9.14 - Brain Structure and its Origins
Spring 2005
Massachusetts Institute of Technology
Instructor: Professor Gerald Schneider

A sketch of the central nervous system and its origins

G. E. Schneider 2005

Part 5: Differentiation of the brain vesicles

MIT 9.14 Class 9b-10a

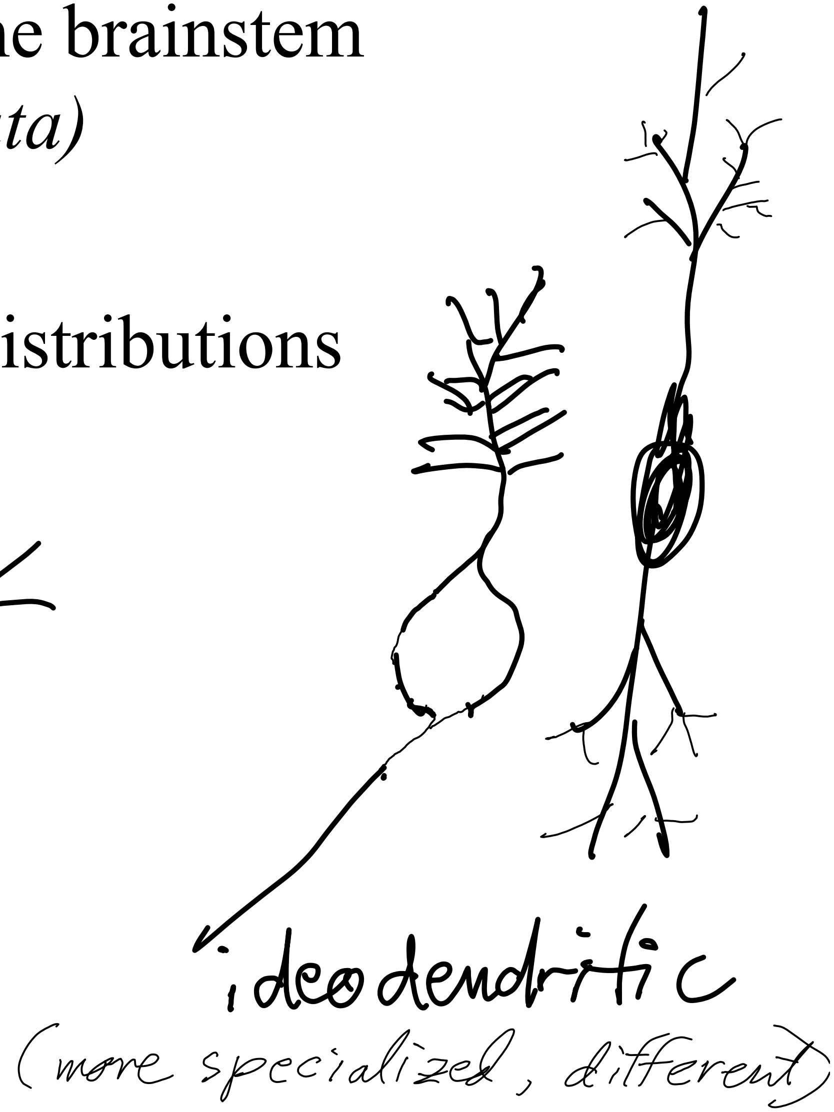
Hindbrain development, elaboration and specializations

Hindbrain functions

- **Routine maintenance**: the support services area of the CNS, for centralized control of spinal functions
  - Vital functions (control of breathing, blood pressure & heart rate, & other visceral regulation)
  - Motor coordination (cerebellum, vestibular system)
  - Fixed Action Pattern generators: swallowing, vomiting, eyeblink, grooming, smiling, frowning, righting, etc.
  - Widespread modulation of brain activity: sleep & waking; arousal effects [See following illustrations]
- **Role in mammalian higher functions**: movement control for functions of more rostral brain systems
  - for speech (tongue, lip, breath control)
  - for emotional displays, especially in facial expressions
  - for eye movements

Neurons of the reticular formation

- "Isodendritic" core of the brainstem *(Ramon-Moliner & Nauta)*
- Neuropil segments
- Axons with very wide distributions



neuropil: space between cell bodies, where synaptic contacts between axons and dendrites are made

Dendritic orientation of reticular formation neurons in hindbrain, forming a series of "neuropil" segments.

Collaterals of pyramidal tract axons have similar distributions.
For contrast, cells of the hypoglossal nucleus are also shown

Figure removed due to copyright reasons.

Golgi stain, parasagittal section of hindbrain, young rat. From Scheibel & Scheibel, 1958

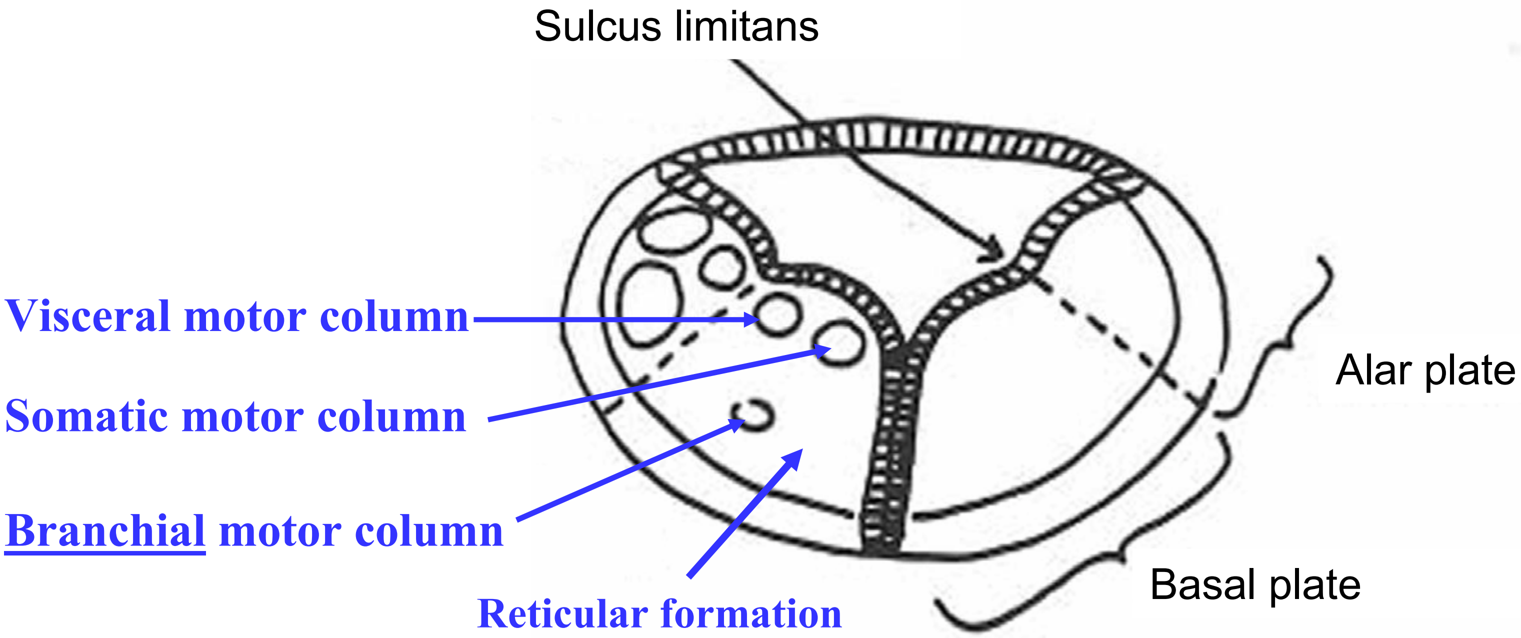
Neuron of hindbrain reticular formation: Axon has ascending and descending branches, each with widespread distribution of terminations

Figure removed due to copyright reasons.

2-day old rat, Rapid Golgi stain, from Scheibel & Scheibel, 1958

Notes on hindbrain origins: *definitions*

- Segmentation above the segments of the spinal cord: The **branchial arches** and the **rhombomeres**
- *See Nauta & Feirtag, ch.11, p. 170, on the "**branchial motor column**" -- in addition to the **somatic and visceral motor columns**.*



Sulcus limitans

Visceral motor column

Somatic motor column

Branchial motor column

Reticular formation

Alar plate

Basal plate

Three segmented systems, 3-day chick embryo:
somites, branchial arches, rhombomeres

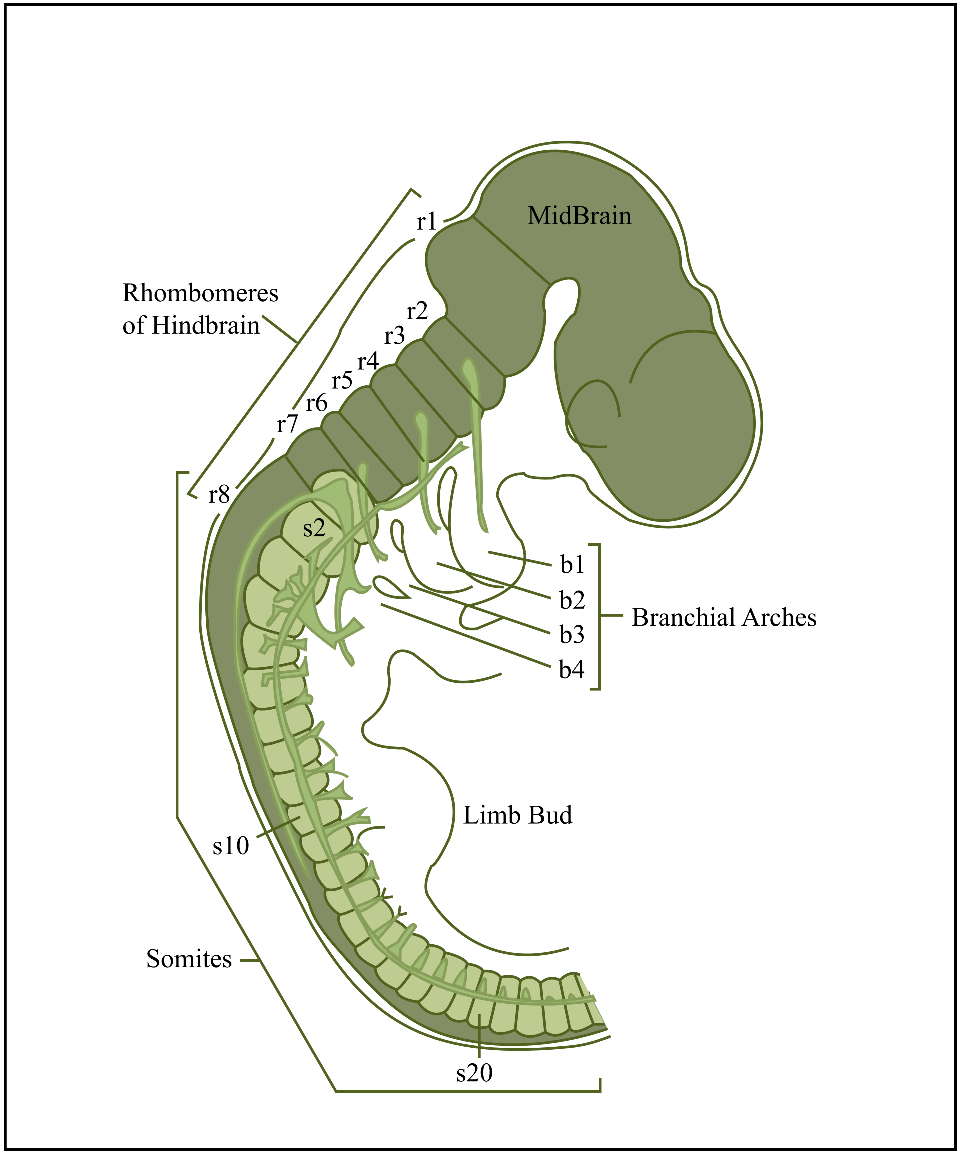


Figure by MIT OCW.

