

Monkey picks up **raisin**, or watches a human pick it up: the neuron fires both times. [MM p171]

Watching **hand movements** with no **object** to pick up: the **mirror neuron** responds less. [MM p171]

Mirror neurons are also found in adult humans and children, in premotor and other cortex. [MM p170]

Significance: may help understand others' actions; maybe part of a neural system for **empathy**. [MM p170, MM p171]

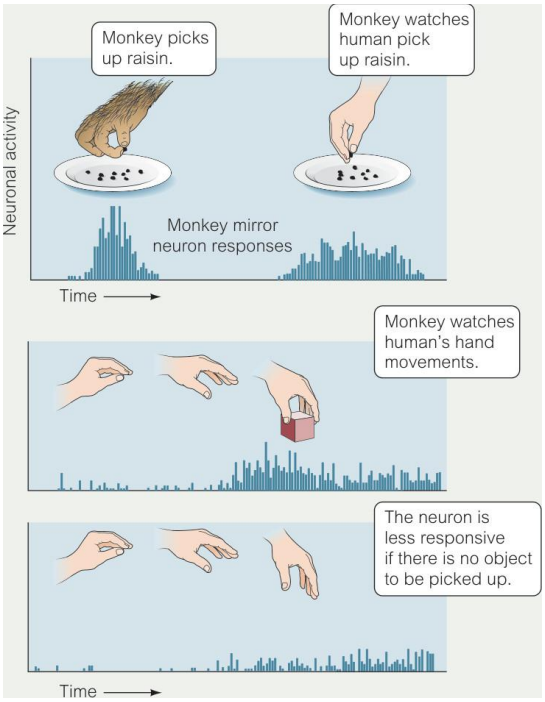
Speculated roles: infant imitation, evolution of language, and other behavior. [MM p170]

Autism spectrum disorder: failure to anticipate others' thinking and actions; maybe a mirror neuron deficit. [MM p170]

Specific functions of mirror neurons remain somewhat controversial. [MM p170]

Extrapyramidal projections are especially important in modulation and ongoing control of movement. [MM p172]

Two of the most important extrapyramidal sources: **basal ganglia** and **cerebellum**. [MM p172]



Mirror neuron firing when a monkey picks a raisin or watches a human do it [MM p171]

On the figure: mirror neuron · raisin · object · hand movements

Basal ganglia: forebrain nuclei deep in the hemispheres: **caudate nucleus**, **putamen**, **globus pallidus**. [MM p172]

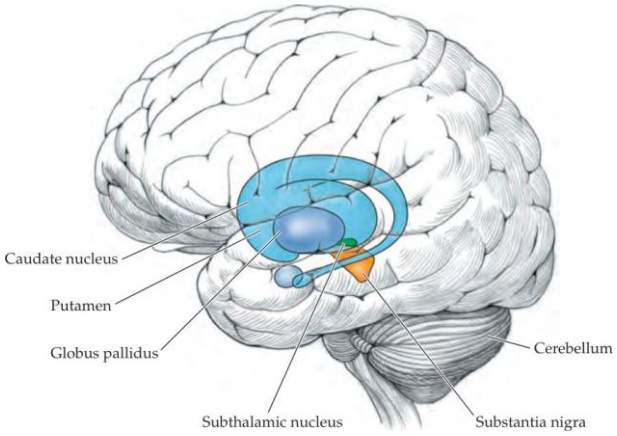
Basal ganglia get strong inputs from the **substantia nigra** and **subthalamic nucleus**. [MM p172]

Basal ganglia loop, in order: [MM p172]

1. Wide expanses of cortex send input toward the basal ganglia. [MM p172]
2. The loop passes through the basal ganglia. [MM p172]
3. Output passes through the thalamus. [MM p172]
4. Back to the cortex, closing the loop. [MM p172]

Basal ganglia help control **amplitude** *(size)* and direction of movement. [MM p172]

Changes in basal ganglia activity appear important for INITIATING movement. [MM p172]



Basal ganglia nuclei, substantia nigra, subthalamic nucleus and cerebellum [MM p172]

On the figure: **caudate nucleus** · **putamen** · **globus pallidus** · **subthalamic nucleus** · **substantia nigra** · **cerebellum**

Much basal ganglia function: modulating activity started by other circuits, such as cortical motor pathways. [MM p172]

Basal ganglia: especially important for movements performed by MEMORY, not those guided by sensory control. [MM p172]

Cerebellum: at the back of the brain, **dorsal** *(behind)* to the pons. [MM p172]

Cerebellum regulates movement centrally and is involved in some forms of learning. [MM p172]

Cerebellum inputs: sensory sources and other brain motor systems. [MM p172]

