Lecture - Neural Development

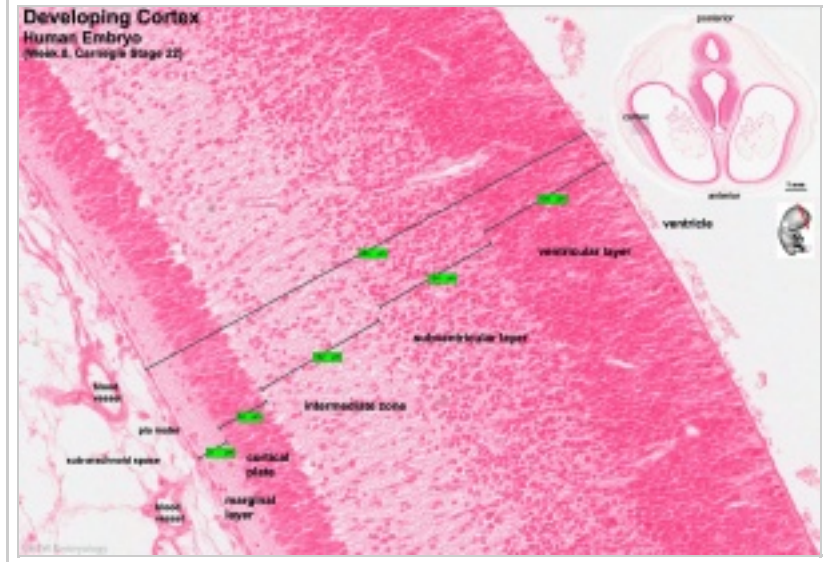
From Embryology

Contents

Introduction

1. Understand early neural development.
2. Understand the formation of the brain; grey and white matter from the neural tube.
3. Understand the formation of spinal cord.
4. Understand the role of migration of neurons during neural development.

- Detailed structure of the adult nervous system is provided in other Anatomy courses.
- History - Santiago Ramón y Cajal



Cerebrum development human embryo (week 8, Stage 22)

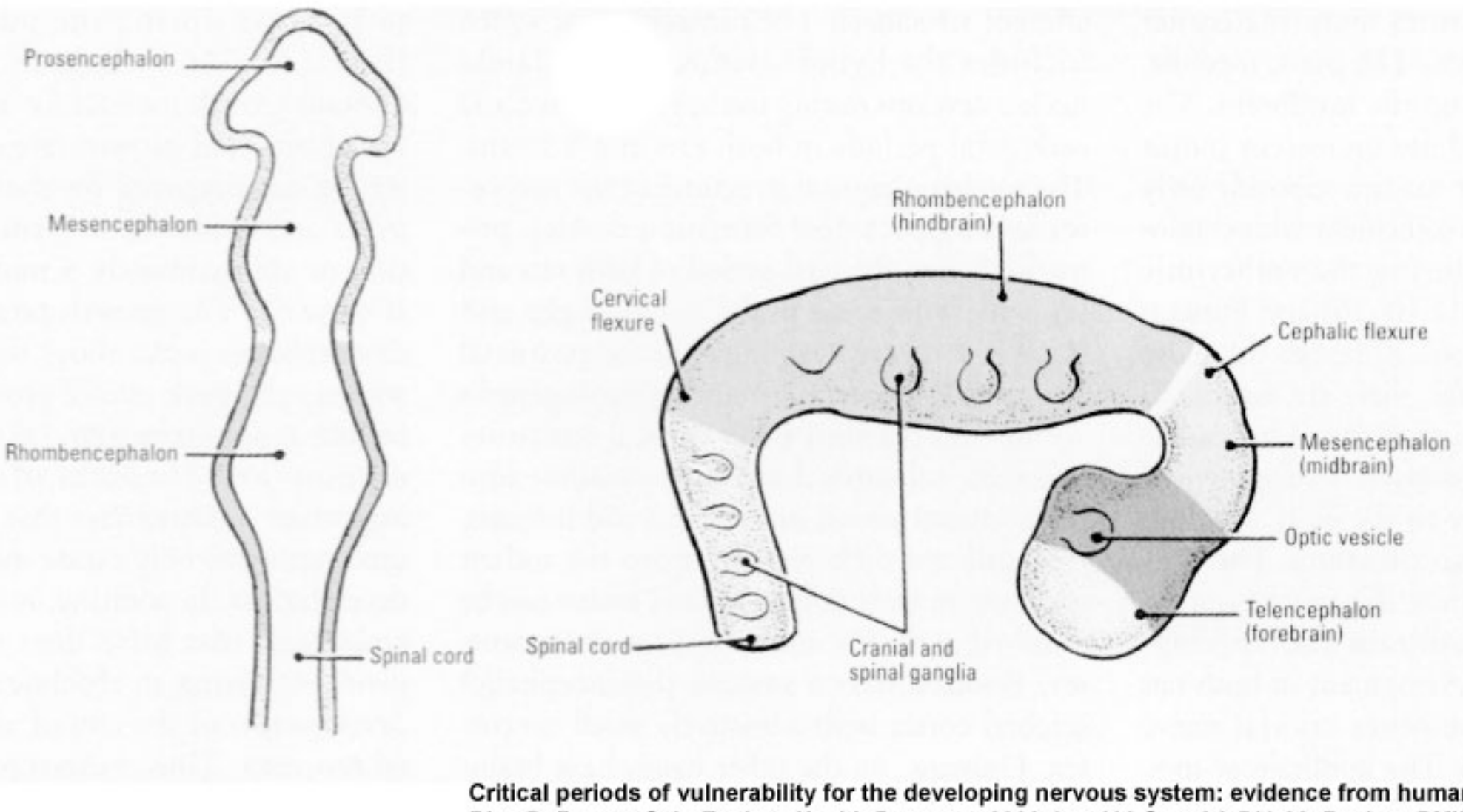
Lecture Resources

Movies[Expand]

References [Collapse]	
Hill, M.A. (2015). *UNSW Embryology* (15th ed.) Retrieved October 12, 2015, from https://embryology.med.unsw.edu.au	**Neural Links**: Introduction | Ventricular System | Stage 22 | Gliogenesis | Fetal | Lecture - Early Neural | Lecture - Neural Crest | Lab - Early Neural | Neural Crest | Sensory | Abnormalities | Folic Acid | Iodine Deficiency | Fetal Alcohol Syndrome | Postnatal | Postnatal - Neural Examination | Histology | Historic Neural | Category:Neural **Neural Parts**: Introduction | Prosencephalon | Telencephalon | Amygdala | Hippocampus | Basal Ganglia | lateral ventricles | Diencephalon | Epithalamus | Thalamus | Hypothalamus | Pituitary | Pineal | third ventricle | Mesencephalon | Mesencephalon | Tectum | cerebral aqueduct | Rhombencephalon | Metencephalon | Pons | Cerebellum | Myelencephalon | Medulla Oblongata | Spinal Cord | Vascular | Meninges | Category:Neural Archive: 2014 (https://embryology.med.unsw.edu.au/embryology/index.php?title=Lecture_-_Neural_Development&oldid=172709) | 2014 Lecture 19 PDF
Moore, K.L., Persaud, T.V.N. & Torchia, M.G. (2011). *The developing human: clinically oriented embryology* (9th ed.). Philadelphia: Saunders.	The following chapter links only work with a UNSW connection. ▪ Chapter 5 - Fourth to Eighth Weeks of Human Development (http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=93) ▪ Chapter 6 - Ninth Week to Birth: The Fetal Period (http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=115) ▪ Chapter 17 - Nervous System (http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=411)
Schoenwolf, G.C., Bleyl, S.B., Brauer, P.R. & Francis-West, P.H. (2009). *Larsen's human embryology* (4th ed.). New York; Edinburgh: Churchill Livingstone.	UNSW students have full access to this textbook edition through UNSW Library subscription (http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/FullRecord.aspx?p=2074524) (with student Zpass log-in). ▪ Chapter 4 - Fourth Week: Forming the Embryo ▪ Chapter 9 - Development of the Central Nervous System ▪ Chapter 10 - Development of the Peripheral Nervous System

Early Brain Structure

Primary Vesicles



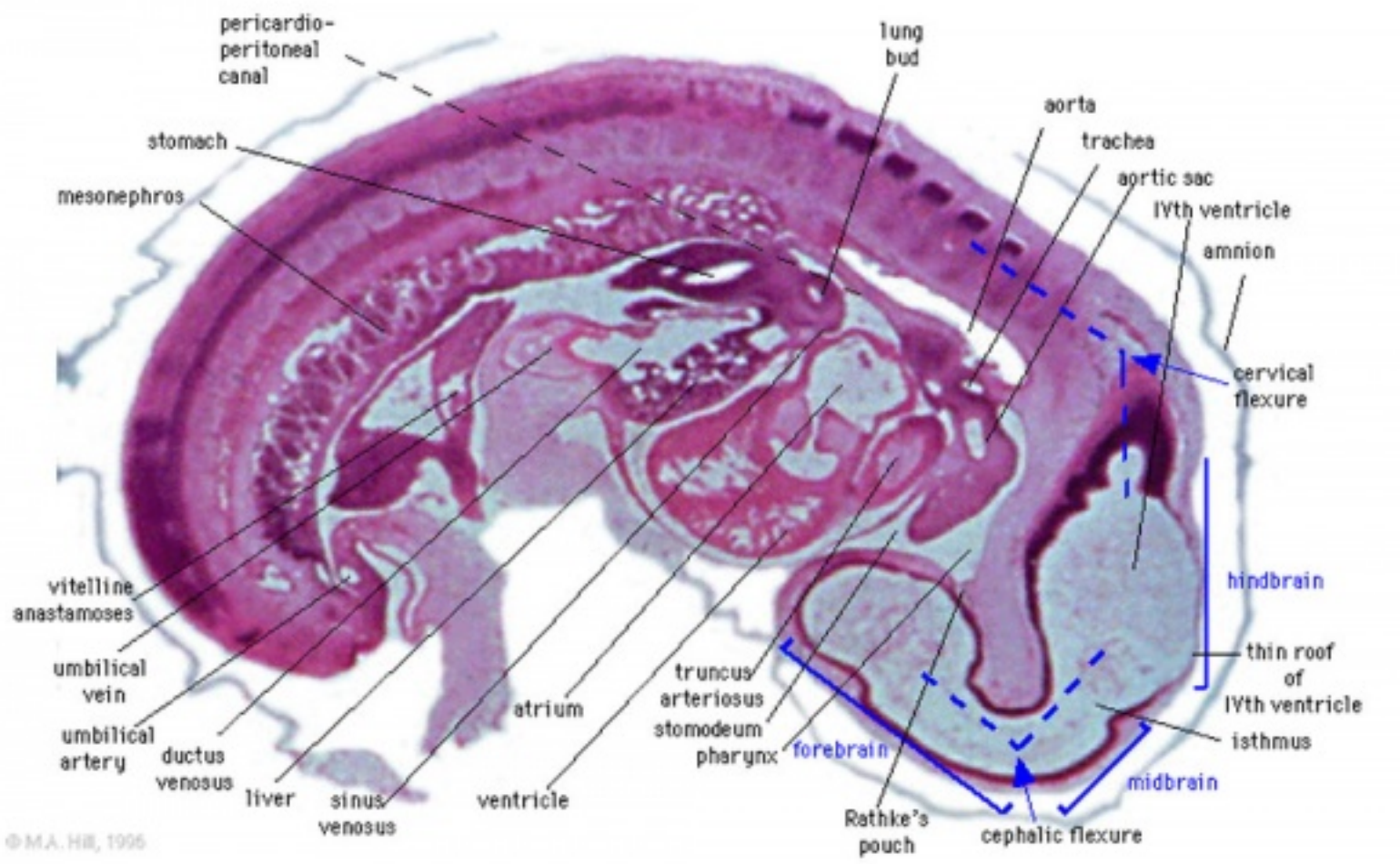
Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Rice D, Barone S Jr. Environ Health Perspect. 2000 Jun;108 Suppl 3:511-33. Review. PMID: 10852851