5th n.

Branchial arches, innervated by Trigeminal Motor & Facial 7th Nucleus and by Nucleus Ambiguus.

(Function of Nuc. Ambiguus: swallowing and vocalization)

Somites,
2-day chick embryo

Figure removed due to copyright reasons.
Please see:
Wolpert, Lewis, et al. *Principles of Development*. 2nd ed.
Oxford, UK: Oxford University Press, 2002, p. 22. ISBN: 0198792913.

Genes underlying hindbrain segmentation

topics

- Ancient origins of segmentation along the A-P axis, with corresponding nervous system differentiation
- The homeobox genes: What are they?
- Examples of gene expression patterns

Homeobox genes in Drosophila, and 13 paralogous groups in 4 chromosomes of mouse

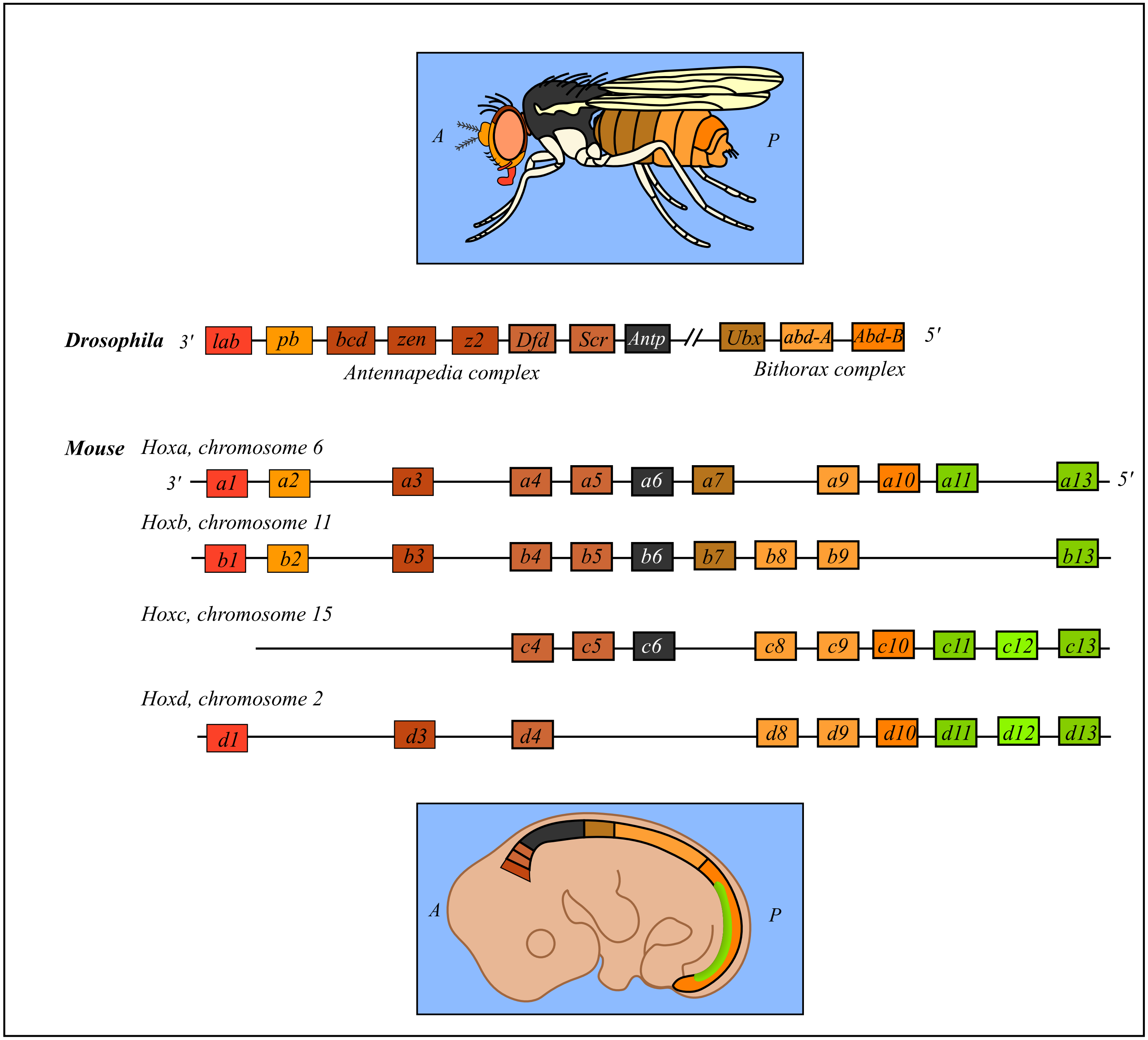


Figure by MIT OCW.

Hox gene expression in the mouse embryo after neurulation

Figure removed due to copyright reasons.
Please see:
Figure 4.11 from Wolpert, Lewis, et al. *Principles of Development*. 2nd ed.
Oxford, UK: Oxford University Press, 2002. ISBN: 0198792913.

E 9.5 mouse embryos, immunostained using antibodies specific For the protein products of the indicated Hox genes.

Hox gene expression along the antero-posterior axis of the mouse mesoderm

Figure removed due to copyright reasons.

Please see:

Figure 4.12 from Wolpert, Lewis, et al. *Principles of Development*. 2nd ed. Oxford, UK: Oxford University Press, 2002. ISBN: 0198792913.

Rhombomeres

Figure removed due to copyright reasons.

Allman, John Morgan. "Scanning Electron Microscope Photo." *Evolving Brains*. New York, NY: Scientific American Library: Distributed by W.H. Freeman and Co., 1999. ISBN: 0716750767.

Figure removed due to copyright reasons.

Gene Expression
and
Rhombomeres

(Lumsden & Krumlauf '96)

The hindbrain neuromeres:

A) Expression of transcription factor genes;

B) Fate of embryonic precursor cells injected before and after rhombomere formation

Figures removed due to copyright reasons.

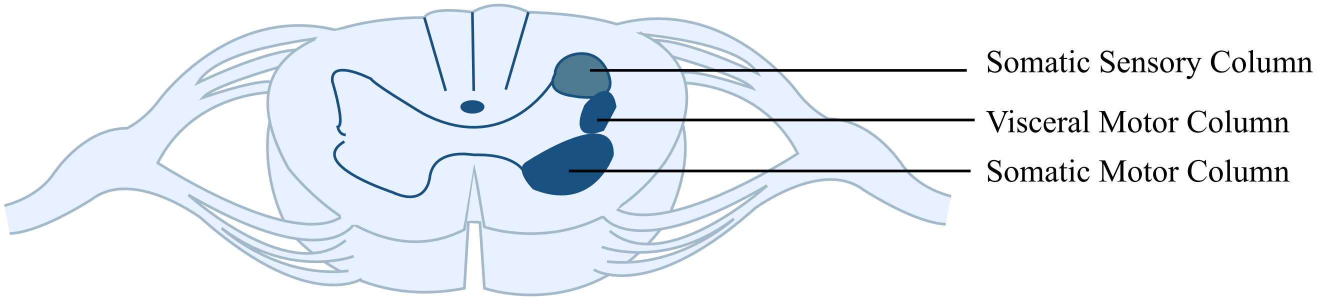
Please see:

Striedter, Georg F. *Principles of Brain Evolution*. Sunderland, MA: Sinauer Associates, 2005, p. 79. ISBN: 0878938206.

Columns of
secondary sensory and motor neurons

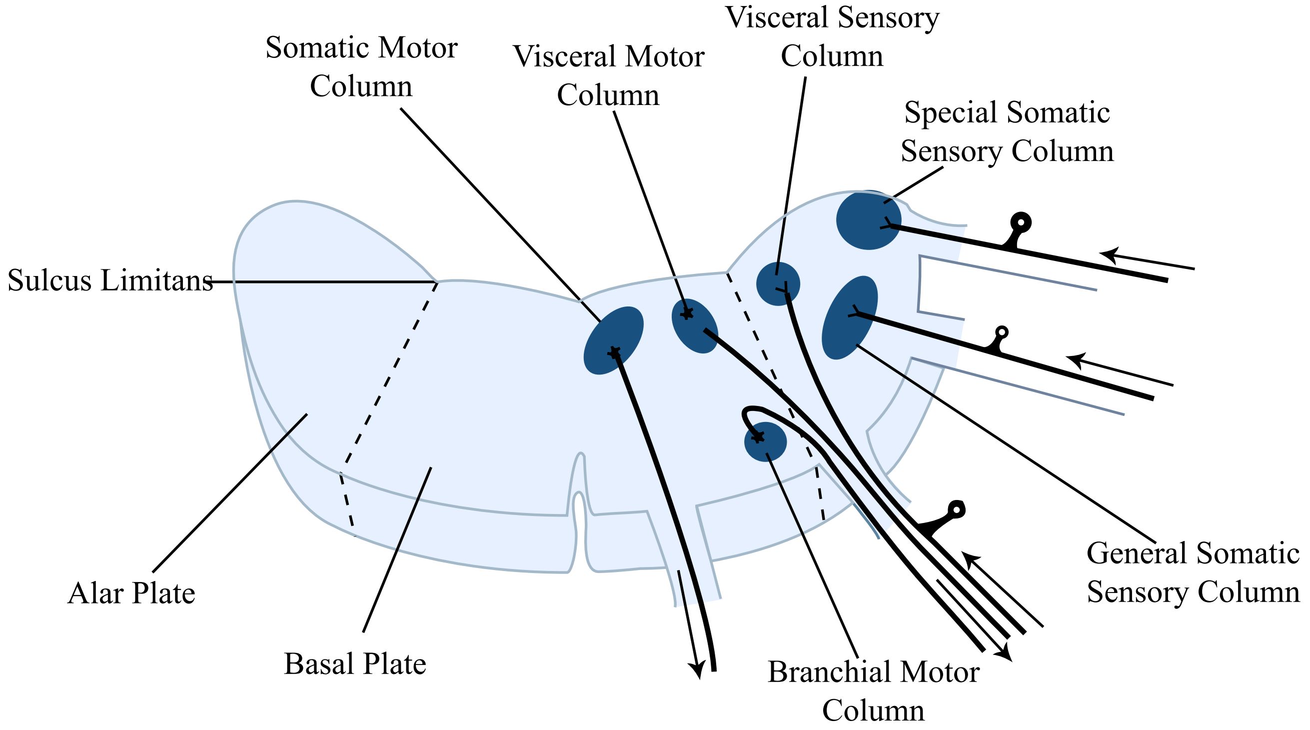
- This time, these should begin to enter your long-term memory!
- Trajectories of associated cranial nerves have been added in the following figure from Nauta & Feirtag.

