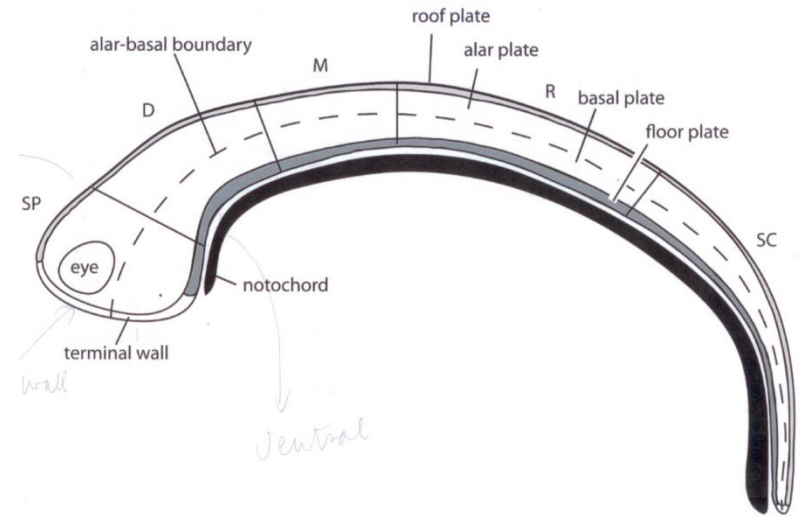# Differentiation of brain vesicles

Compiled by:
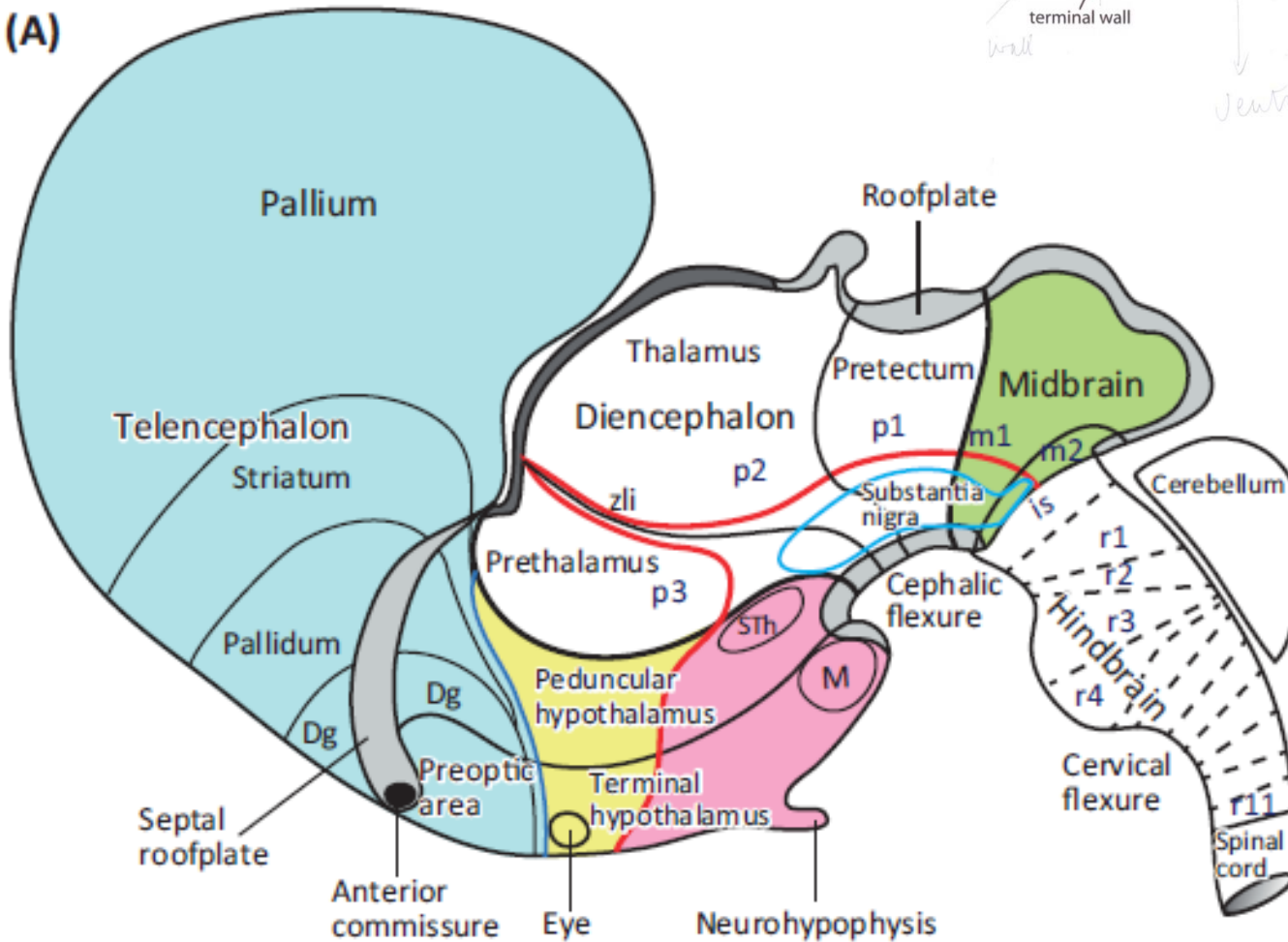