- rostral neural tube forms 3 primary brain vesicles (week 4)
- 3 primary vesicles: **prosencephalon** (forebrain), **mesencephalon** (midbrain), **rhombencephalon** (hindbrain)

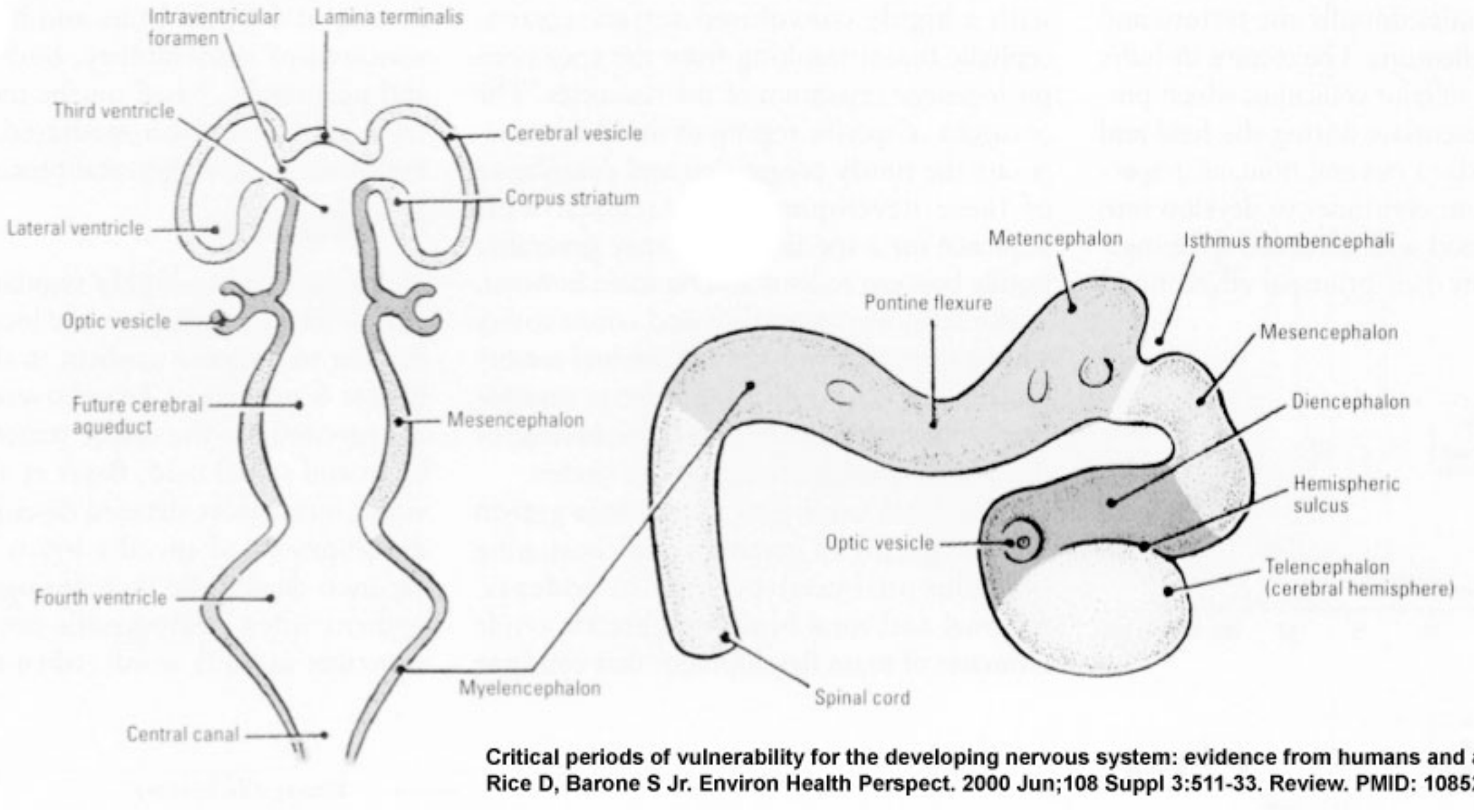
Brain Flexures

Rapid growth folds the neural tube forming 3 brain flexures

- **cephalic flexure** - pushes mesencephalon upwards
- **cervical flexure** - between brain stem and spinal cord
- **pontine flexure** - generates 4th ventricle



Secondary Vesicles



Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models.
Rice D, Barone S Jr. Environ Health Perspect. 2000 Jun;108 Suppl 3:511-33. Review. PMID: 10852851

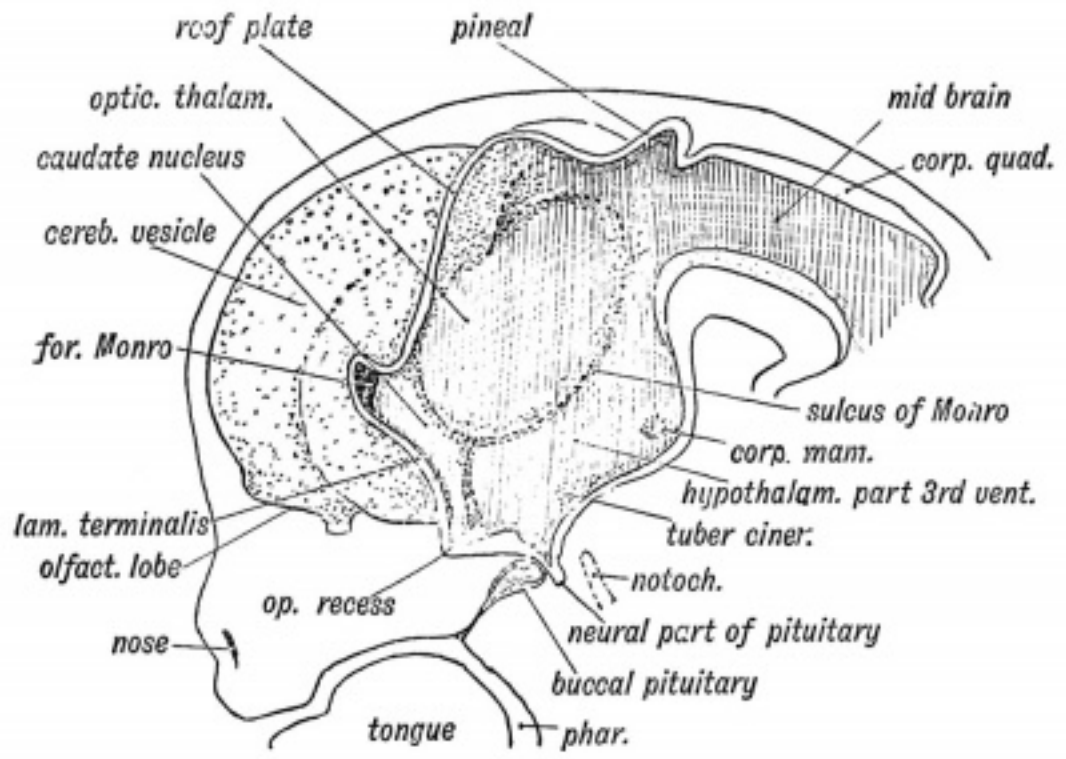
From the 3 primary vesicles developing to form 5 secondary vesicles

- prosencephalon- **telencephalon** (endbrain, forms cerebral hemispheres), **diencephalon** (betweenbrain, forms optic outgrowth)
- **mesencephalon**
- rhombencephalon- **metencephalon** (behindbrain), **myelencephalon** (medullabrain)

Carnegie stage 13 Embryo showing neural tube and brain flexures.

Neural Tube	Primary Vesicles	Secondary Vesicles	Adult Structures
	Prosencephalon	Telencephalon	Rhinencephalon, Amygdala, Hippocampus, Cerebrum (Cortex), Basal Ganglia, lateral ventricles
		Diencephalon	Epithalamus, Thalamus, Hypothalamus, Subthalamus, Pituitary, Pineal,

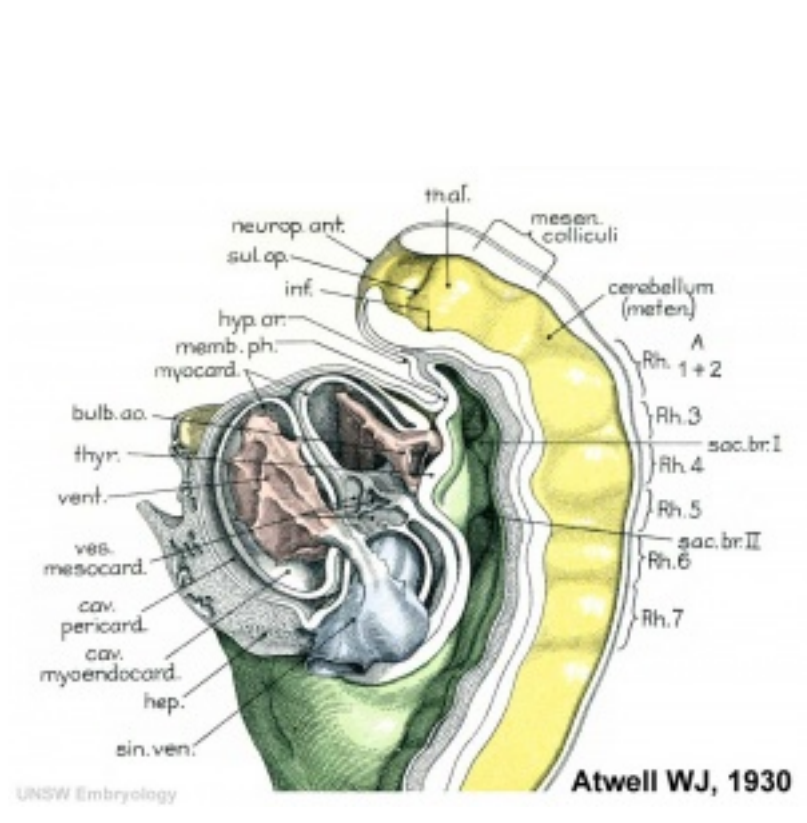
Brain			third ventricle
	Mesencephalon	Mesencephalon	Tectum, Cerebral peduncle, Pretectum, cerebral aqueduct
	Rhombencephalon	Metencephalon	Pons, Cerebellum
		Myelencephalon	Medulla Oblongata
Spinal Cord			



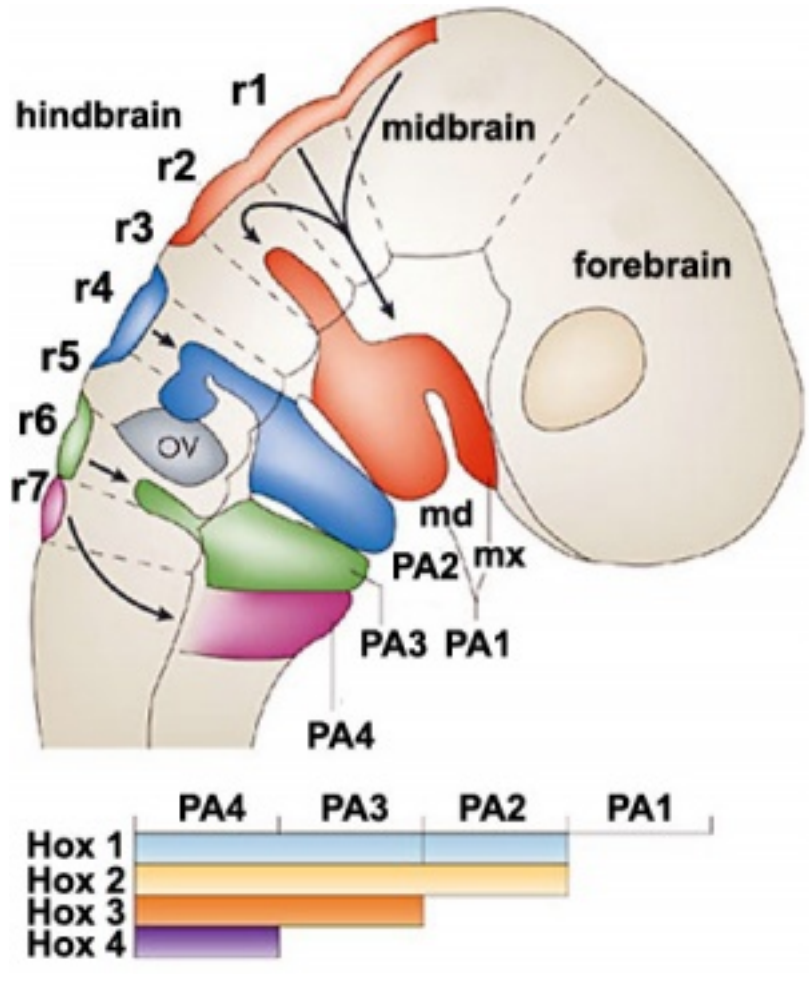
Historic figure showing the parts derived from the walls of the fore-brain. (After Wilhelm His (1831-1904))