Sensory inputs: muscle and joint receptors, vestibular, somatosensory, visual, and auditory systems. [MM p172]

Pyramidal and nonpyramidal pathways send inputs to the cerebellum. [MM p172]

Those pathways receive outputs from the deep cerebellar nuclei, all of which are inhibitory. [MM p172]

Cerebellum establishes and fine-tunes neural programs for SKILLED movements. [MM p172]

Especially rapid, repeated movements that become automatic. [MM p172]

Some people appear born without a cerebellum, yet develop normal motor skills. [MM p172]

Presumably due to the great plasticity of the brain during development. [MM p172]

Visual Summary: extrapyramidal = basal ganglia, substantia nigra, brainstem nuclei, and cerebellum. [MM p174]

Brainstem nuclei listed: thalamic nuclei, reticular formation, and red nucleus. [MM p174]

Review, mirror neurons: fire for own and observed movement; may support understanding others. [MM p170, MM p173]

M1 vs SMA vs premotor cortex

Area	Location	Role
M1	Precentral gyrus	Initiates movement; maps specific movements
SMA	Medial hemisphere surface	Starts internally planned sequences; basal ganglia input
Premotor cortex	Just anterior to M1	Externally guided sequences; maps behaviors

Table source: [MM p168, MM p169, MM p170]

Plegia vs paresis vs apraxia

Disorder	Meaning	Damage site
Plegia	Paralysis	Motor cortex
Paresis	Weakness	Motor cortex
Apraxia	Cannot sequence complex movements	Parietal or frontal association cortex

Table source: [MM p170]

Basal ganglia vs cerebellum

Feature	Basal ganglia	Cerebellum
Location	Deep forebrain nuclei	Back of brain, dorsal to pons
Parts or inputs	Caudate, putamen, globus pallidus; nigra input	Sensory plus motor system inputs
Main role	Amplitude, direction, initiation of movement	Fine-tunes skilled, rapid, automatic movements
Best for	Movements performed by memory	Rapid repeated skilled movements
Damage	Parkinson's, Huntington's	Ataxia, decomposition of movement

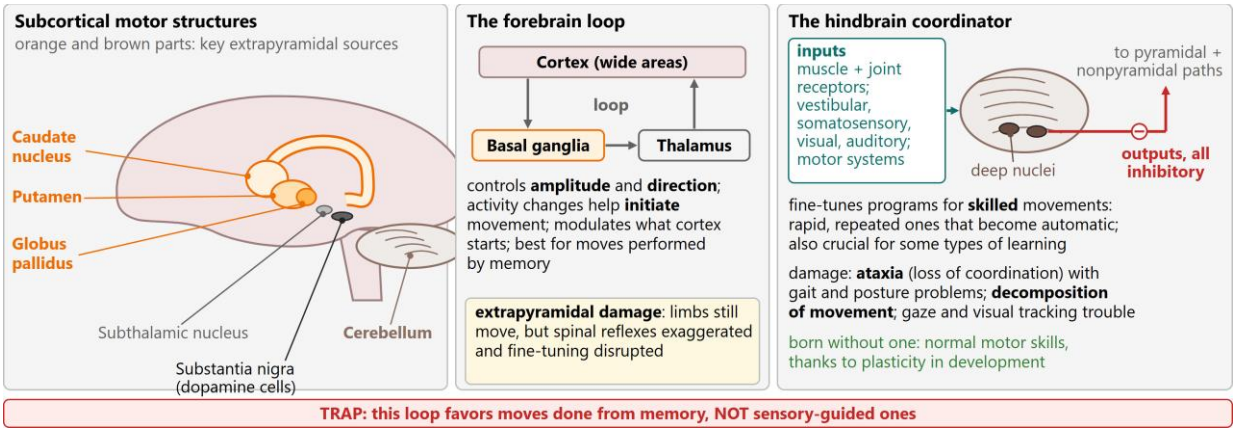
Table source: [MM p172, MM p173]

5.3.5 Describe the behavioral symptoms and underlying pathology of two major motor disorders

⚠ Do not mix up: Parkinson's REDUCES movement (substantia nigra loss); Huntington's causes EXCESSIVE movement (caudate, putamen). [MM p172, MM p173]

Different symptom clusters come from damage to different extrapyramidal structures. [MM p172]

Cerebellar damage effects depend on which part is damaged. [MM p172]



Cerebellar damage and the basal ganglia loop [MM p172]

On the figure: ataxia · decomposition of movement · substantia nigra · caudate nucleus · putamen

Common cerebellar symptoms: abnormal gait and posture, especially **ataxia** of the legs. [MM p172]