András Csillag

Scheme of segmental development
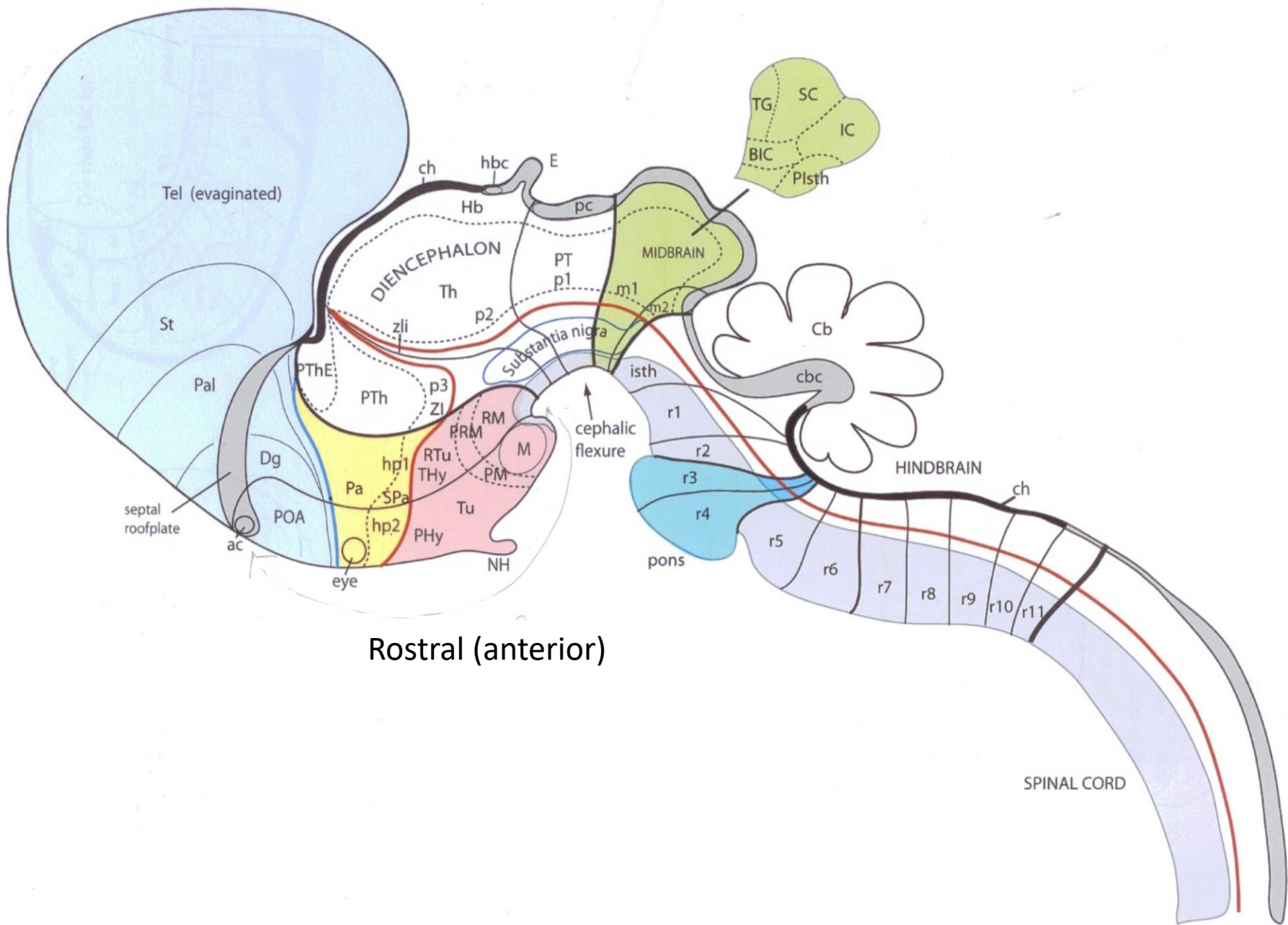
(based on mouse model)