Rhombomeres

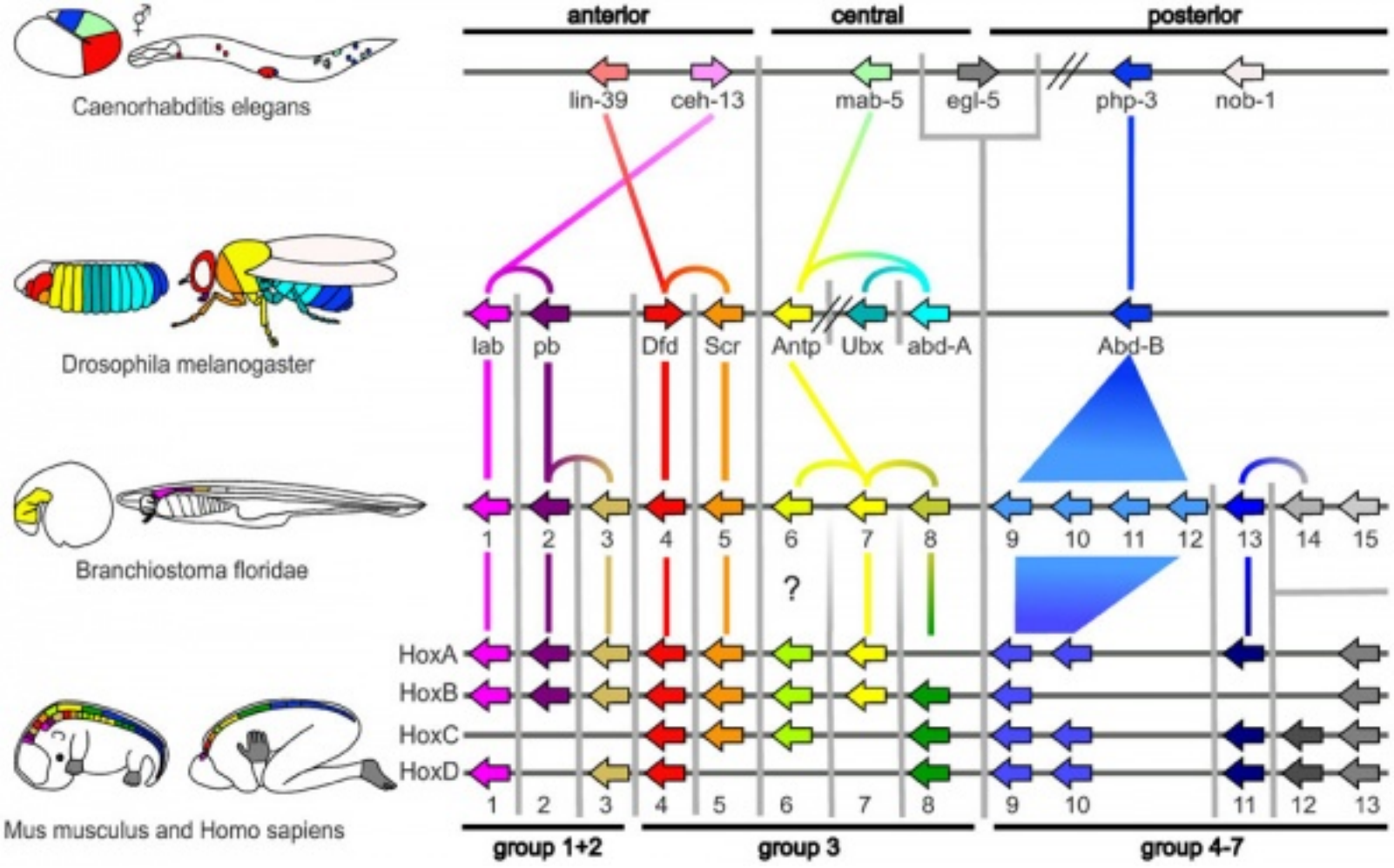
- Hindbrain - Rhombomeres represent the crania-caudal segmentation of the neural tube at the levee lot the hindbrain.
- Historic - Identified morphologically as identifiable regions.
- Modern - Represent the different expression levels of Hox genes and levels of neural crest migration.



Historic image of embryonic rhombomeres



Hindbrain neural crest migration

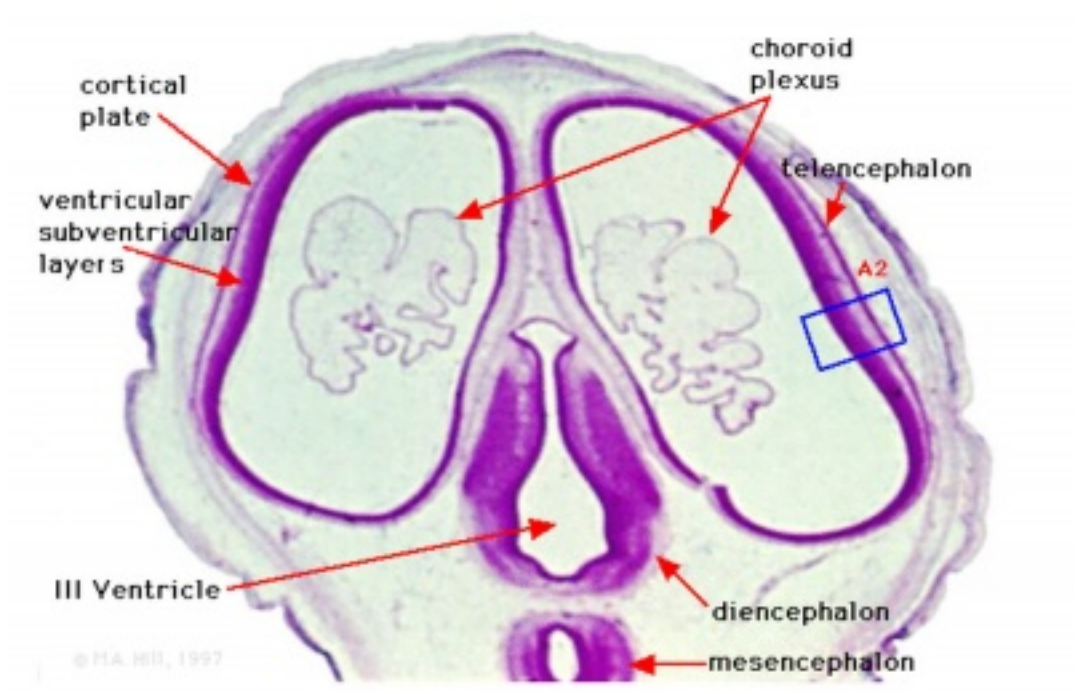


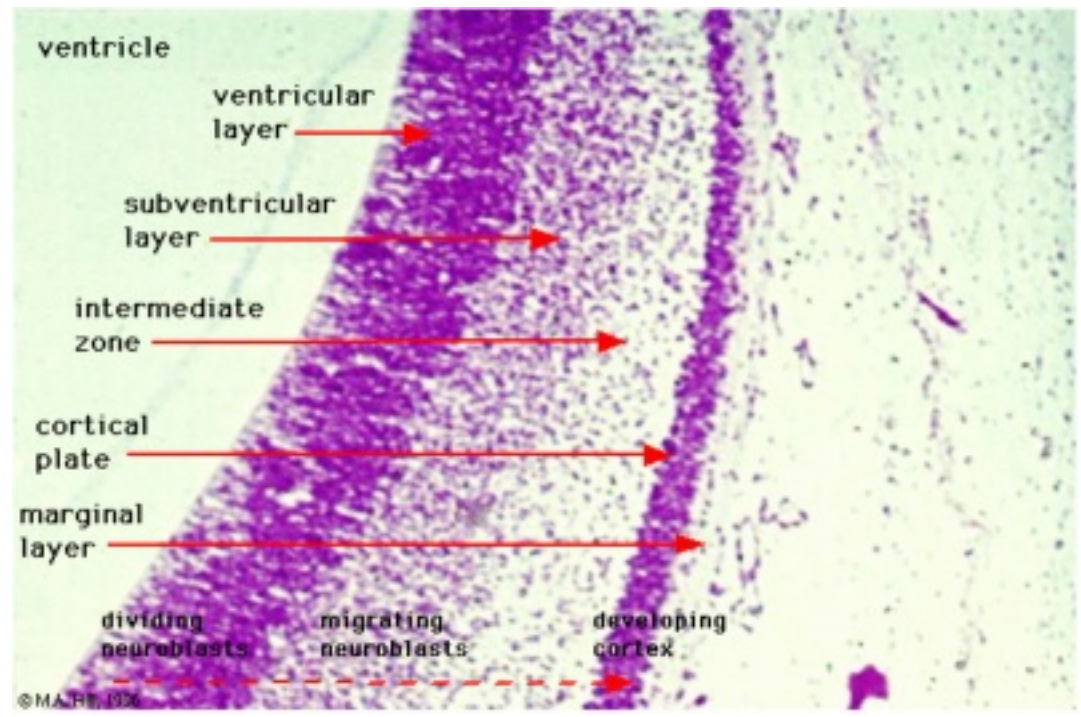
Hox-proteins crania-caudal expression (species comparison)

Neural Layers

- **Ventricular Germinal Zone** (VGZ) - mitosis at the ventricular luminal surface, produces early-generated macroneurons
- **Subventricular Zone** (SVZ) - mitosis away from the ventricular surface, produces later-generated microneurons and glia