Columns in spinal cord



Know these figures!

Columns in Hindbrain



Figures by MIT OCW.

The variety of cranial nerve types

- Study previous picture (fig. 71) from Nauta & Feirtag ch. 11. Note the four types of cranial nerves depicted (p. 172). The figure is a good one to memorize.

- Next, some more details about hindbrain: Names of cell groups; fibers passing through, between the cord and more rostral brain structures.

The inadequacy of the **traditional enumeration of 12 cranial nerves** *(a note from Butler & Hodos)*

- More than 12 are seen in embryonic development.
- *See Butler & Hodos, p. 134 table:* **25 cranial nerves** are listed. But some are found only in certain groups of vertebrates.
- *P. 127:* The facial (#7), glossopharyngeal (#9) and vagus (#10) each contain two distinct parts.
- However, it has become traditional to list just 12 cranial nerves. For the adult human brain, it is an adequate description.

The caudal hindbrain of an adult mammal

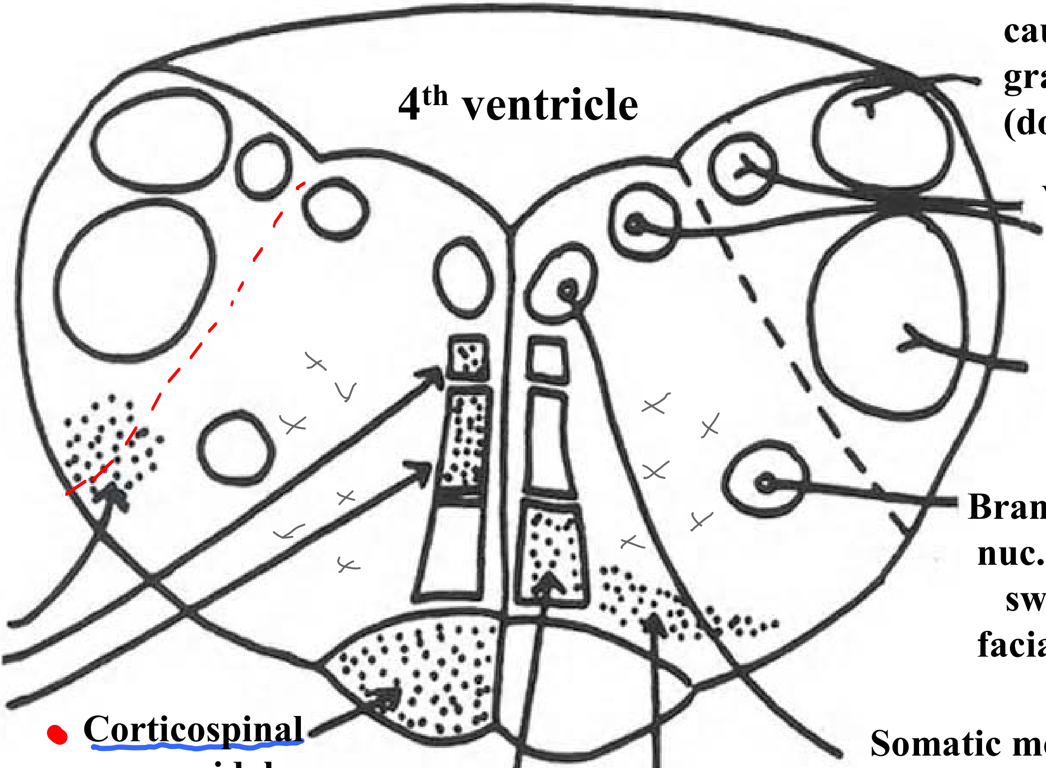
- Locations of cell groups
  - Secondary sensory neurons in the alar plate
  - Motor neurons in the basal plate
- Locations of axons passing through

The neuroanatomical names add to the apparent complexity of the following picture, but it will seem simpler as we study the brain more and more.

Use the figure for reference. Understand it, but you don't have to memorize it.

Adult caudal hindbrain (*medulla oblongata*):

principle cell columns and fiber tracts (schematic)



4th ventricle

Vestibular, auditory (VIII);
caudally—nuc.
gracilis & cuneatus
(dorsal column nuclei)

Visceral sensory & motor
(III in midbrain; VII, IX
& X – parasympathetic

Trigeminal (V, sensory
from face)

Branchial motor column:
nuc. ambiguus (IX, X –
swallowing & vocalization)
facial (VII), masticatory (V)

Descending
pathways:
Rubrospinal
Vestibulospinal
Tectospinal

● **Corticospinal**
=pyramidal
tract

Medial
lemniscus

Spinothalamic
tract

Somatic motor column:
III, IV (midbrain) & VI – eye
movements
XII – tongue movements

Reticulospinal:
not shown

x Spinoreticular axons

Locations in human brainstem

- Imagine the brainstem to be transparent, and that the secondary sensory cell groups and the motor nuclei are bright or dark objects *(figure from Nauta & Feirtag)*
- You should understand the following two figures, but there is no need to memorize them.

Brainstem Nuclei: secondary sensory and motor neuron columns

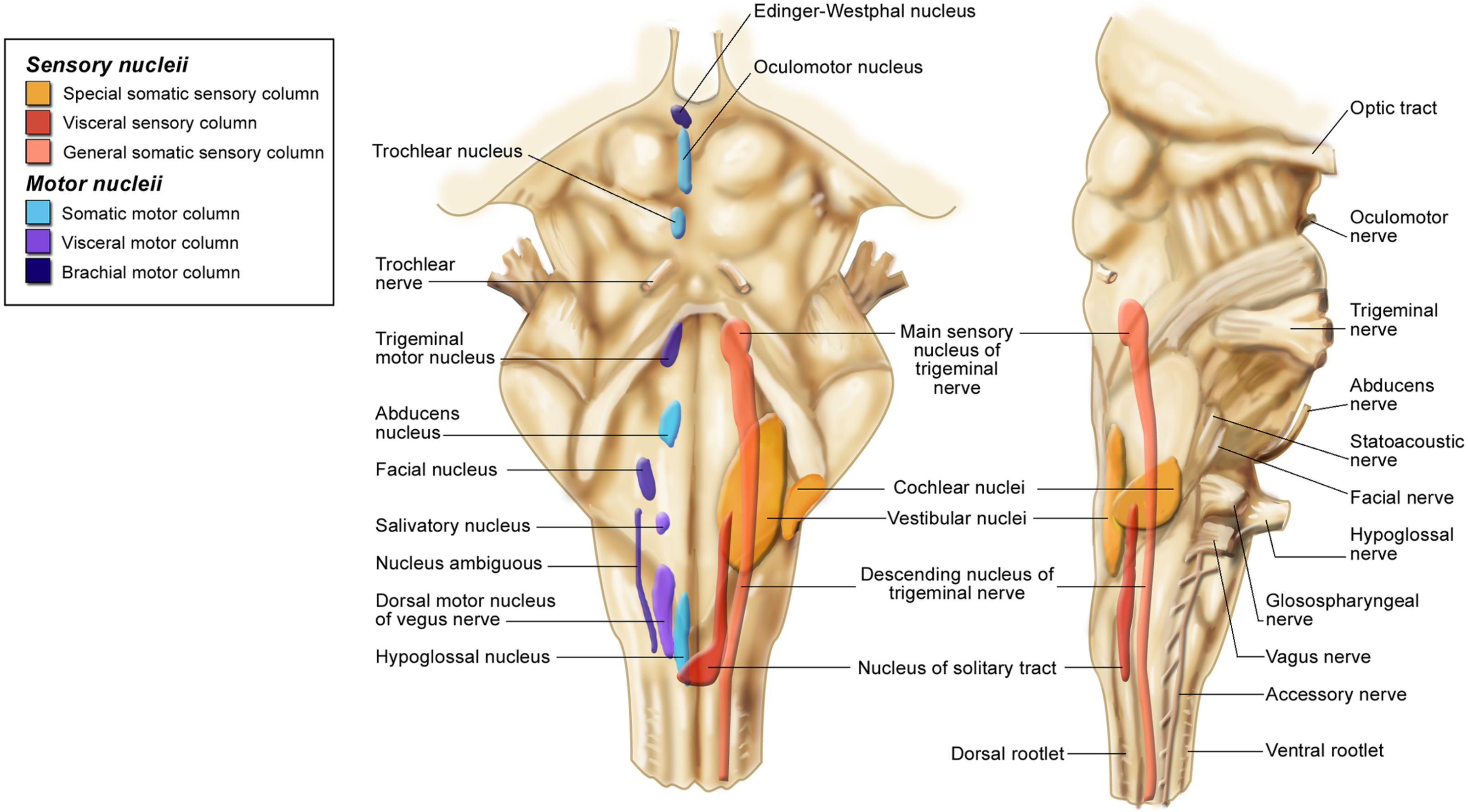
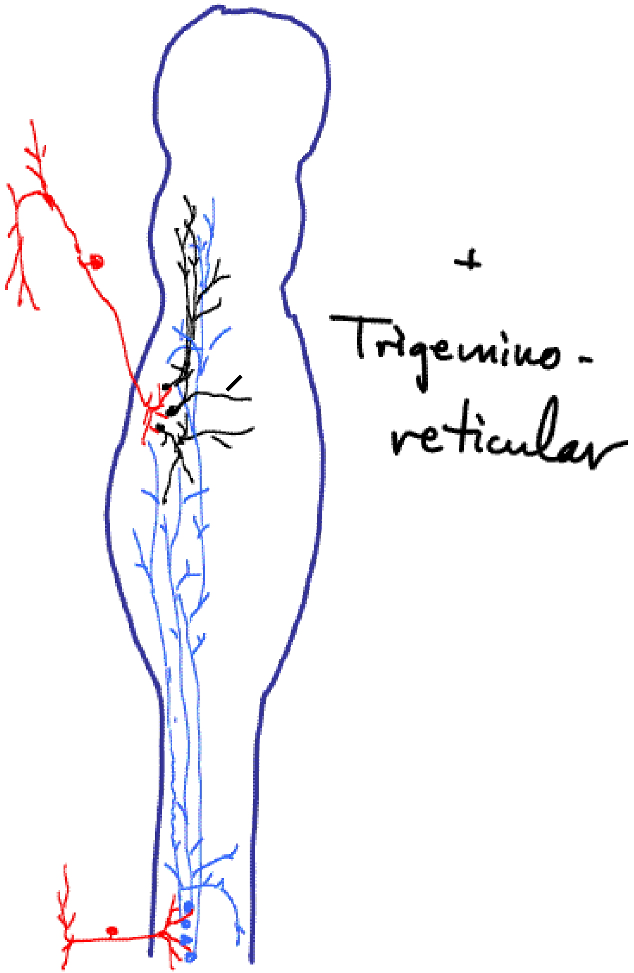


Figure by MIT OCW.