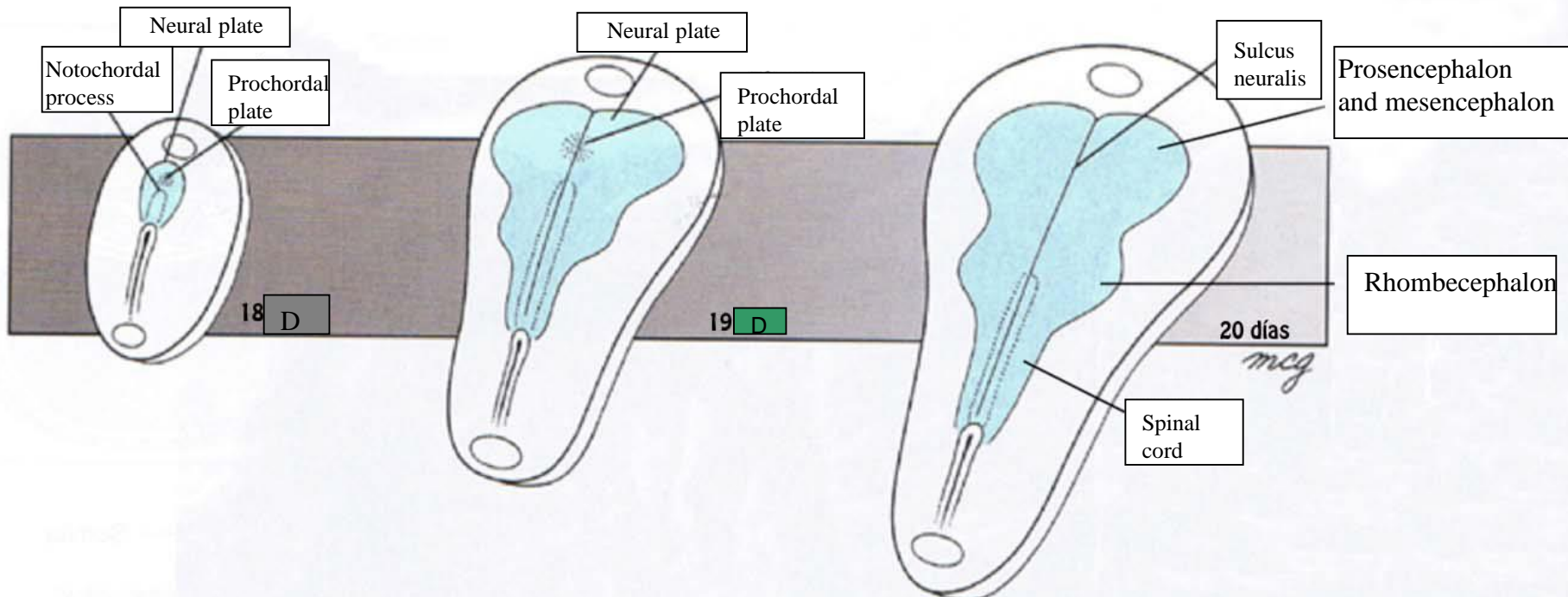*Puelles et al, Trends in Neurosci, 2013.*

Rostral (anterior)

Labels within the figure:

Tel (evaginated)