Brain



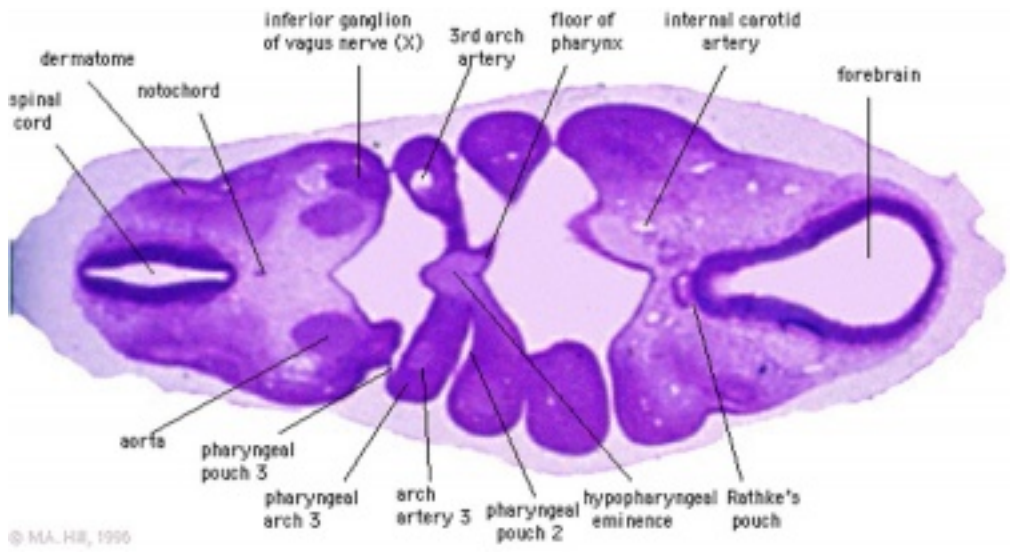


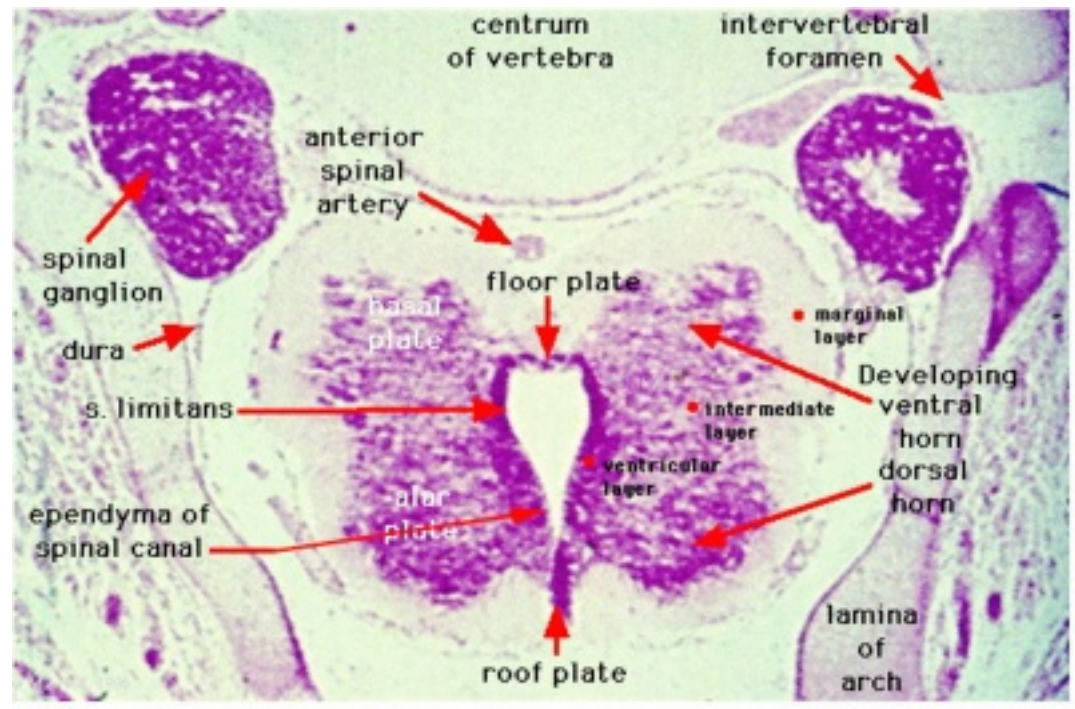
Human Embryo developing head cross section (Week 8, Stage 22) Detail of developing cortex (shown in blue box)

- Neural progenitor cells migrate from the ventricular layer along **radial glia**.
- Cortex layers develops inside (first) outside (last)
- Glial progenitor cells develop later from the same ventricular stem cells.

Spinal Cord

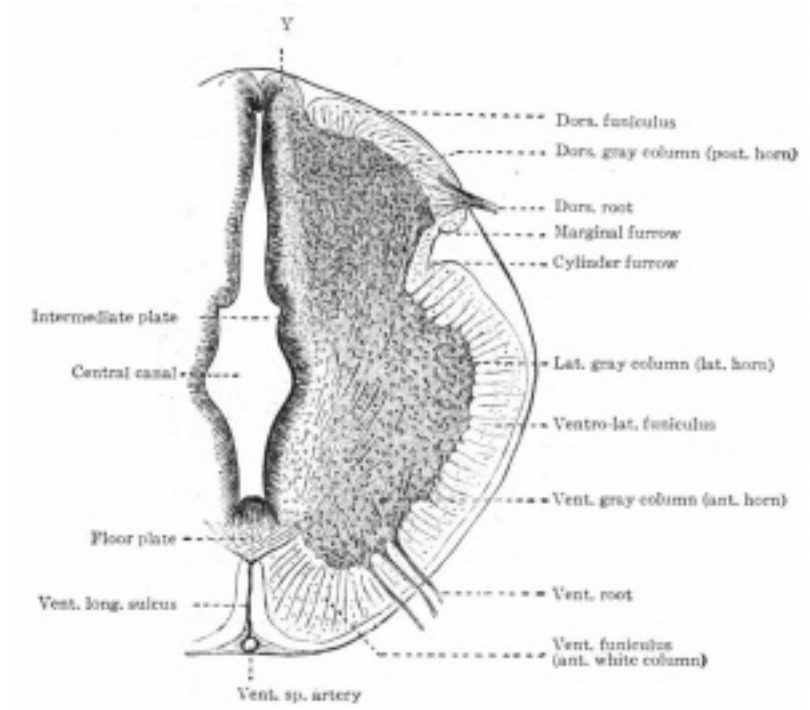
- Similar processes to those described for brain.
- Remember notochord ventral patterning by SHH and dorsal ectoderm (dorsalisation).
- Identify the different regions within the neural tube (floor plate, basal plate, alar plate, roof plate)



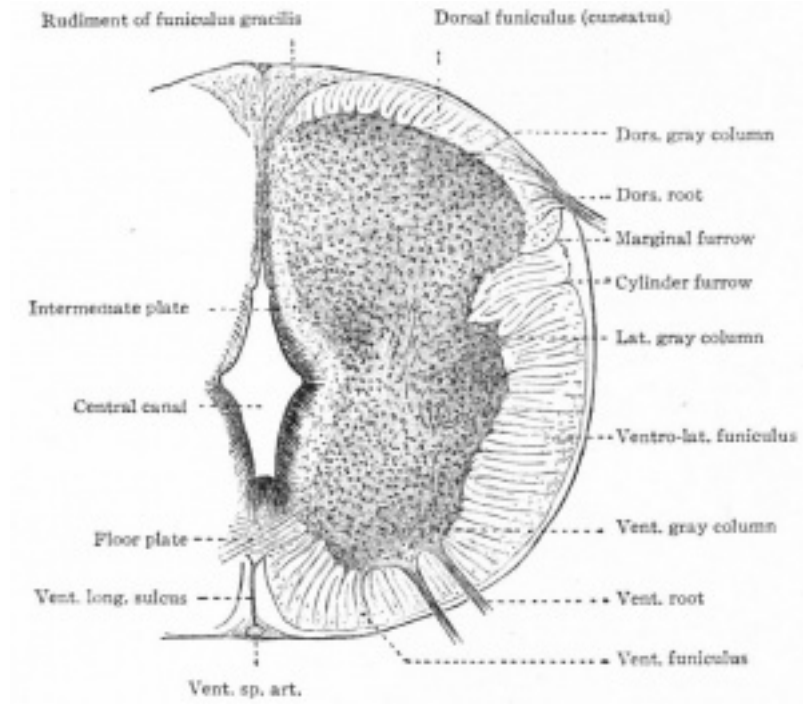


Stage 13 Stage 22

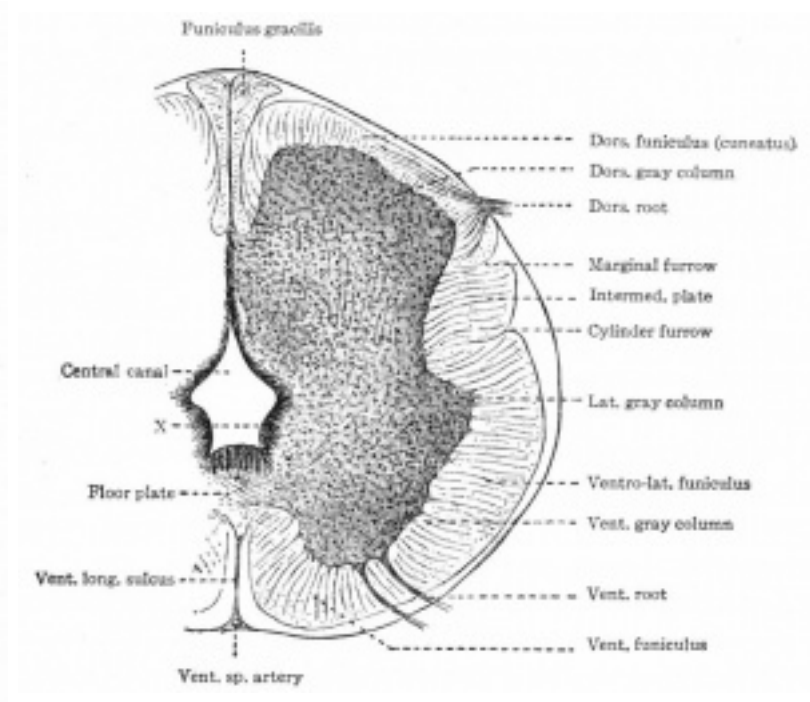
Half of a transverse section of the spinal cord



Human embryo of 18.5 mm (7.5 weeks).



Human embryo of 24 mm (8.5 weeks).



Human fetus of about 3 months.

Wilhelm His (1831-1904)

Ventricular Development

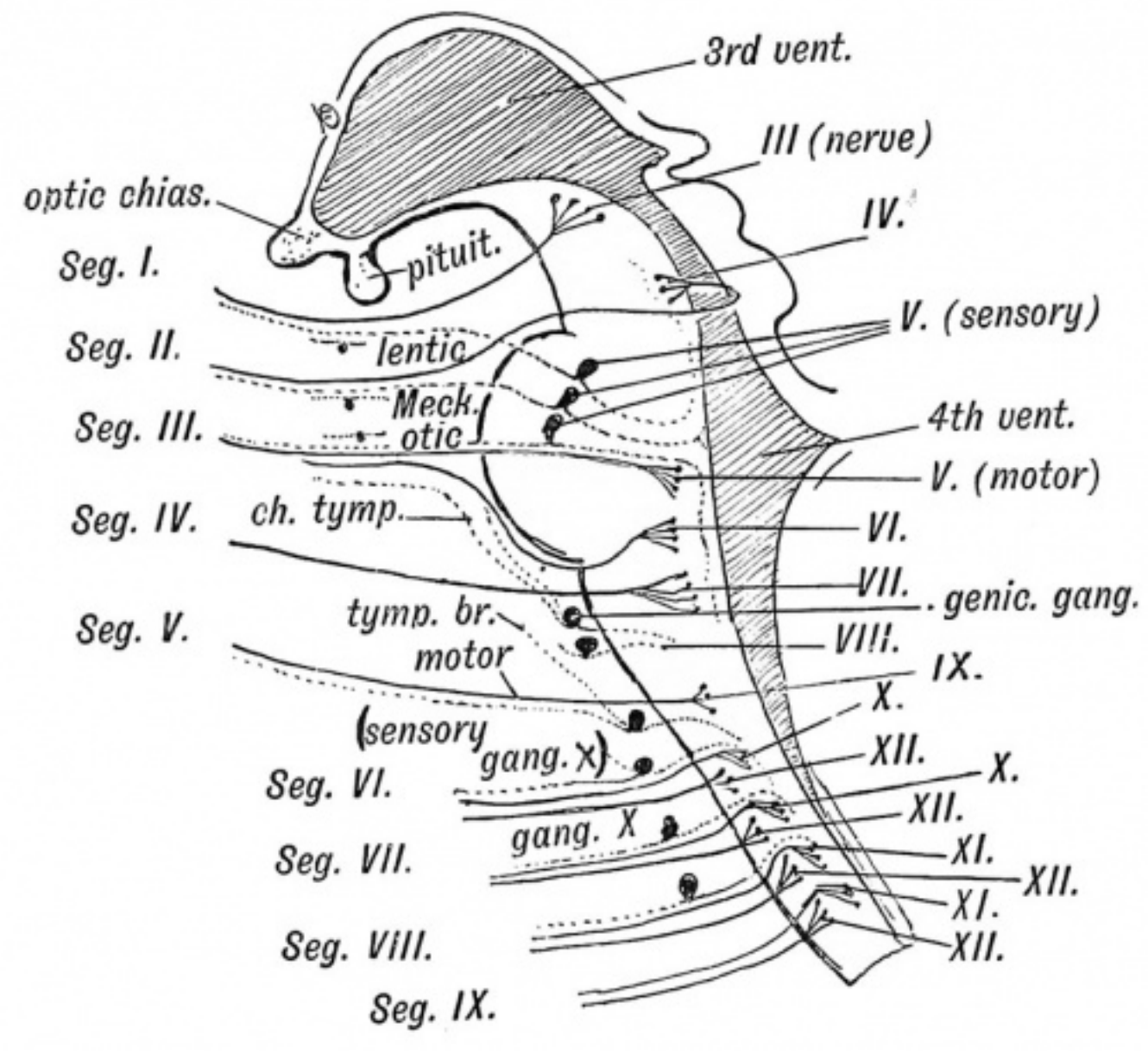
- The ventricular system develops from the single cavity formed from the hollow neural tube.
- This fluid-filled space is separated from the amnion following fusion of the neural tube and closure of neuropores.
- At different regions sites within the wall (**floor of lateral ventricle** and **roof of the third and fourth ventricles**) differentiate to form **choroid plexus** a modified vascular structure which will produce Cerebrospinal fluid (CSF)
- **choroid plexus** is a modified vascular structure which will produce Cerebrospinal fluid (CSF)