Sensory channels:
the trigeminal nerve input (from the face)

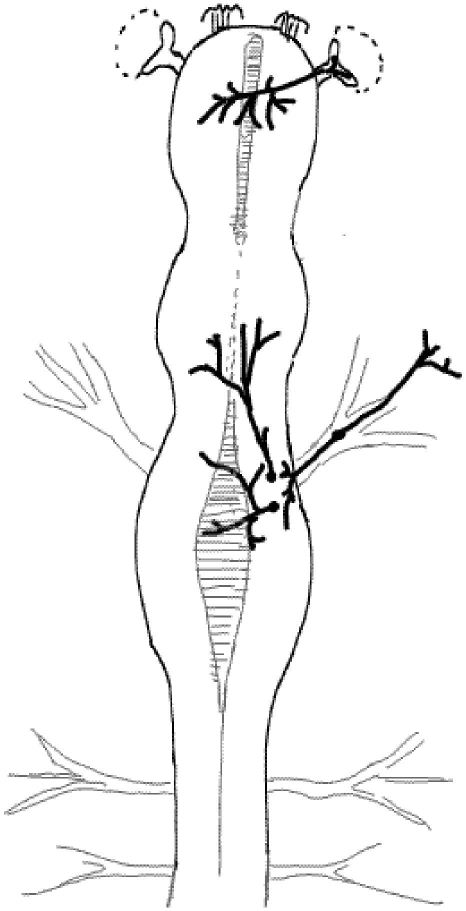
- Local reflex channel: see following figures
  - Example: Pathway for eyeblink reflex
  - There is also a role of endogenous activity in eyeblink control.
- Lemniscal pathways:
  - Mammalian "trigeminal lemniscus", leading to the ventrobasal nucleus of thalamus (the part called VPM, or *ventralis posteriomedialis*).
  - Hypothesis: The decussation evolved with or after the evolution of the crossed retinal projection to the midbrain tectum.
  - The earliest inputs were ipsilateral or bilateral.

A lemniscal pathway in mammals, bilateral, inherited from ancient chordates, carrying sensory information from the face (right-hand figure)

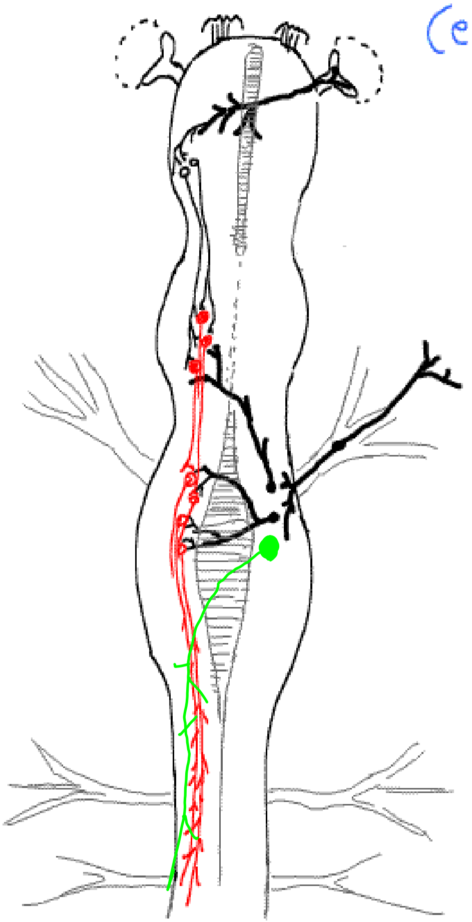


Some bilateral projections become mostly contralateral for eliciting rapid escape/avoidance

1. Bilateral optic and somatosensory connections



2. Contralateral optic and SS → body flexion (escape)

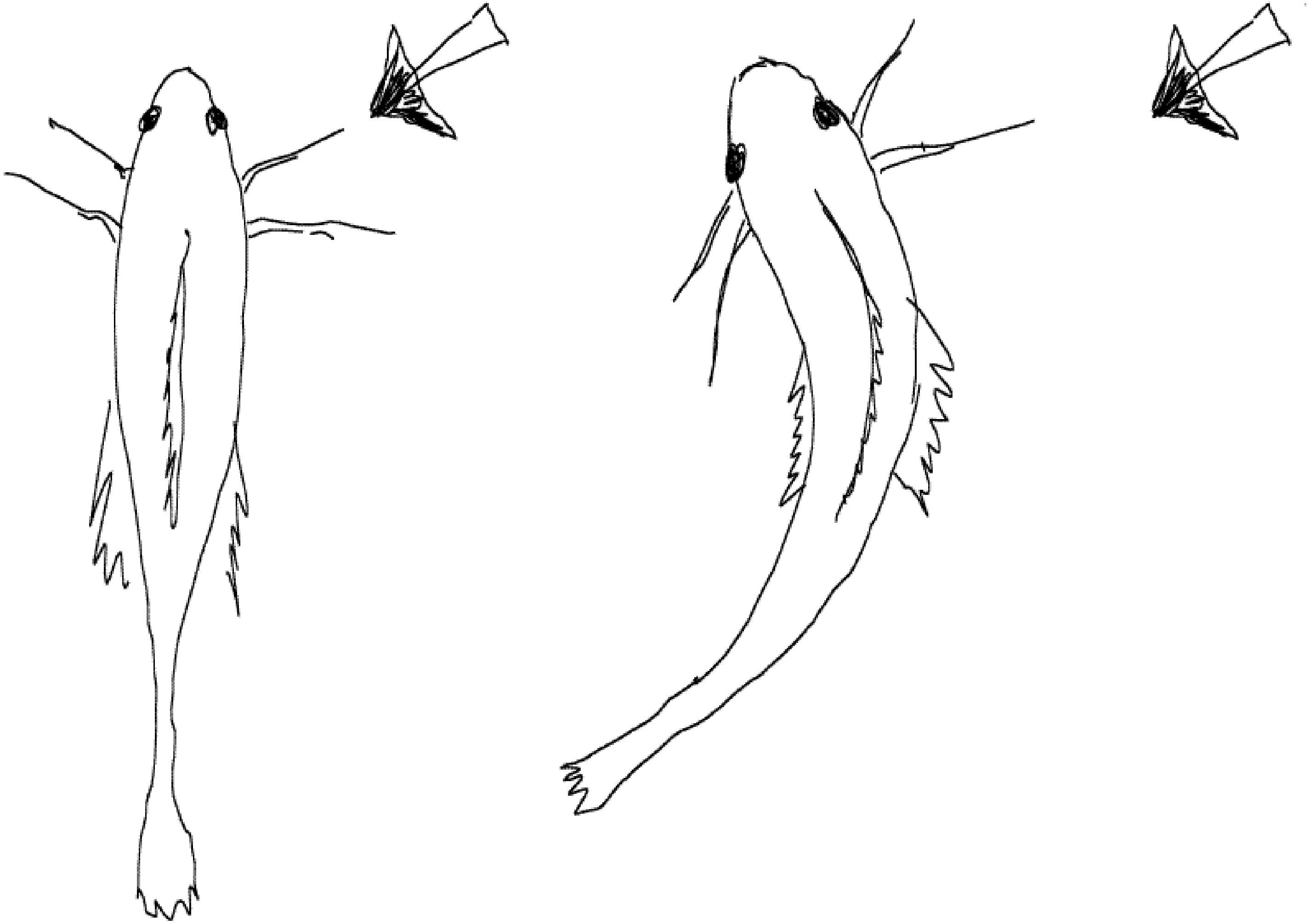


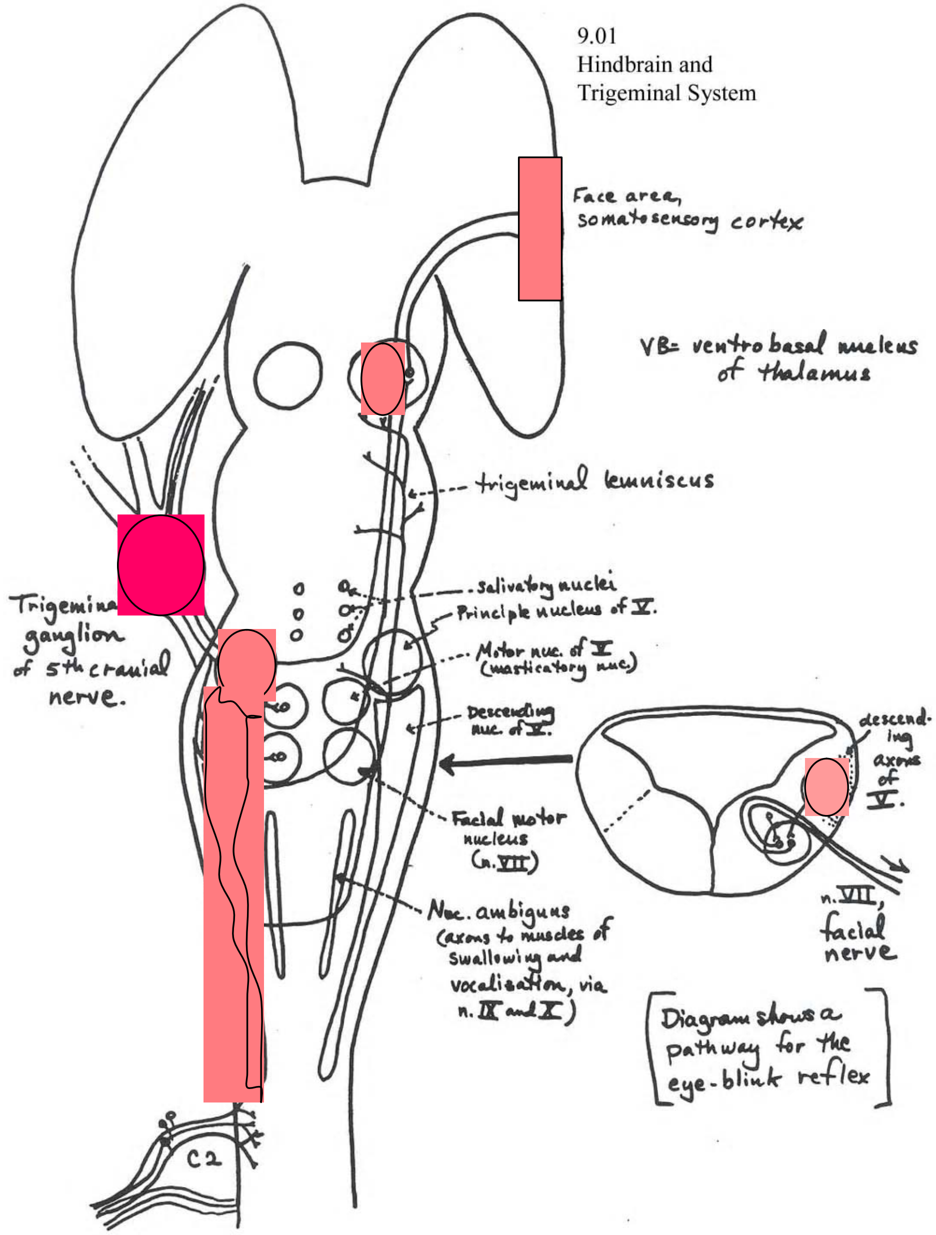
Optic stimuli:
Shadows moving,
sudden novelty,
intense light.