St

Pal

Dg

septal roofplate

ac

POA

eye

PThE

Pa

hp1

hp2

PHy

NH

PTh

ZI

p3

SPa

RTu

THy

RM

PRM

PM

M

Tu

zli

Th

DIENCEPHALON

ch

hbc

Hb

E

pc

PT

p1

p2

m1

m2

MIDBRAIN

Substantia nigra

cephalic flexure

isth

r1

r2

r3

r4

r5

r6

r7

r8

r9

r10

r11

pons

HINDBRAIN

ch

Cb

cbc

TG

SC

IC

BIC

Plsth

SPINAL CORD

Differentiation and early segmentation of the neural plate

Neural plate

Notochordal process

Prochordal plate

Neural plate

Prochordal plate

Sulcus neuralis

Prosencephalon and mesencephalon

Rhombecephalon

Spinal cord

18 D

19 D

20 días

mcg

BMPs from ectoderm determine migration into surface ectoderm
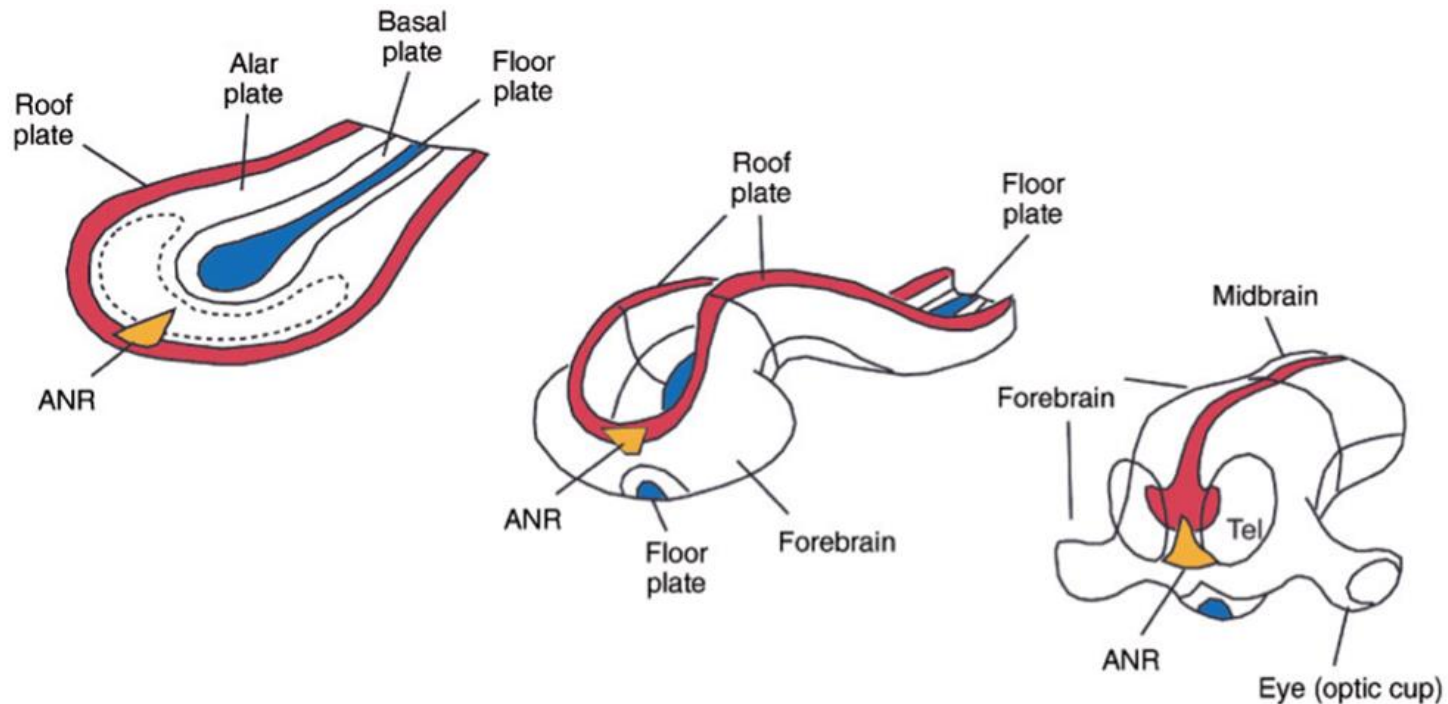
1. Planar induction by

Primitive node – anti-BMP factors – migration to surface prevented, neural plate forms

2. Vertical induction

 - Rostrally by the prochordal plate (mesendoderm)

 - Caudally by the notochord (mesoderm)

After Larsen, 2003

Rostrocaudal regionalization of neural tube

Early formation of prosencephalon and mesencephalon

ANR – anterior neural ridge (crista neuralis anterior)

Important organizer area emitting signals of rostralization, necessary for the development of secondary prosencephalon and its derivatives (telencephalon, optic vesicle, hypothalamus)