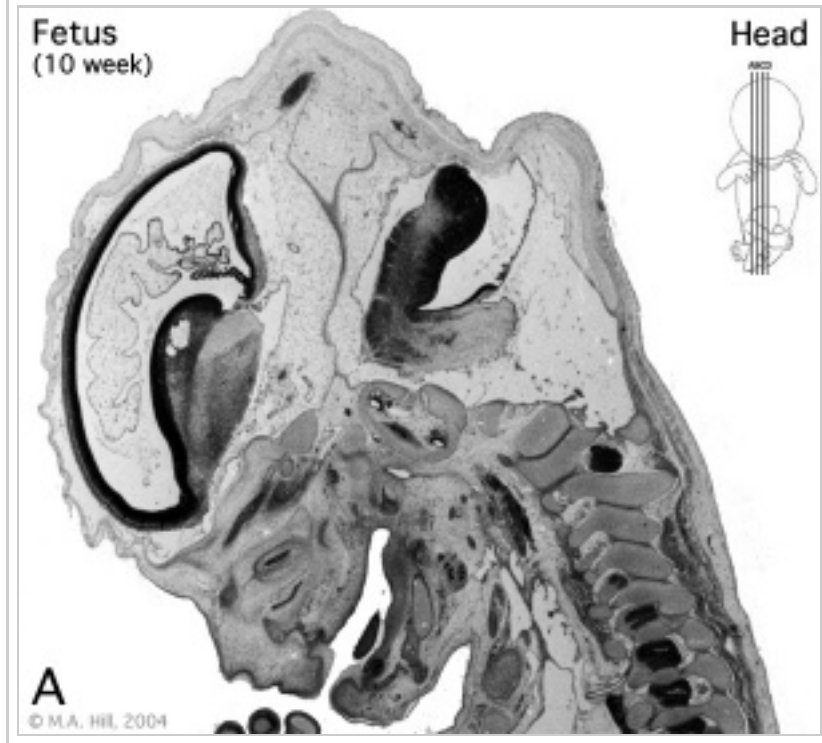
(FYI - you do not need to know detailed stage development)

Human Ventricular Development Timeline[Expand]

Human Embryo (week 8, Stage 22) ventricular system

Cranial Nerves

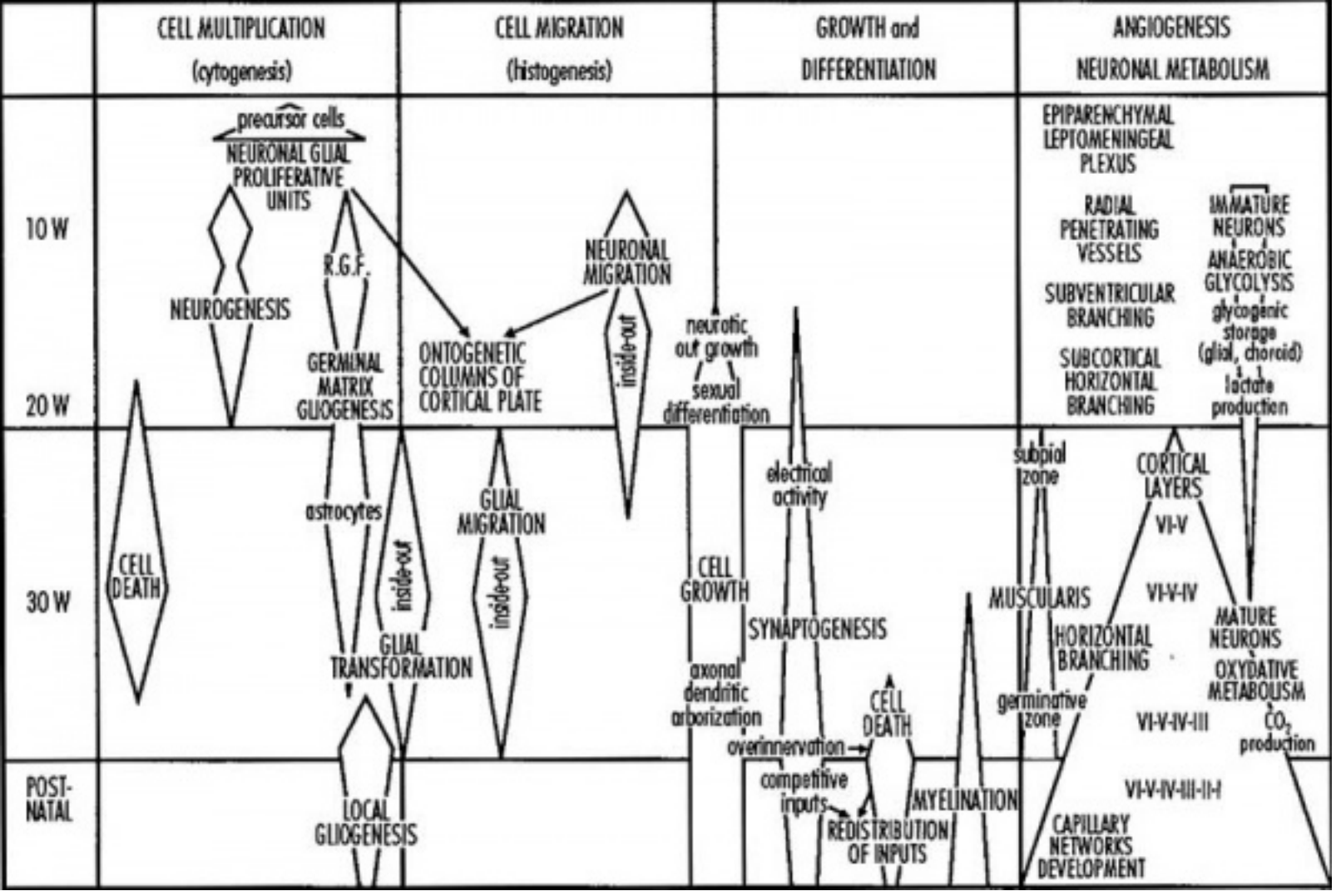




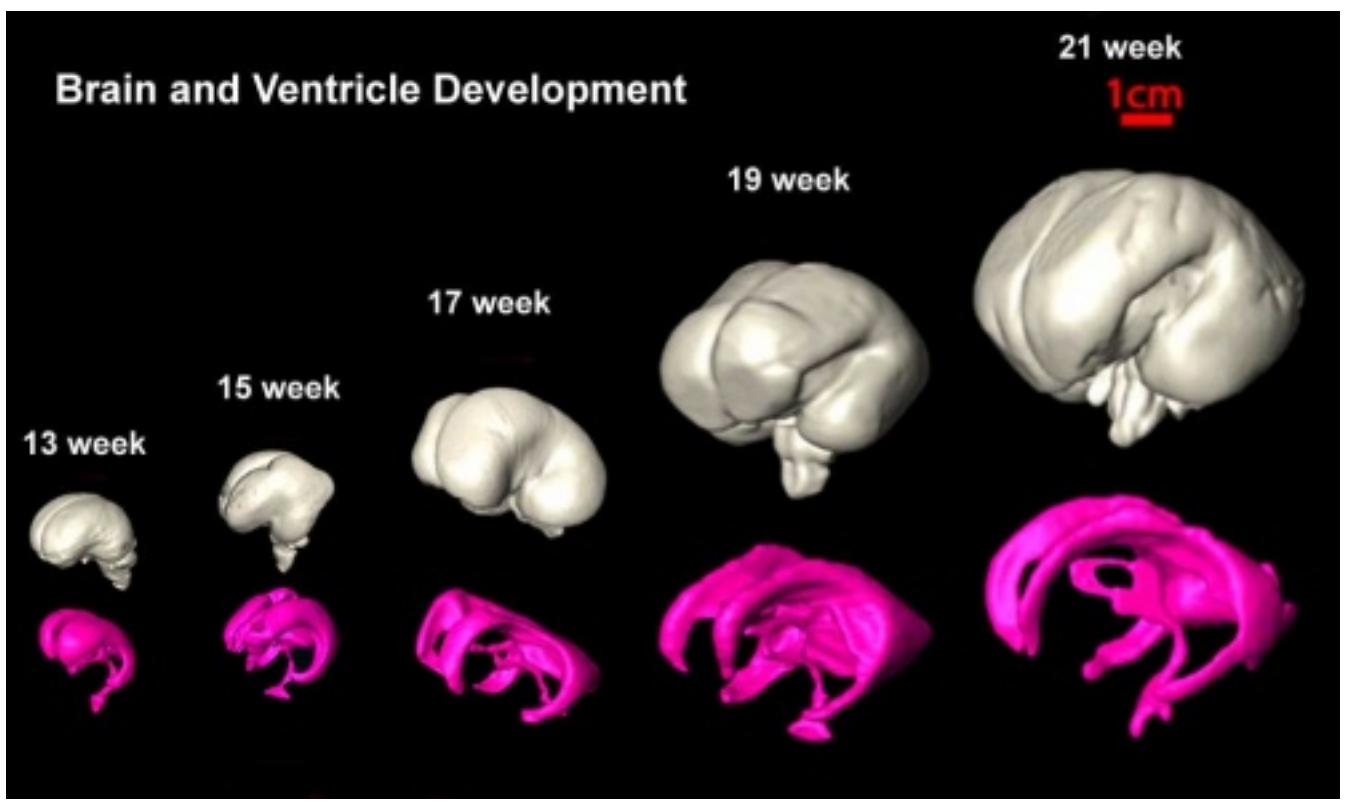
Human Fetus (week 10) showing choroid plexus and early ventricular system