SS stimuli:
Novel, sudden,
intense or
painful.

Also note: Mauthner cells of fish & amphibia

The primitive escape response



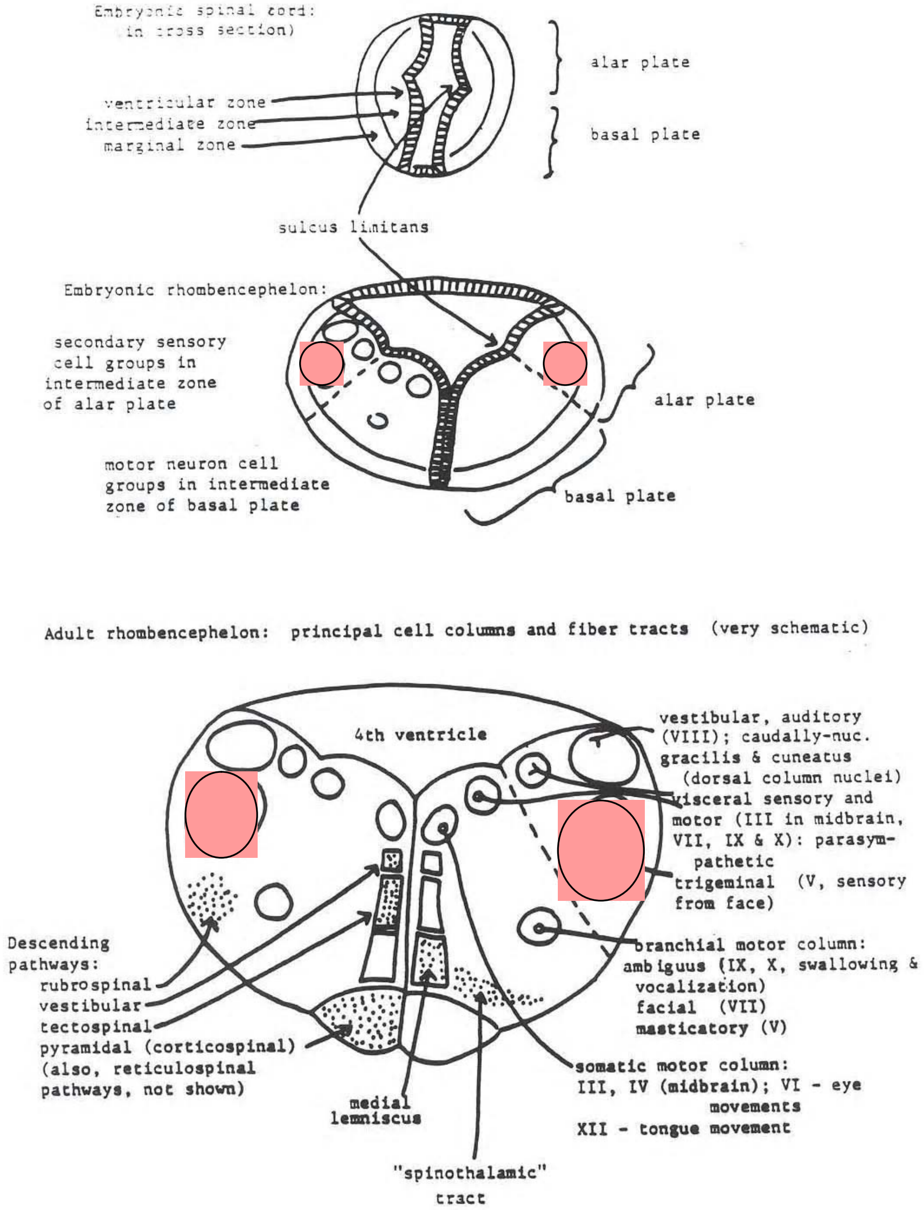


Hindbrain and Trigeminal system of mammals

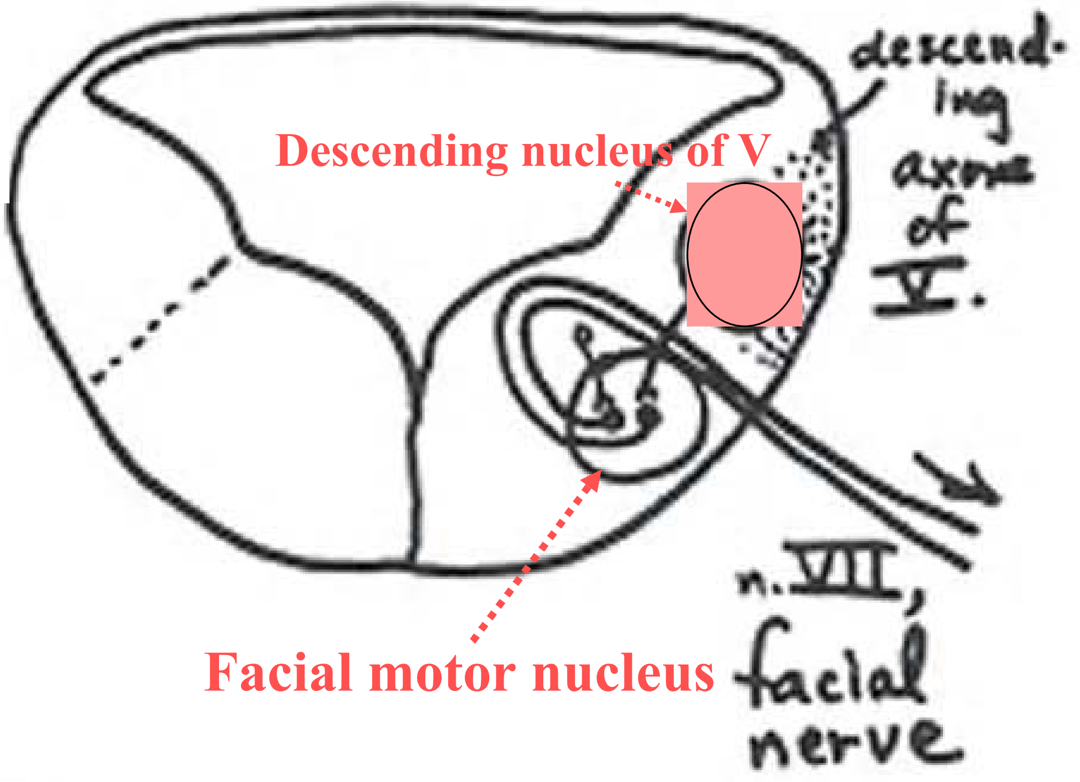
Sensory channels are like those of spinal cord, including extensive bilateral connections with neurons of the reticular formation of hind- and midbrain (not shown).

The figure is not as complex as it first appears. The elongated secondary sensory cell group of the trigeminal nerve makes it seem complicated.

Mammalian trigeminal nuclei (of the 5th cranial nerve)



Pathway for the eyeblink reflex



Descending nucleus of V

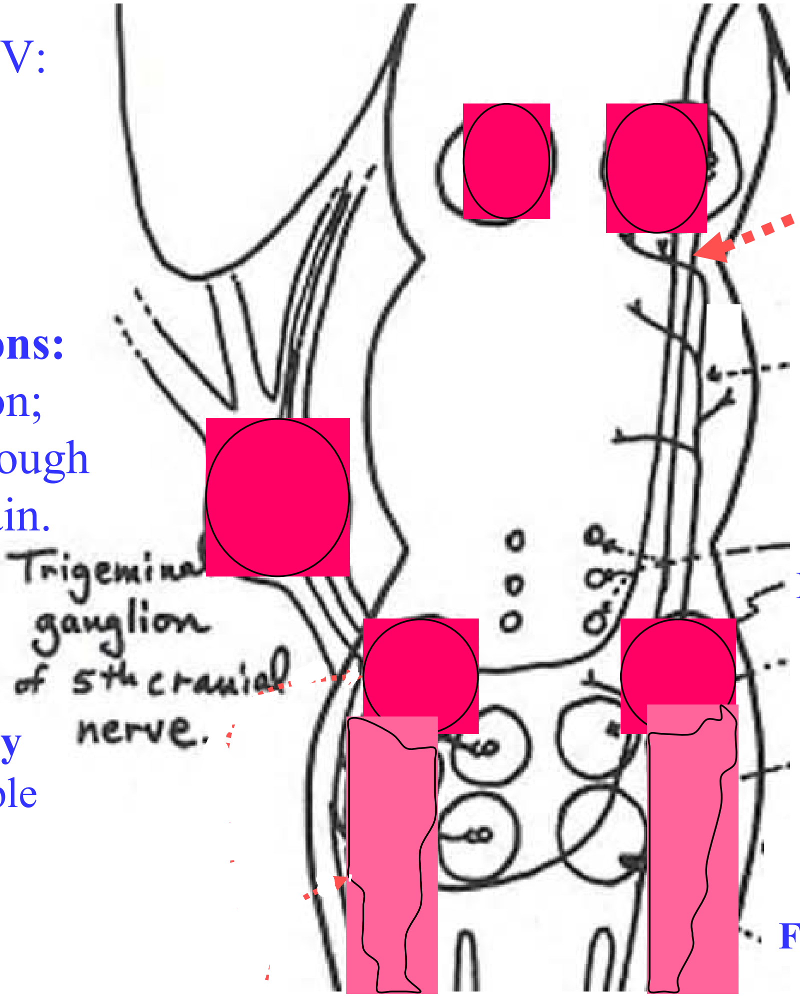
Facial motor nucleus

Trigeminal nerve (cranial nerve 5): Lemniscal channel

Three main branches of V:
  Opthalmic branch
  Maxillary branch
  Mandibular branch

Primary sensory neurons: in the trigeminal ganglion; axons enter the CNS through the pons (rostral hindbrain.