Main secondary organizing centres determining rostrocaudal regionalization in the brain
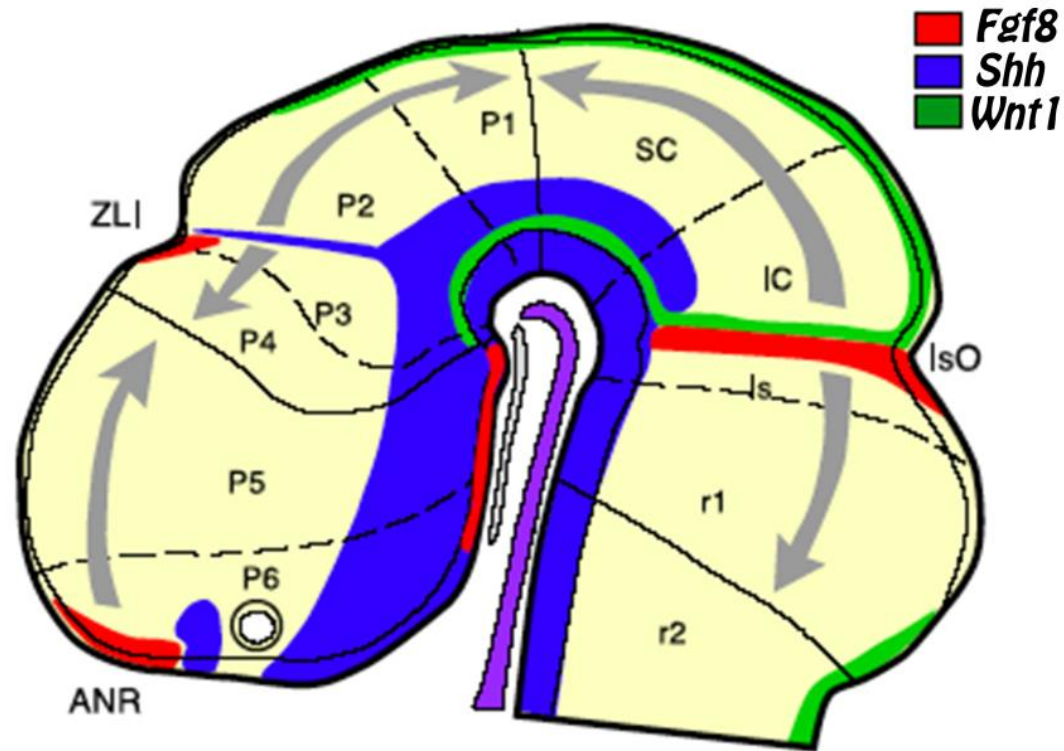
ANR – anterior neural ridge *(defines ant. border of neural plate, antagonizes 'caudalization' signals, e.g. Wnt, and promotes prosencephalic factor Six3)*
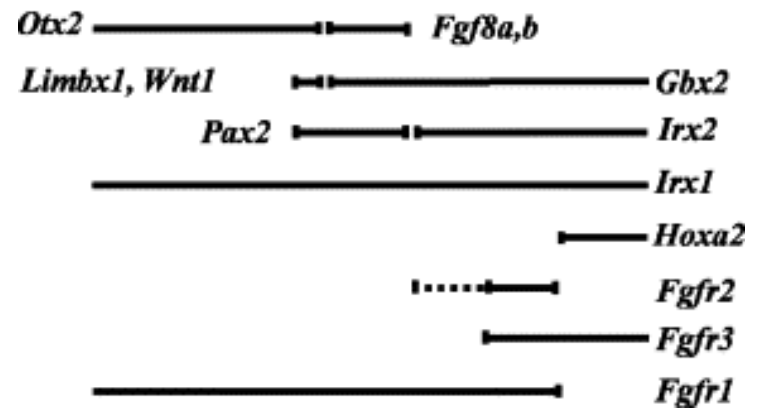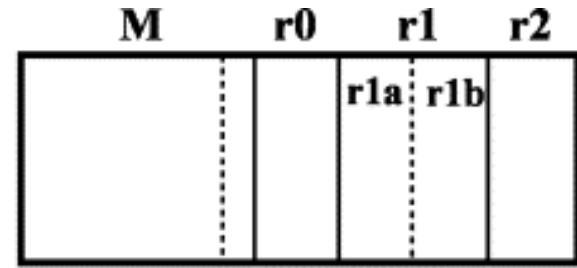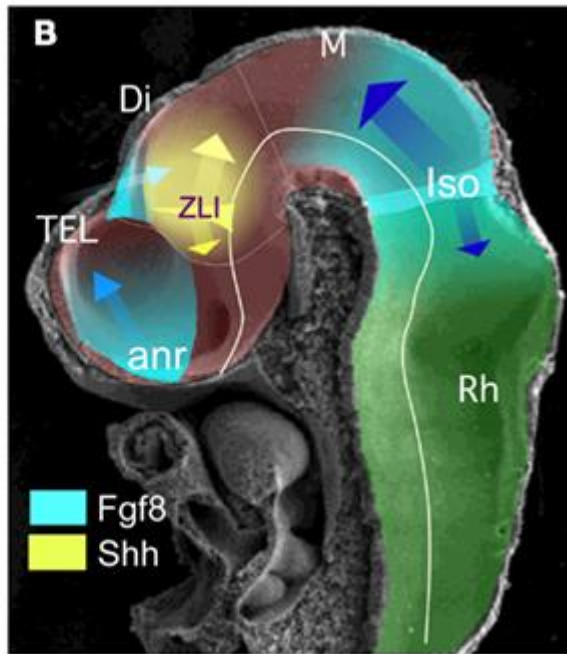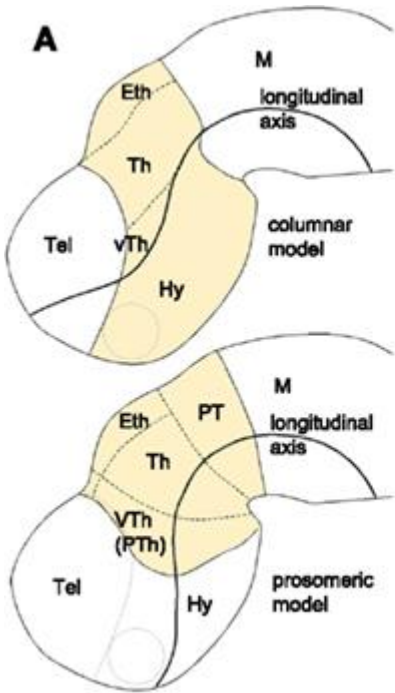
ZLI – zona limitans anterior *(defines border P2/P3)*

IsO – isthmic organizer *(defines prosencephalic/rhombencephalic border, produces Fgf8 for r1 – cerebellar development and Wnt1 for mesencephalon – development of colliculi)*