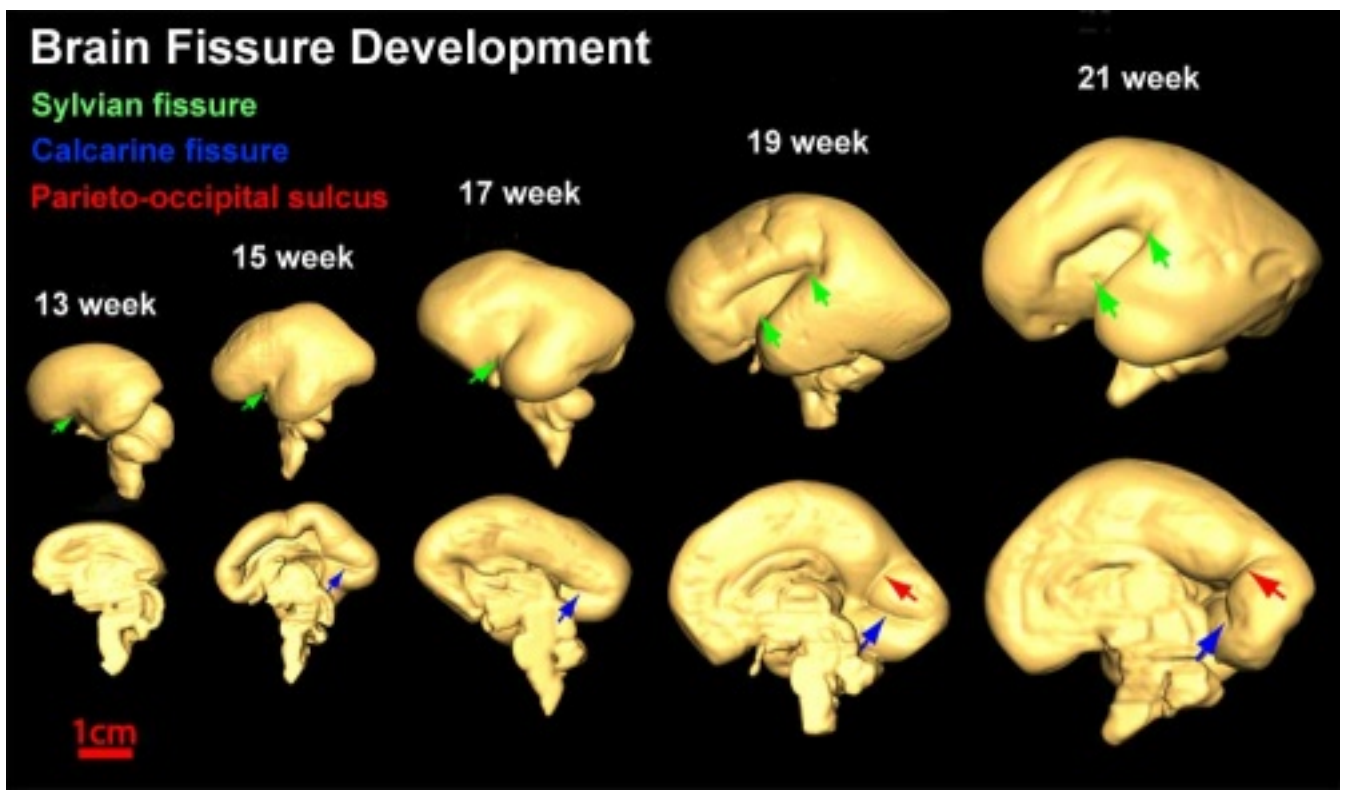
Historic diagram showing the relationship of the Cranial Nerves to the Primitive Segments of the Head.

Fetal Neural



Timeline of events in Human Neural Development





During the fetal period there is ongoing growth in size, weight and surface area of the brain and spinal cord. Microscopically there is ongoing: cell migration, extension of processes, cell death and glial cell development.

Cortical maturation (sulcation and gyration) and vascularization of the lateral surface of the brain starts with the insular cortex (insula, insulary cortex or insular lobe) region during the fetal period. This cerebral cortex region in the adult brain lies deep within the lateral sulcus between the temporal lobe and the parietal lobe.

- **sulcation** - The process of brain growth in the second to third trimester which forms sulci, grooves or folds visible on fetal brain surface as gyri grow (gyration). Abnormalities of these processes can lead to a smooth brain (lissencephaly).
- **gyration** - The development of surface folds on the brain (singular, gyrus)

Insular Gyral and Sulcal Development

- 13-17 gestational weeks - appearance of the first sulcus
- 18-19 gestational weeks - development of the periinsular sulci
- 20-22 gestational weeks - central sulci and opercularization of the insula
- 24-26 gestational weeks - covering of the posterior insula
- 27-28 gestational weeks - closure of the laeteral sulcus (Sylvian fissure or lateral fissure)

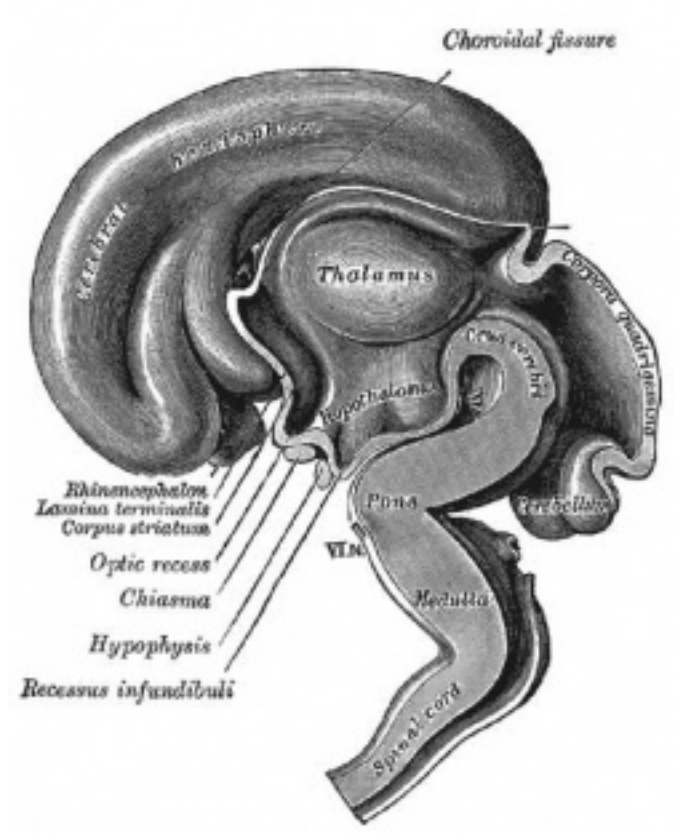
(Data from[2])

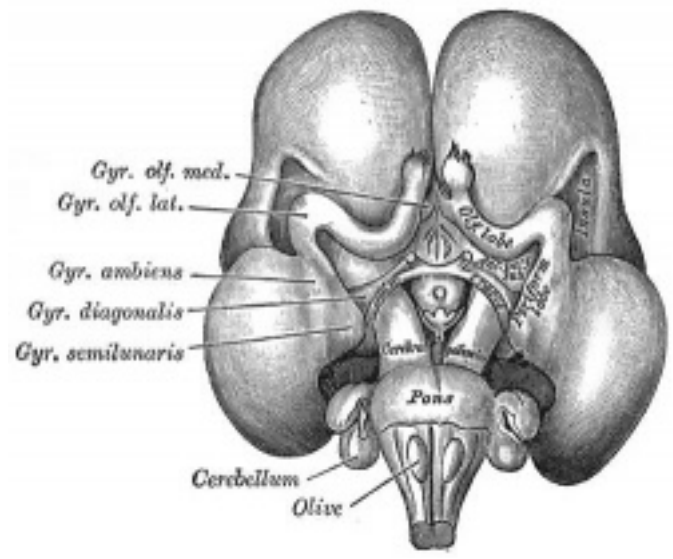
- Between 29-41 weeks volumes of: total brain, cerebral gray matter, unmyelinated white matter, myelinated, and cerebrospinal fluid (from MRI)
  - grey matter- mainly neuronal cell bodies; white matter- mainly neural processes and glia.
- total brain tissue volume increased linearly over this period at a rate of 22 ml/week.
- Total grey matter also showed a linear increase in relative intracranial volume of approximately 1.4% or 15 ml/week.
- The rapid increase in total grey matter is mainly due to a fourfold increase in cortical grey matter.
- Quantification of extracerebral and intraventricular CSF was found to change only minimally.

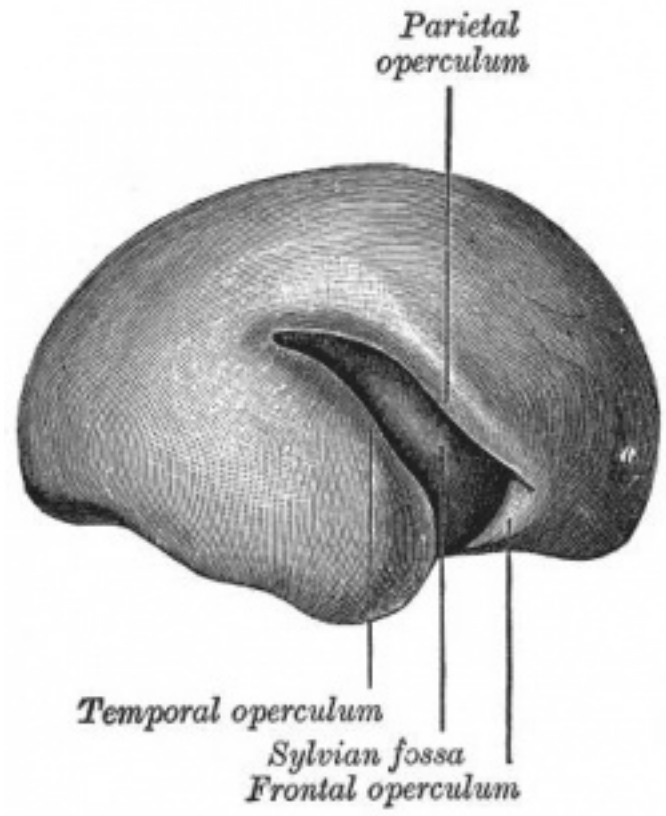
(Text - modified from [3])

Neural development will continue after birth with substantial glial development, growth, death and reorganization occuring during the

postnatally.







Human brain at three months (median sagittal section) Human brain at four months (inferior surface) Human brain at five months (outer surface)

Links: Neural System - Fetal | Neuroscience - Regional specification of the developing brain (http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=neurosci&part=A1465&rendertype=figure&id=A1466)

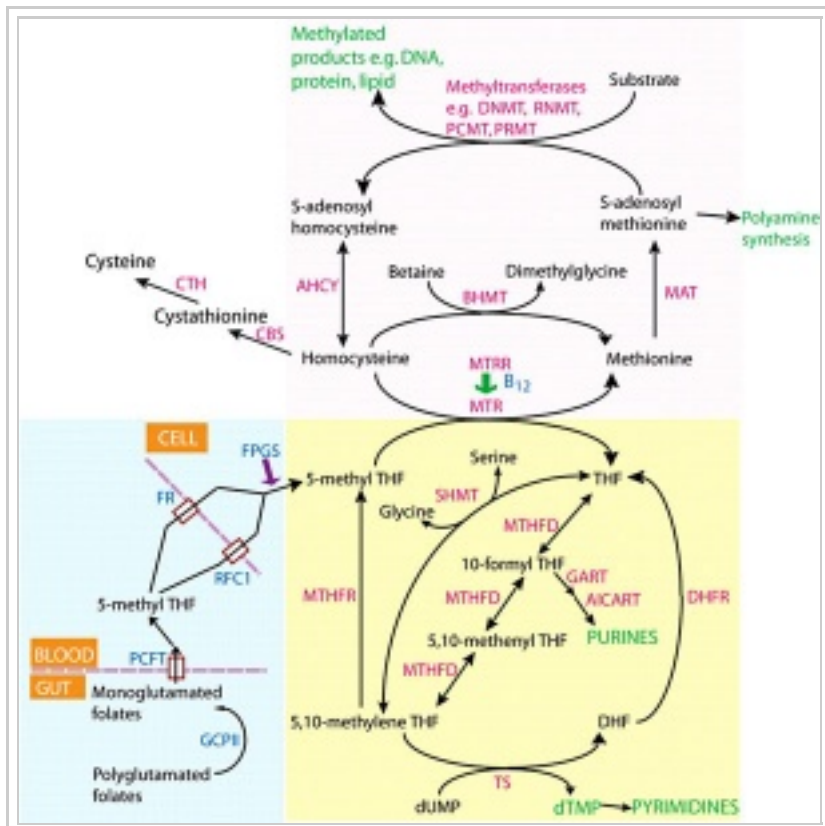
Folate and Neural Development

Research over the last 20 years had suggested a relationship between maternal diet and the birth of an affected infant. Recent evidence has confirmed that folic acid, a water soluble vitamin (vitamin B_9) found in many fruits (particularly oranges, berries and bananas), leafy green vegetables, cereals and legumes, may prevent the majority of neural tube defects.

Required for DNA metabolism in rapidly dividing cells.