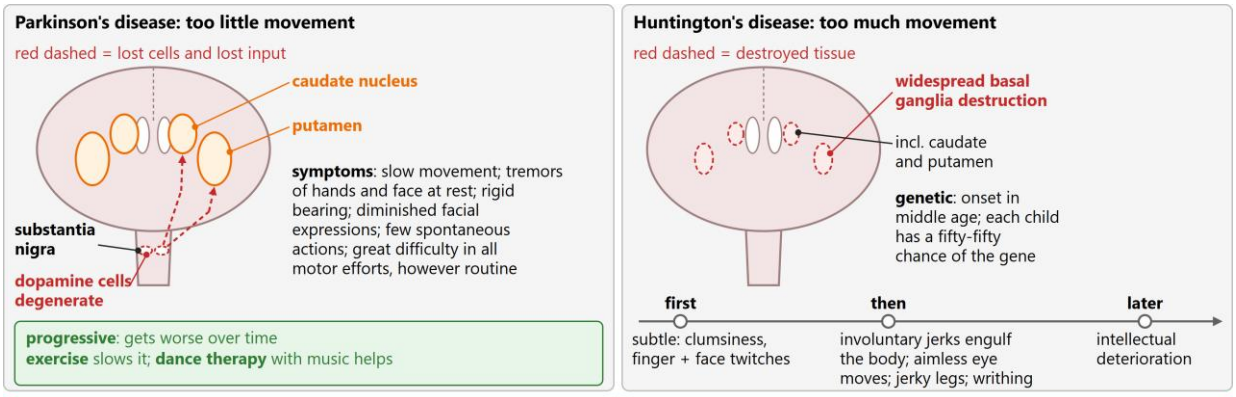
Ataxia: loss of movement coordination, often caused by cerebellar disease. [MM p172]

Decomposition of movement: gestures broken into individual segments instead of executed smoothly. [MM p172, MM p173]

Decomposition of movement is a symptom of cerebellar lesions. [MM p173]

Other cerebellar lesions: difficulty with gaze and visual tracking of objects. [MM p172]

Two basal ganglia diseases reveal extrapyramidal contributions to motor control. [MM p172]



Parkinson's disease versus Huntington's disease [MM p173]

On the figure: Parkinson's disease · Huntington's disease · substantia nigra · caudate nucleus · putamen · dance therapy

Parkinson's disease: degenerative disorder from progressive loss of **dopaminergic** *(dopamine releasing)* **substantia nigra** neurons. [MM p172, MM p173]

Substantia nigra: brainstem structure, a major source of dopamine projections to basal ganglia. [MM p173]

The lost dopamine neurons project to the **caudate nucleus** and **putamen**. [MM p172]

Parkinson's symptoms: slow movement, tremors of hands and face AT REST. [MM p172]

Also a rigid bearing and diminished facial expressions. [MM p172]

Few spontaneous actions; great difficulty in all motor efforts, however routine. [MM p172, MM p173]

Exercise can slow Parkinson's progression. [MM p173]

Dance therapy, using music to encourage movement, helps patients with Parkinson's. [MM p173]

Huntington's disease: genetic disorder, onset in middle age; basal ganglia destruction. [MM p173]

Huntington's causes abrupt, involuntary writhing movements and changes in mental functioning. [MM p173]

First Huntington's symptoms are subtle: clumsiness, twitches in the fingers and face. [MM p173]

As it progresses, a continuing stream of involuntary jerks engulfs the entire body. [MM p173]

Aimless eye movements, jerky leg movements, and body writhing make routine activity hard. [MM p173]

Later stages add intellectual deterioration. [MM p173]

Huntington's pathology: widespread basal ganglia destruction, including caudate nucleus and putamen. [MM p173]

Not just the substantia nigra, as in Parkinson's. [MM p173]

Children of a parent with Huntington's have a fifty-fifty chance of inheriting the gene. [MM p173]

Research into both diseases may pave the way to new therapies. [MM p173]

Review, Parkinson's: slow movement, rest tremor, rigidity; from substantia nigra dopamine cell loss. [MM p172, MM p173]

Review, Huntington's: involuntary jerks and writhing, mental decline; from caudate and putamen destruction. [MM p173]

Review, testing question: a personal choice; the risk of inheriting is fifty-fifty. [MM p173]

Parkinson's vs Huntington's disease

Feature	Parkinson's disease	Huntington's disease
Cause	Degenerative; dopamine neuron loss	Genetic; onset in middle age
Brain damage	Substantia nigra dopamine cells	Widespread basal ganglia: caudate, putamen
Movement	Reduced, slow	Excessive, involuntary jerks
Key signs	Rest tremor, rigidity, flat face	Writhing, twitches, clumsiness
Mental changes	Not mentioned	Later intellectual deterioration
Helps	Exercise, dance therapy	No treatment named

Table source: [MM p172, MM p173]