Echevarría et al., 2003
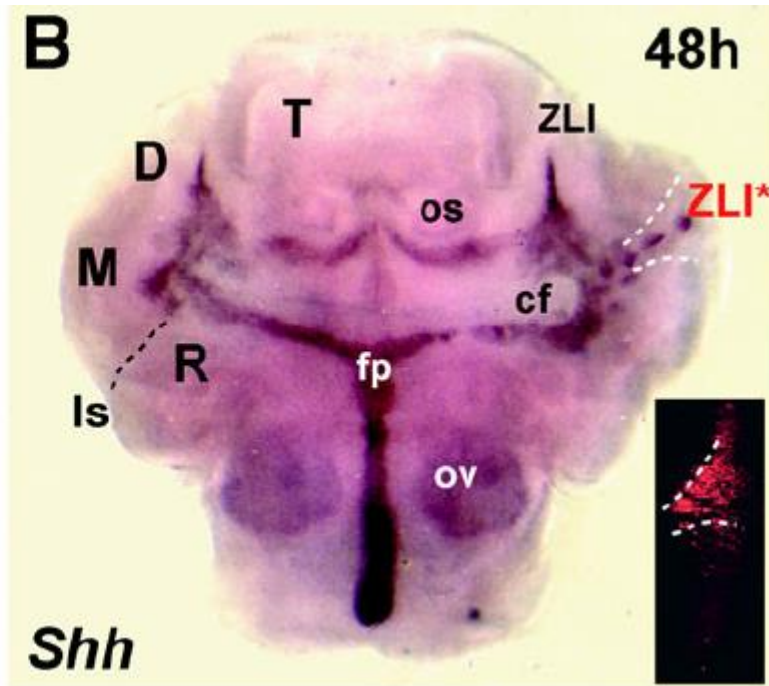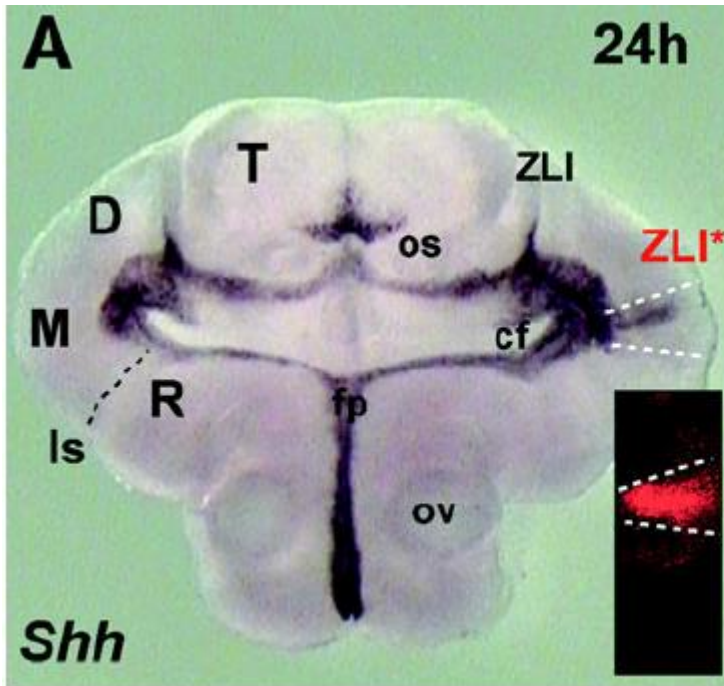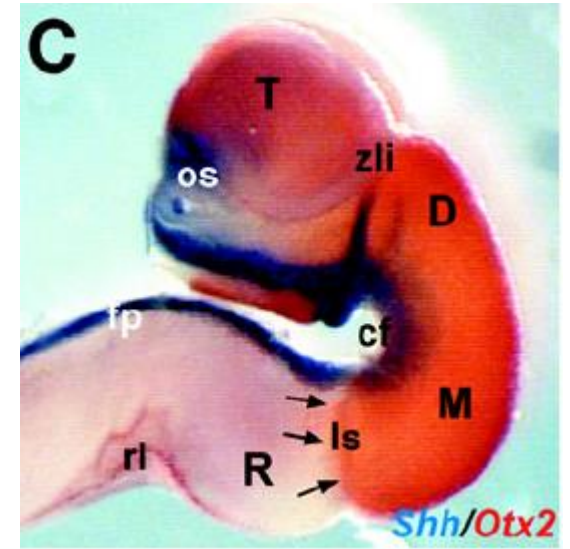
'The isthmic organizer'

anr (ant. neural ridge) and Iso (isthmic organizer)

Fgf8 (fiber growth factor 8) → Otx2 → caudal

→ Gbx2 → rostral

Morphogenetic gradient principle

Martínez-Ferre és Martínez, *Front. Neurosci*, 2012.

Aroca és Puelles, 2005.