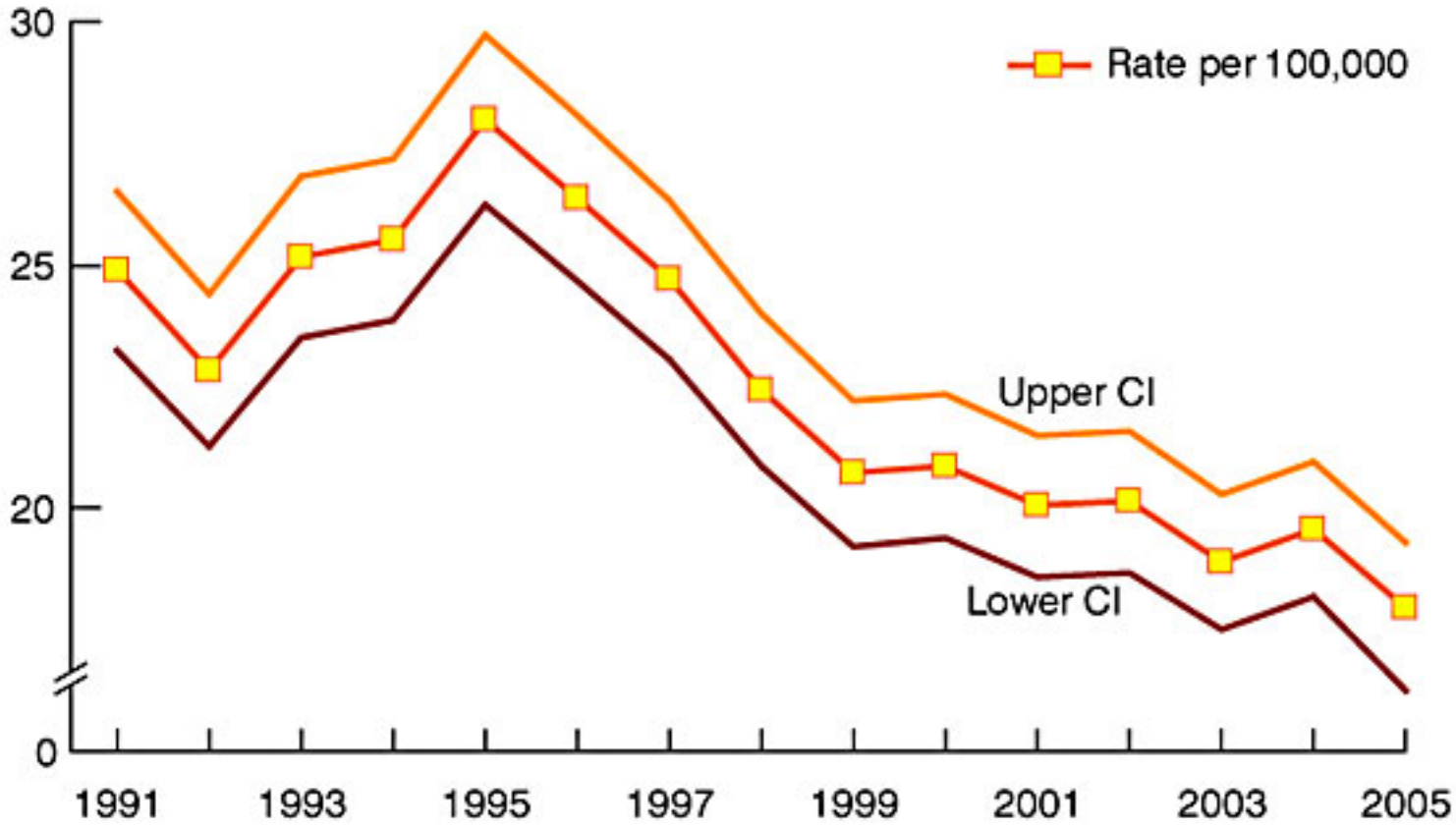
USA Statistics

In the U.S.A. the Food and Drug Administration in 1996 authorized that all enriched cereal grain products be fortified with folic acid, with optional fortification beginning in March 1996 and mandatory fortification in January 1998. The data below shows the subsequent changes in anencephaly and spina bifida rate over that period.



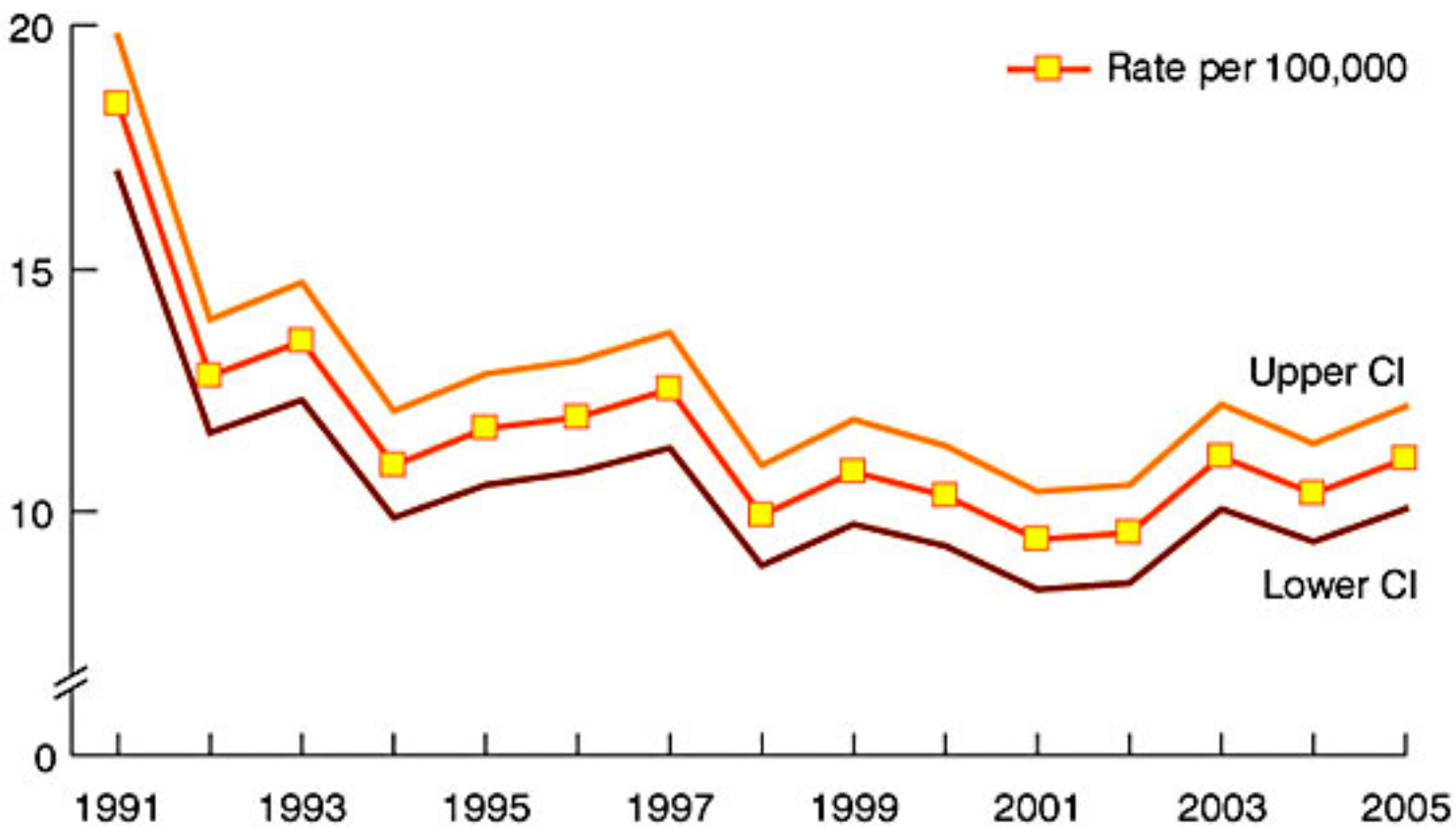
Folate one-carbon metabolism

Figure 1. Spina bifida rates, 1991–2005



NOTES: Excludes data for Maryland, New Mexico, and New York, which did not require reporting for spina bifida for some years.
CI is 95% confidence interval.
SOURCE: CDC/NCHS, National Vital Statistics System.

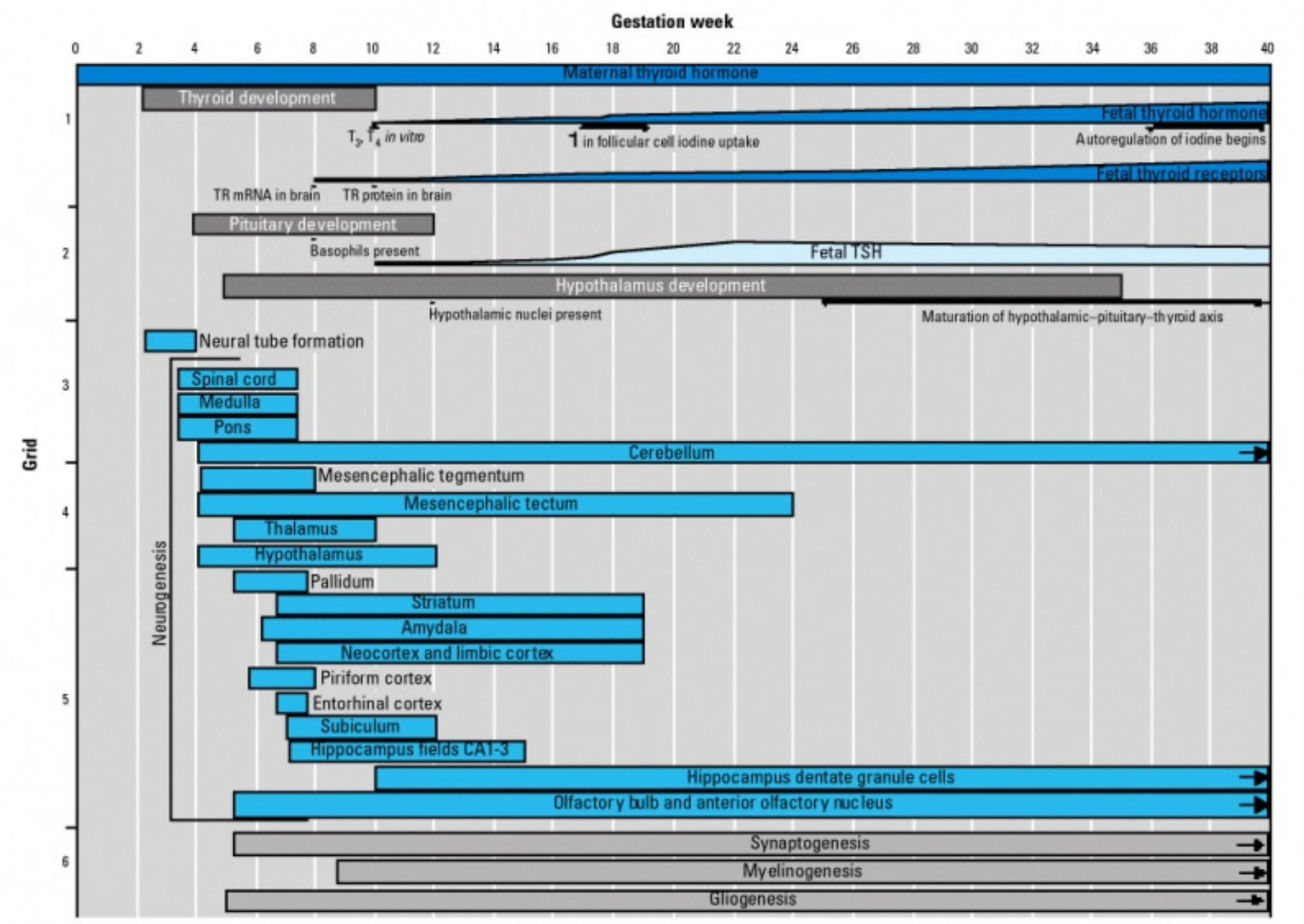
Figure 2. Anencephalus rates, 1991–2005



NOTES: Excludes data for Maryland, New Mexico, and New York, which did not require reporting for anencephalus for some years.
CI is 95% confidence interval.
SOURCE: CDC/NCHS, National Vital Statistics System.