They synapse on **secondary sensory cells** of the principle nucleus of V, and the descending nucleus of V.



The <u>Trigeminal Lemniscus:</u> projections From the principle & Descending nuclei of V to the thalamus (longest axons end in the Ventrobasal nucleus)

Salivatory nuclei (parasympathetic)

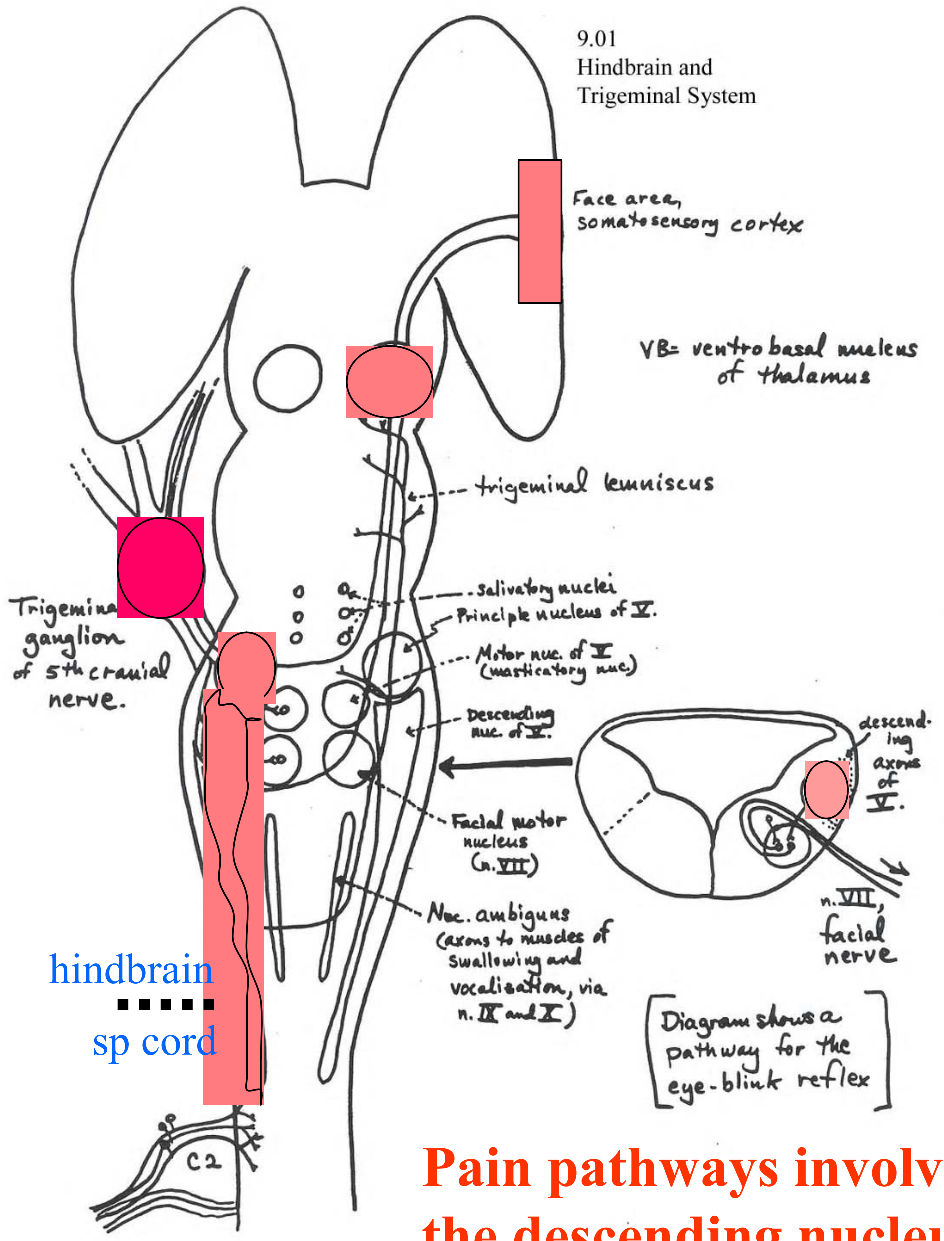
Principal nucleus of V

Masticatory nucleus

Descending nuc. of V

Facial motor nucleus

Hindbrain and Trigeminal system of mammals



Sensory channels resemble those of spinal cord

Pain pathways involve mainly the spinal portion of the descending nucleus of V

At this point, we need a change of pace!

- For some more fun: We will look at some specializations of the 5th cranial nerve and the structures it innervates in some species.
- (Some of this was mentioned earlier.)

Sensory specializations, 5th cranial nerve
and other hindbrain specializations

- Snake sensory pit (in pit vipers) for infrared radiation detection
- Rodent vibrissae, for sensing space around the head
- Recall also some other specializations of the hindbrain:
  - for taste functions in some fishes,
  - electrosensory abilities in weakly electric fish,
  - cerebellar expansions in large animals with highly developed manipulatory abilities

Rattlesnake trigeminal nerve: innervation of a specialized distance sense

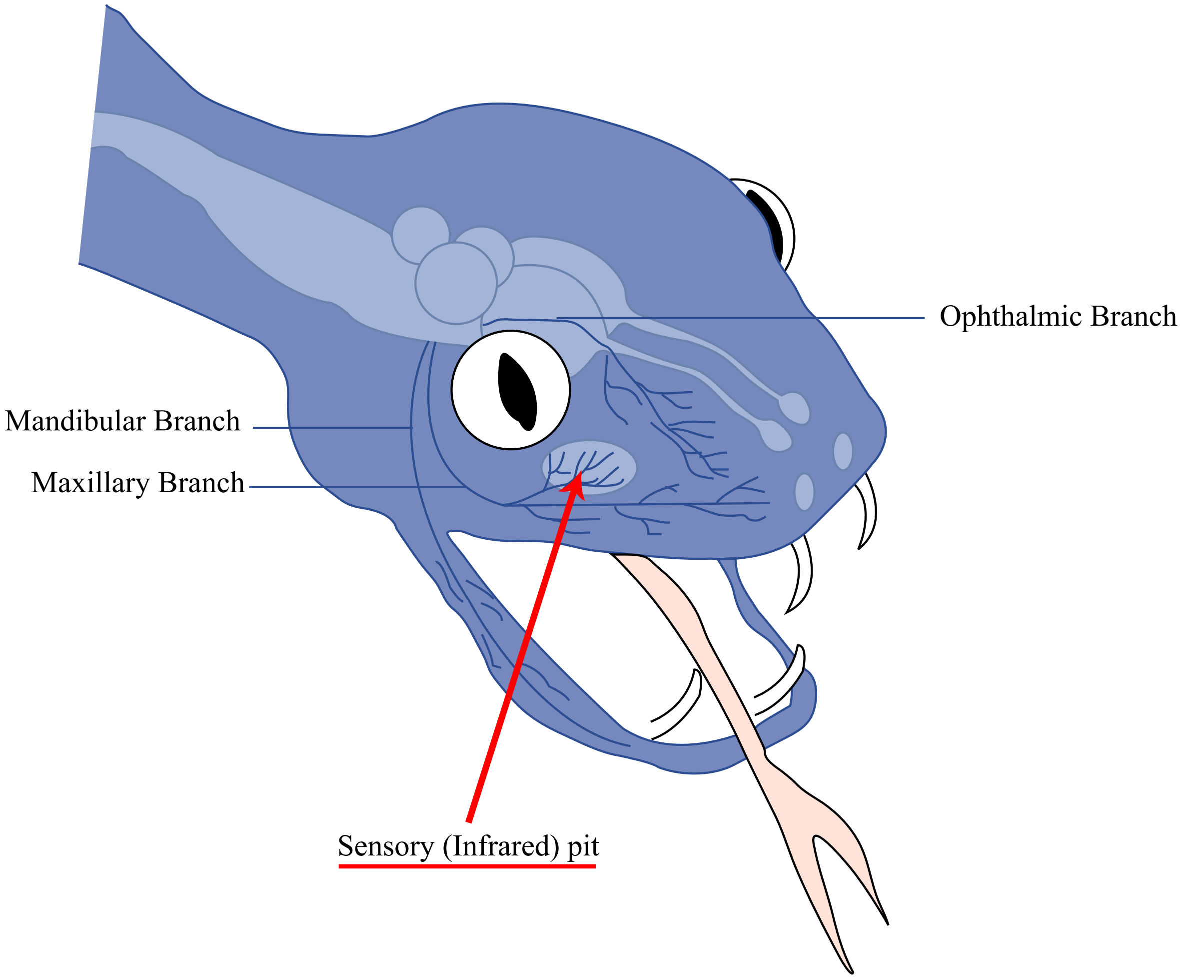


Figure by MIT OCW.

End class 9

The evolution of changes in brain involve both size and architectural details

- The trigeminal system of moles and rodents
  - Relative size of central maps and sensory acuity are correlated.
  - Organizational specializations: the barrel fields representing the vibrissae

Somatosensory representation in mole neocortex

Figure removed due to copyright reasons.
Please see:
Figure 22-12 from Zigmond, Michael J., et al., eds. *Fundamental Neuroscience.*
San Diego, CA: Academic Press, 1999, part III. ISBN: 0127808701. (Illustrations by Robert S. Woolley.)

Somatosensory representation in a mouse or rat, from whiskers to “barrels”

Figure removed due to copyright reasons.

Please see:

Figure 1 in Li, Y., R. S. Erzurumlu, C. Chen, S. Jhaveri, and S. Tonegawa. "Whisker-related Neuronal Patterns Fail to Develop in the Trigeminal Brainstem Nuclei of NMDAR1 Knockout Mice." *Cell* 76, no. 3 (February 11, 1994): 427-37.

P4 rat neocortex, coronal section, DiI in VB

Figure removed due to copyright reasons.

Please see:

Jhaveri, S., R. S. Erzurumlu, and K. Crossin. "Barrel construction in rodent neocortex: role of thalamic afferents versus extracellular matrix molecules." *Proc Natl Acad Sci USA* 88, no. 10 (May 15, 1991): 4489-93.