Organotypic culture technique
Mouse neural tube explants

Echevarría et al, Int. J. Dev. Biol., 2001

Scheme of rostrocaudal subdivisions of the neural tube
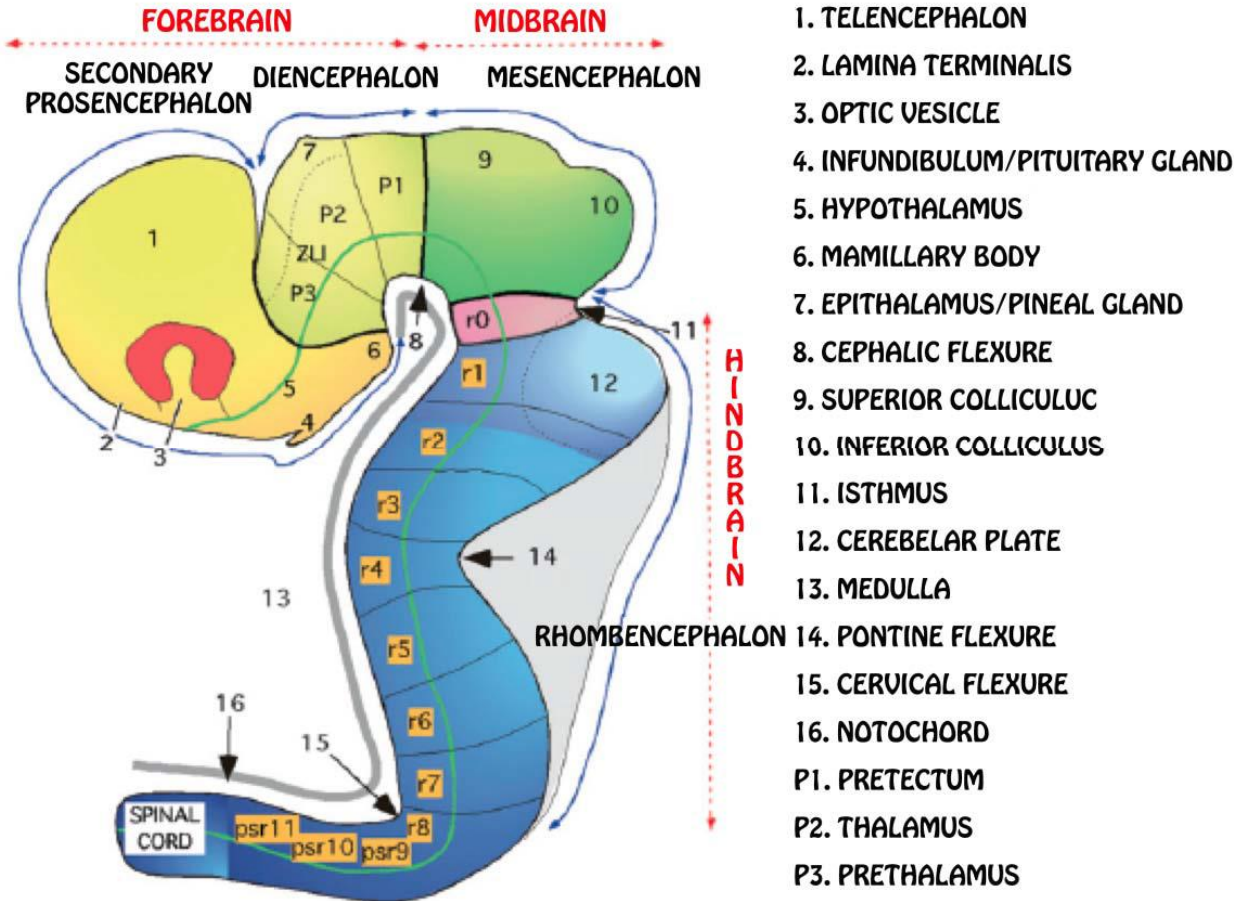
1. TELENCEPHALON
2. LAMINA TERMINALIS
3. OPTIC VESICLE
4. INFUNDIBULUM/PITUITARY GLAND
5. HYPOTHALAMUS
6. MAMILLARY BODY
7. EPITHALAMUS/PINEAL GLAND
8. CEPHALIC FLEXURE
9. SUPERIOR COLLICULUC
10. INFERIOR COLLICULUS
11. ISTHMUS
12. CEREBELAR PLATE
13. MEDULLA
14. PONTINE FLEXURE
15. CERVICAL FLEXURE
16. NOTOCHORD
P1. PRETECTUM
P2. THALAMUS
P3. PRETHALAMUS