Links: Folic Acid and Neural Tube Defects

Thyroid System and Neural Development

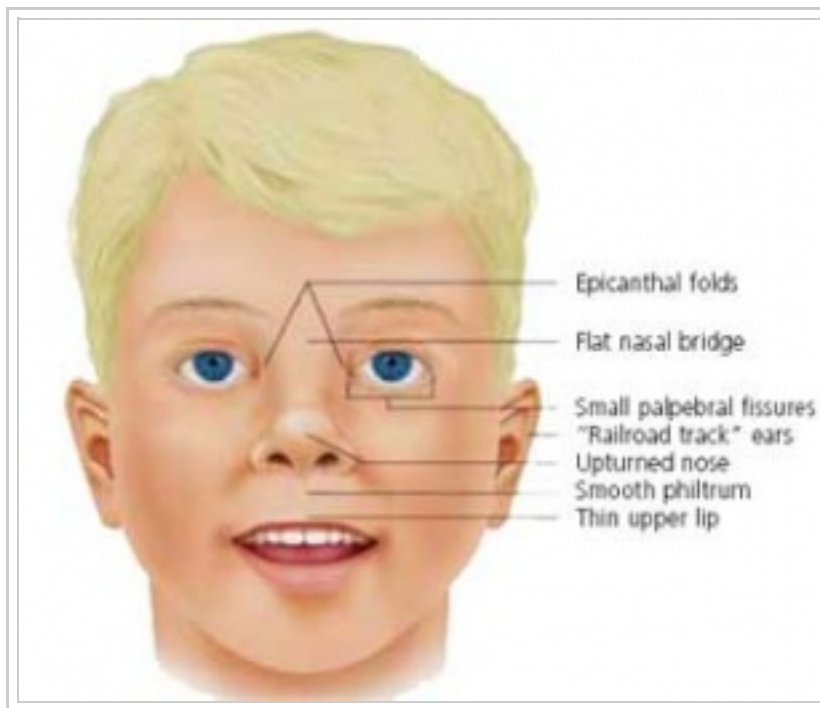


Timeline of human thyroid system and brain development from conception to birth.[4] (Estimation of neurogenesis adapted from Bayer et al.[5])

Links: Endocrine - Thyroid Development

Environmental Effects and Neural Development

The developmental environment can also impact upon neural growth; maternal drugs such as alcohol and heavy metals such as lead (mining, historically both petrol and paint).

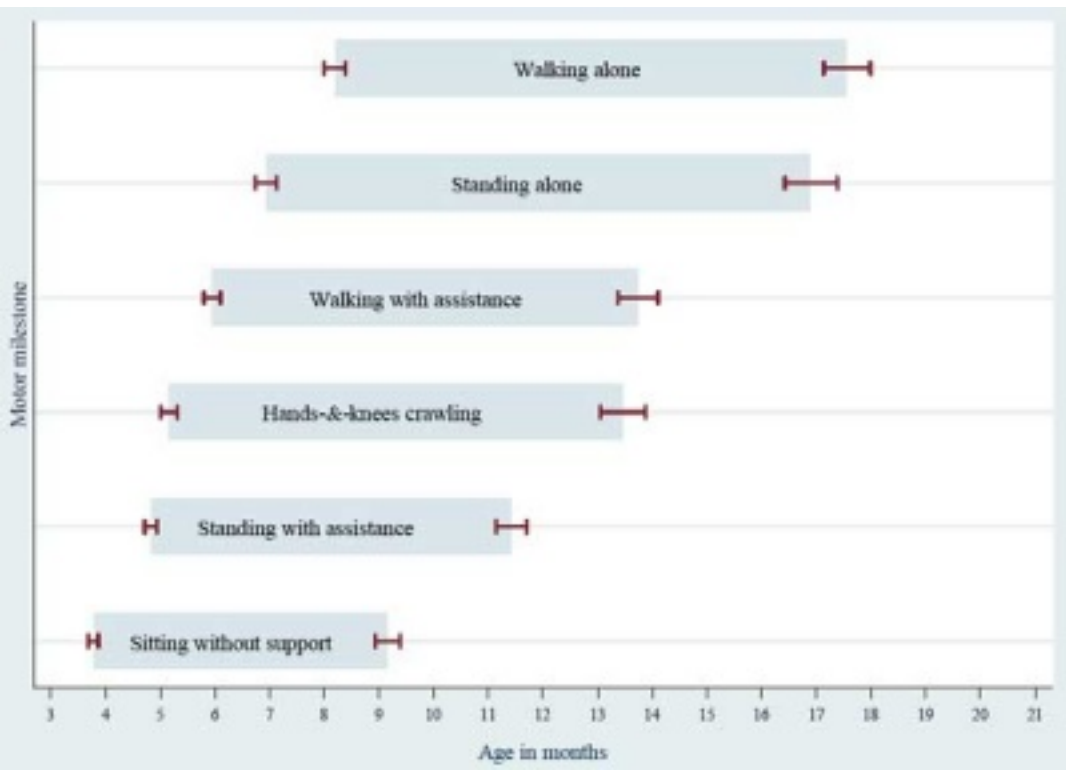


Fetal Alcohol Syndrome (FAS) facial features[6]

Postnatal

Postnatal environment, diet and other sensory abnormalities (hearing) can also impact on achieving developmental milestones.

- Neural System - Postnatal



WHO motor development milestones

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2. ↑ A Afif, R Bouvier, A Buenerd, J Trouillas, P Mertens **Development of the human fetal insular cortex: study of the gyration from 13 to 28**

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3. ↑ P S Hüppi, S Warfield, R Kikinis, P D Barnes, G P Zientara, F A Jolesz, M K Tsuji, J J Volpe **Quantitative magnetic resonance imaging of brain development in premature and mature newborns.** Ann. Neurol.: 1998, 43(2);224-35 PubMed 9485064
4. ↑ Kembra L Howdeshell **A model of the development of the brain as a construct of the thyroid system.** Environ. Health Perspect.: 2002, 110 Suppl 3;337-48 PubMed 12060827
5. ↑ S A Bayer, J Altman, R J Russo, X Zhang **Timetables of neurogenesis in the human brain based on experimentally determined patterns in the rat.** Neurotoxicology: 1993, 14(1);83-144 PubMed 8361683
6. ↑ Daniel J Wattendorf, Maximilian Muenke **Fetal alcohol spectrum disorders.** Am Fam Physician: 2005, 72(2);279-82, 285 PubMed 16050451

Historic Embryology

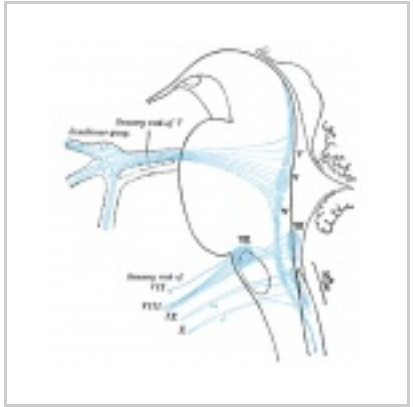
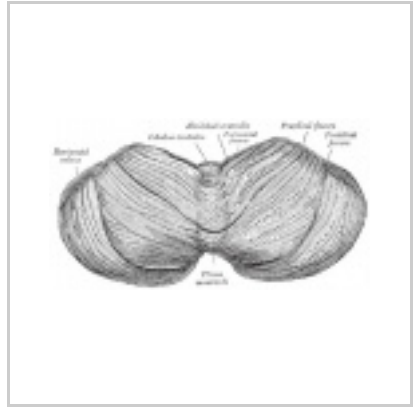
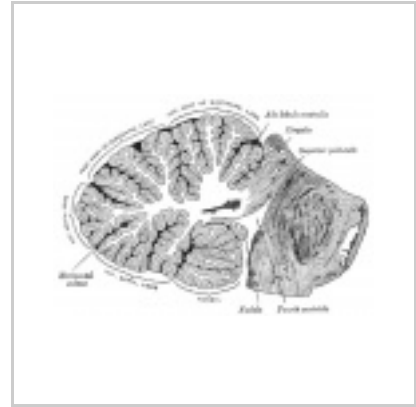
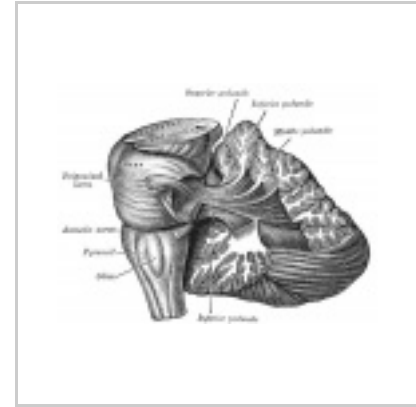
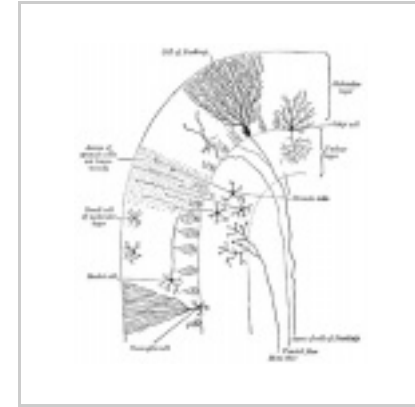
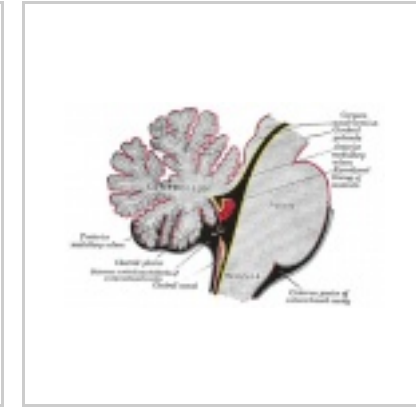
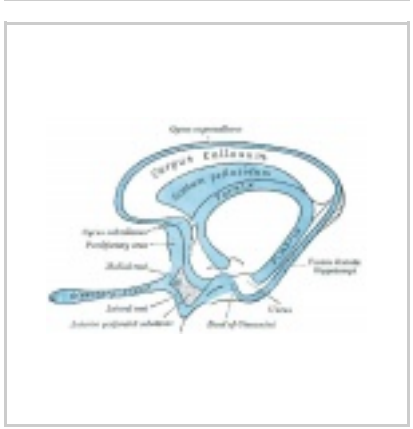
Historic Disclaimer - information about historic embryology pages [Expand]

- Chapter XV. The Brain and Spinal Cord Human Embryology and Morphology. Keith, A. (1902) London: Edward Arnold.
- Contributions to Embryology Carnegie Institution No.59 Relative Weight and Volume of the Component Parts of the Brain of the Human Embryo at Different Stages of Development. Jenkins, G.B. (1921). pp5-54.

Images

Text-Book of Embryology - 1921[Expand]

} Gray, Henry. Anatomy of the Human Body. Philadelphia: Lea & Febiger, 1918.

Anatomy of the Human Bod - 1918[Expand]

2015 Course: **Week 2** Lecture 1 Lecture 2 Lab 1 | **Week 3** Lecture 3 Lecture 4 Lab 2 | **Week 4** Lecture 5 Lecture 6 Lab 3 | **Week 5** Lecture 7 Lecture 8 Lab 4 | **Week 6** Lecture 9 Lecture 10 Lab 5 | **Week 7** Lecture 11 Lecture 12 Lab 6 | **Week 8** Lecture 13 Lecture 14 Lab 7 | **Week 9** Lecture 15 Lecture 16 Lab 8 | **Week 10** Lecture 17 Lecture 18 Lab 9 | **Week 11** **Lecture 19** Lecture 20 Lab 10 | **Week 12** Lecture 21 Lecture 22 Lab 11 | **Week 13** Lecture 23 Lecture 24 Lab 12 | **Projects**: Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Students | Student Designed Quiz Questions | Moodle page (http://moodle.telt.unsw.edu.au/course/view.php?id=15814)

Glossary Links

A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z | Numbers | Symbols

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