Similar case, tangential section

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Please see:

Jhaveri, S., R. S. Erzurumlu, and K. Crossin. "Barrel construction in rodent neocortex: role of thalamic afferents versus extracellular matrix molecules." *Proc Natl Acad Sci USA* 88, no. 10 (May 15, 1991): 4489-93.

P5 rat barrel fields, AChE stain, tangential section

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Please see:

Jhaveri, S., R. S. Erzurumlu, and K. Crossin. "Barrel construction in rodent neocortex: role of thalamic afferents versus extracellular matrix molecules." *Proc Natl Acad Sci USA* 88, no. 10 (May 15, 1991): 4489-93.

Rat barrel fields, Cytochrome C tangential section

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Please see:

Jhaveri, S., R. S. Erzurumlu, and K. Crossin. "Barrel construction in rodent neocortex: role of thalamic afferents versus extracellular matrix molecules." *Proc Natl Acad Sci USA* 88, no. 10 (May 15, 1991): 4489-93.

From whiskers to barrlettes to barreloids to barrels

Figure removed due to copyright reasons.

Please see:

Figure 1 in Li, Y., R. S. Erzurumlu, C. Chen, S. Jhaveri, and S. Tonegawa. "Whisker-related Neuronal Patterns Fail to Develop in the Trigeminal Brainstem Nuclei of NMDAR1 Knockout Mice." *Cell* 76, no. 3 (February 11, 1994): 427-37.

The evolution of changes in brain: Many examples of size increases and changes in architectural details within hindbrain systems

- Cerebellum of electric fish
- Cerebellum of mammals
- Somatosensory system of rodents
- Specializations of taste reception (7th, 9th, 10th n.)
  - Ray-finned fishes: vagal lobes and facial lobes of hindbrain, with specialized receptors for bottom feeding
- Lateral line receptor systems:
  - Electroreception
  - Mechanoreception

Large variations in size of specific brain parts are examples of "mosaic evolution" (Striedter, 2005, ch 5)

The changes cause "distortions" in the basic organization of the hindbrain

- **Variations in relative size of parts**
  - **Huge vagal lobe of the fresh-water buffalofish** [Review]
  - **Vagal and facial lobes of the catfish** [Review]
  - Electric fish have an enormous and specialized cerebellum. [Review]
  - The cerebellum is very large in mammals, especially in humans.
- Cell migrations from the alar plate:
  - Cerebellum
  - Pre-cerebellar cell groups – especially the cells of the pons

Illustrations from C.J. Herrick

- Brain of a freshwater buffalo fish:
  - Huge "vagal lobe."
- Brain of a catfish:
  - “Facial lobe" and "vagal lobe".
- Catfish 7th cranial nerve distribution, re:
  - Taste senses (explains facial lobe)

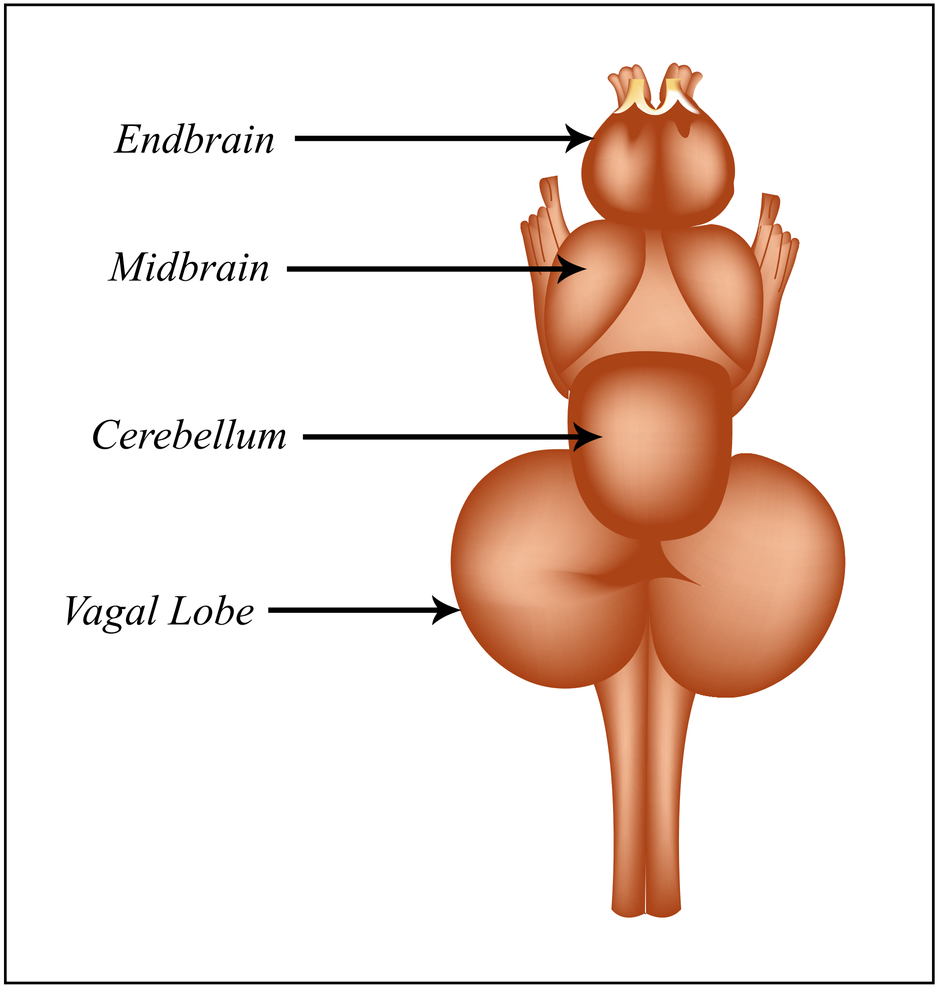


Figure by MIT OCW.

Carpiodes tumidus (buffalofish) has a specialized palatal organ for filtering the water for food; it is innervated by the vagus nerve.

Pilodictis olivaris (catfish)

has taste receptors all over its body innervated by the facial nerve (7th cranial nerve)

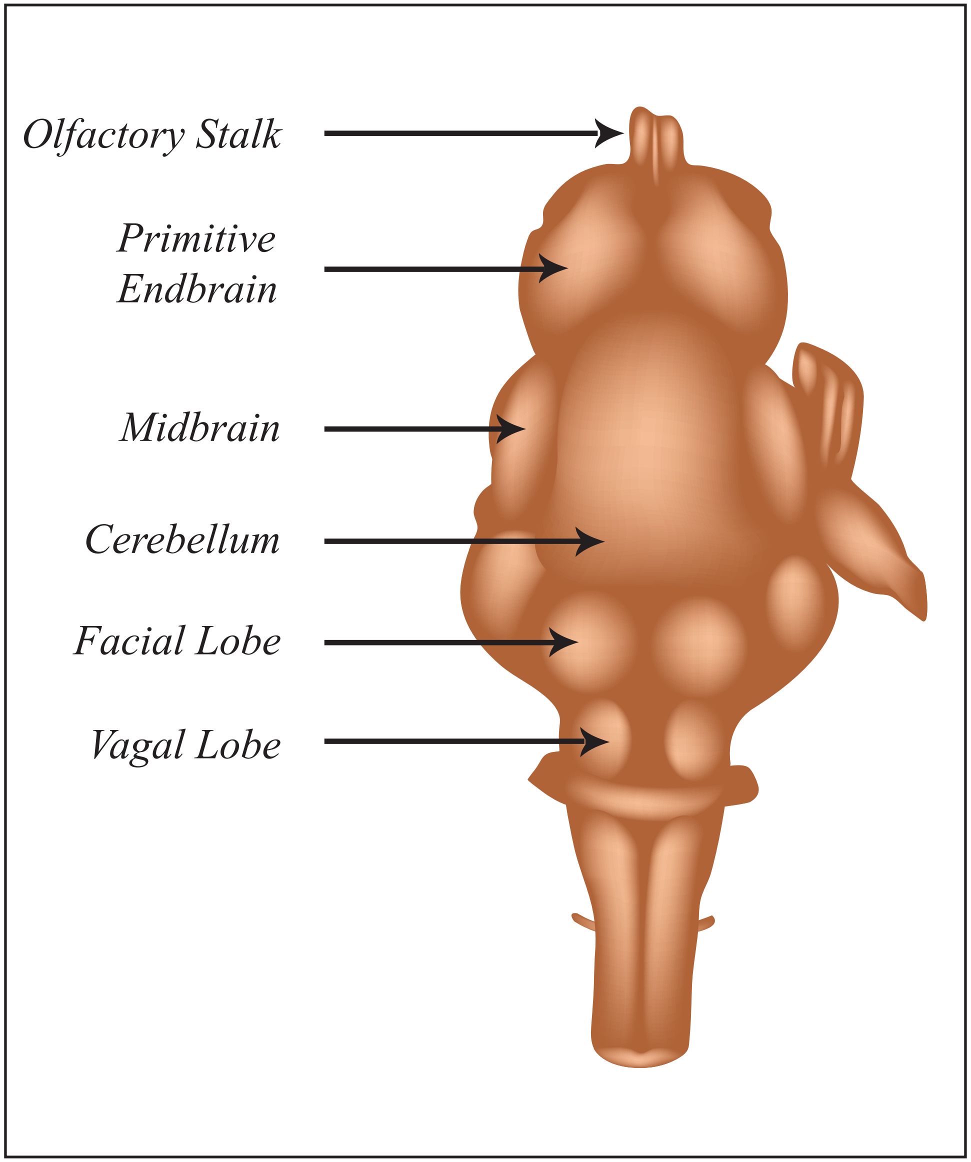
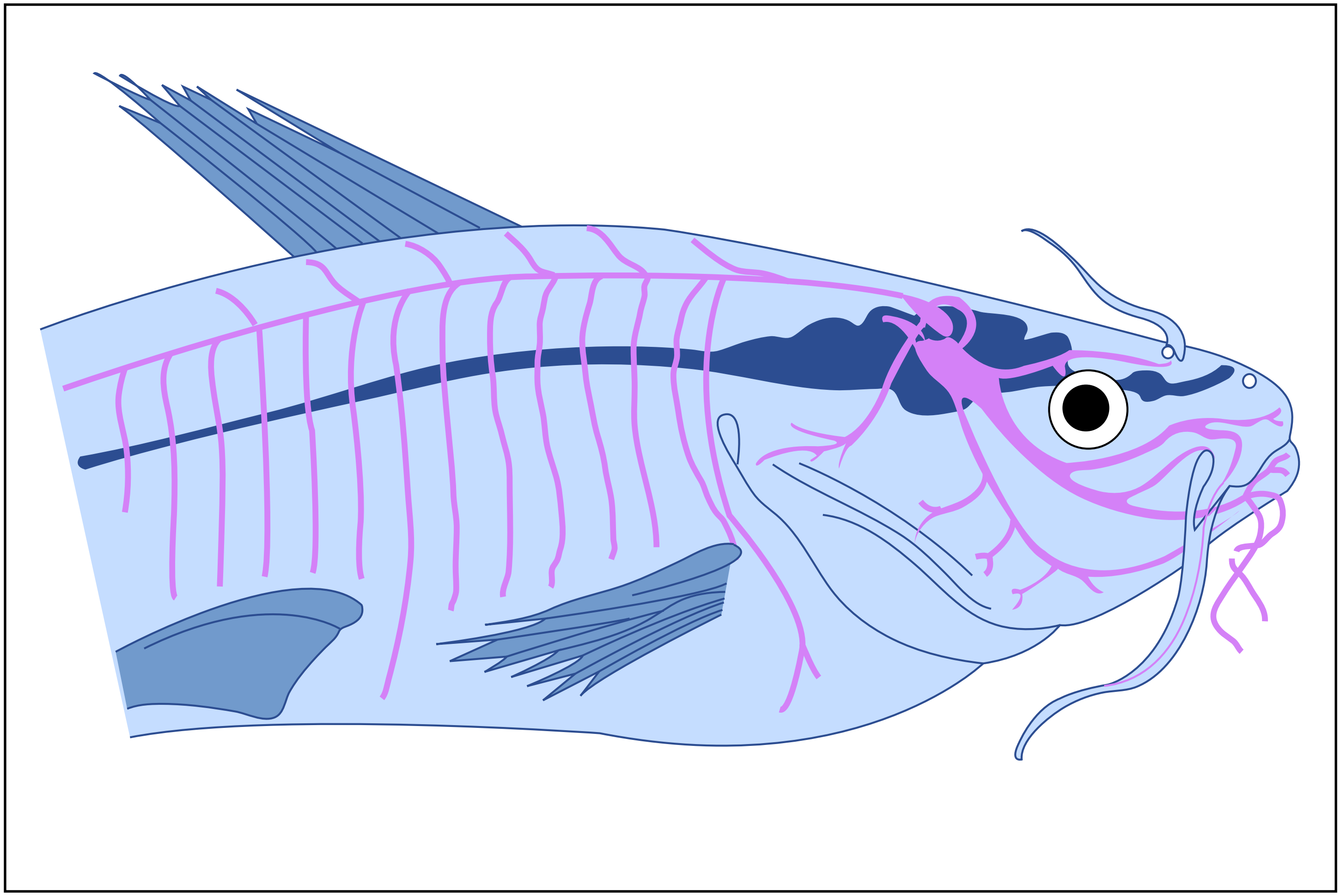


Figure by MIT OCW.

Amiurus melas (the small catfish): 7th cranial nerve (facial nerve) innervating taste buds in skin of entire body



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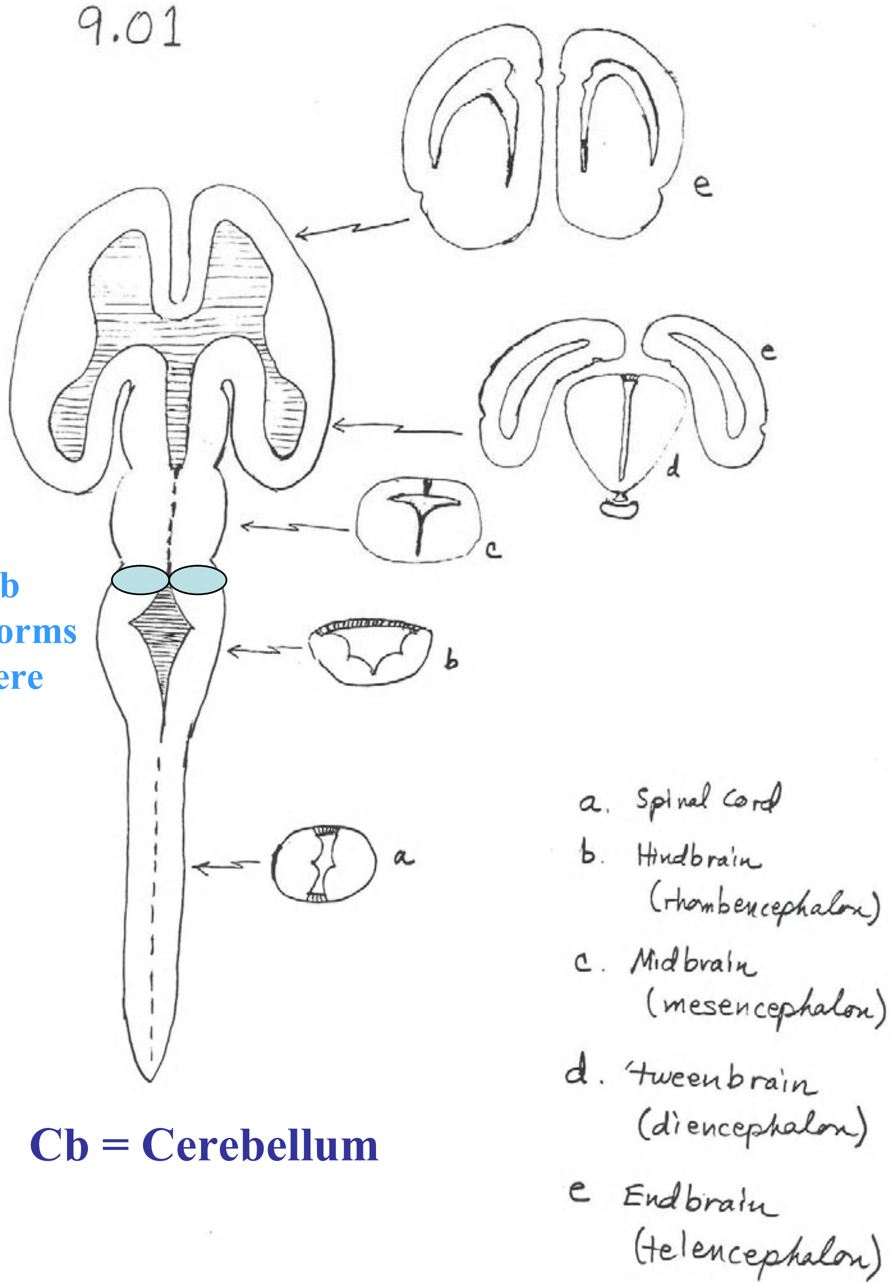
The "distortions" in the basic organization of the hindbrain, continued

- Variations in relative size of parts
  - Huge vagal lobe of the fresh-water buffalofish
  - Vagal and facial lobes of the catfish
  - **Electric fish have an enormous and specialized cerebellum.**
  - **The cerebellum is very large in mammals, especially in humans.**
- **Cell migrations from the alar plate cause major distortions in large mammals**
  - **Migration into the cerebellum**
  - **Migration to pre-cerebellar cell groups – especially the cells of the pons**

Location of the late-developing Cerebellum, in the rostral hindbrain



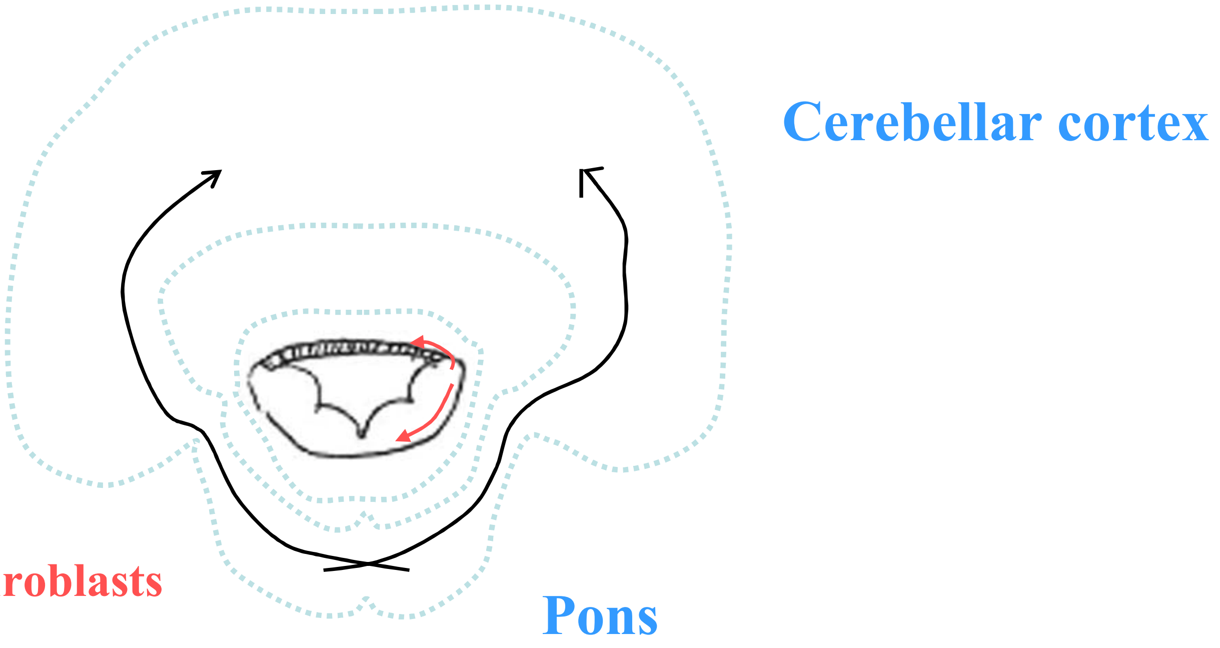
Cb Forms here

Cb = Cerebellum

Specimen slide removed due to copyright reasons.

Human
rostral hindbrain,
with *pons* and
cerebellum →
a quantitative
“distortion” of the
basic plan

Growth of cerebellum and pons in rostral hindbrain, by migration of neuroblasts from the rhombic lip



Red arrows:
  migration of neuroblasts

Black arrows:
  course of axons from
  pontine gray to Cb cortex

Selected References

Slide 7: Wolpert, Lewis, et al. *Principles of Development*. 2nd ed. Oxford, UK: Oxford University Press, 2002, fig. 4.24. ISBN: 0198792913.

Slide 17: Nauta, Walle J. H., and Michael Feirtag. *Fundamental Neuroanatomy*. New York, NY: Freeman, 1986, fig. 71. ISBN: 0716717239.

Slide 23: Nauta, Walle J. H., and Michael Feirtag. *Fundamental Neuroanatomy*. New York, NY: Freeman, 1986. ISBN: 0716717239.

Slide 35: Butler, Ann B., and William Hodos. *Comparative Vertebrate Neuroanatomy: Evolution and Adaptation*. New York, NY: Wiley-Liss, 1996. ISBN: 0471888893.