Martínez et al., 2012

Dorsoventral regionalization of neural tube
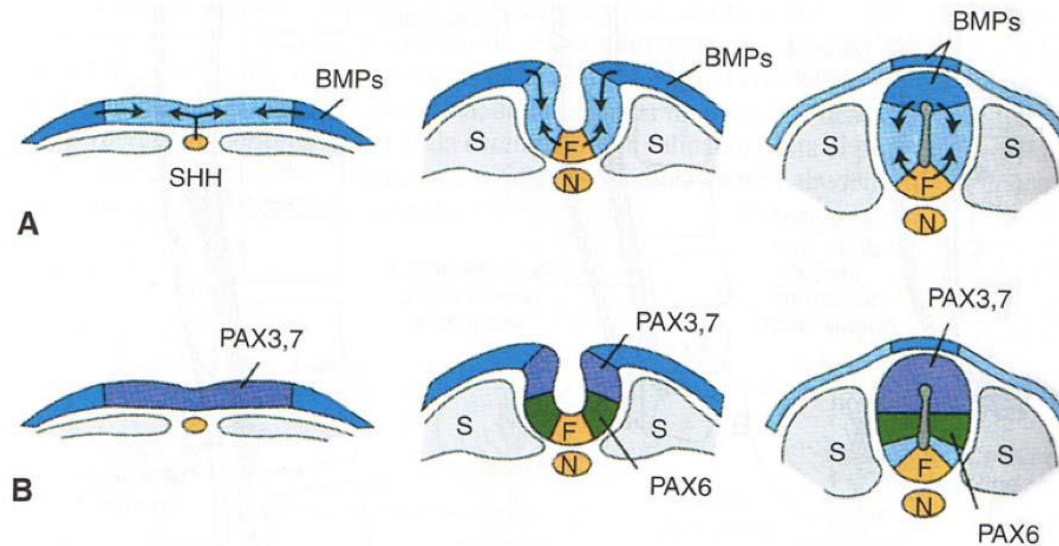
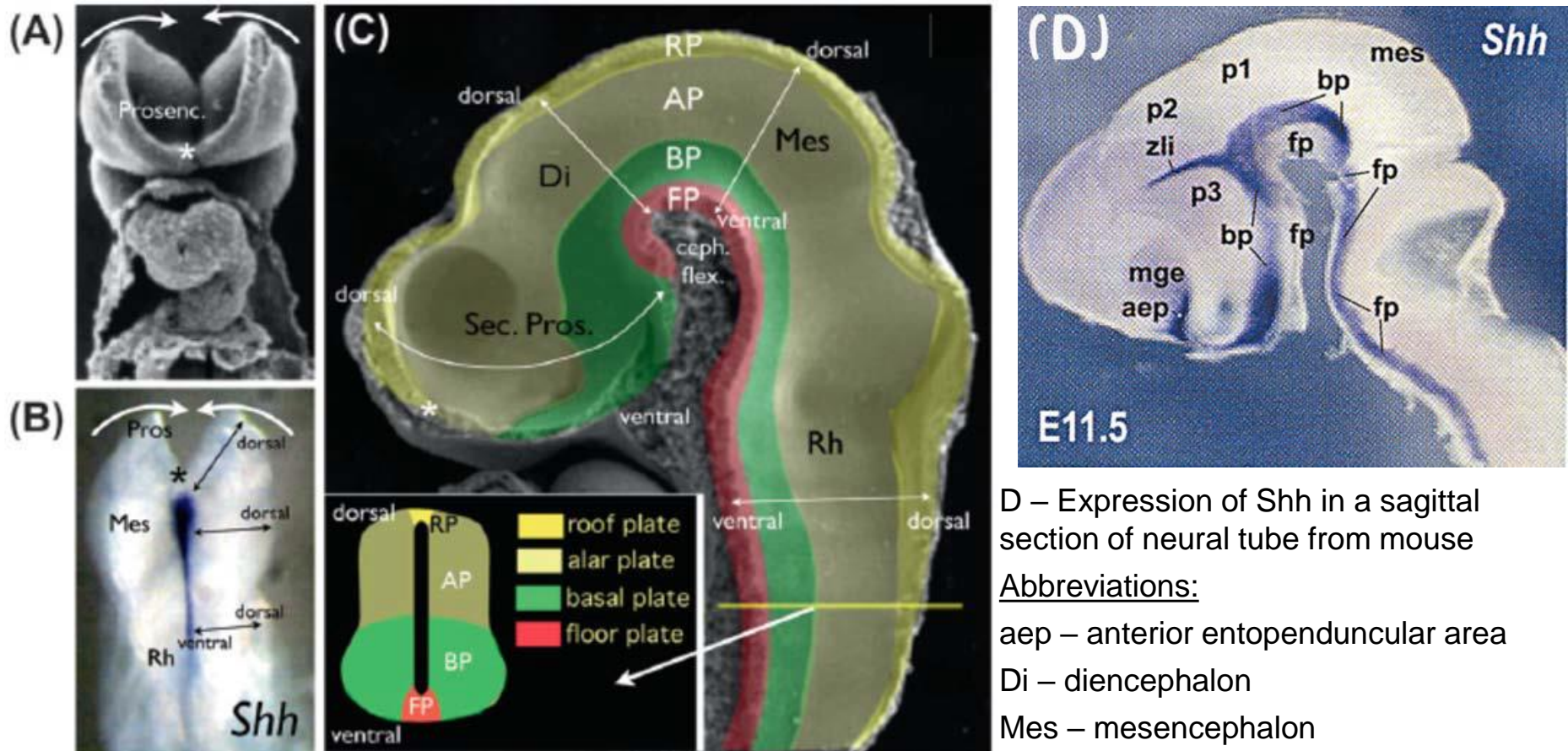Transcription factors:

BMPs from non-neural ectoderm

Sonic hedgehog (Shh) from notochord (N) and floor plate (F)

Retinoic acid from somites (S)

Pax 3,7 from roof plate and then from alar plate

Nk2 (Nkx), then Pax 6 from basal plate

Dorsoventral regionalization of neural tube

D – Expression of Shh in a sagittal section of neural tube from mouse

Abbreviations:

aep – anterior entopenduncular area

Di – diencephalon

Mes – mesencephalon

mge – medial ganglionic eminence

Pros – prosencephalon

Rh – rhombencephalon

Sec. Pros. – secondary prosencephalon

p1-3 – prosomeres

A – Fusion of neural tube, rostral aspect

B – Expression of Shh in the floor plate

C – The four principal dorsoventral units of neural tube (roof plate – RP; alar plate – AP; basal plate – BP; floor plate – FP)

Martínez et al., 2012

Puelles et al., 2004
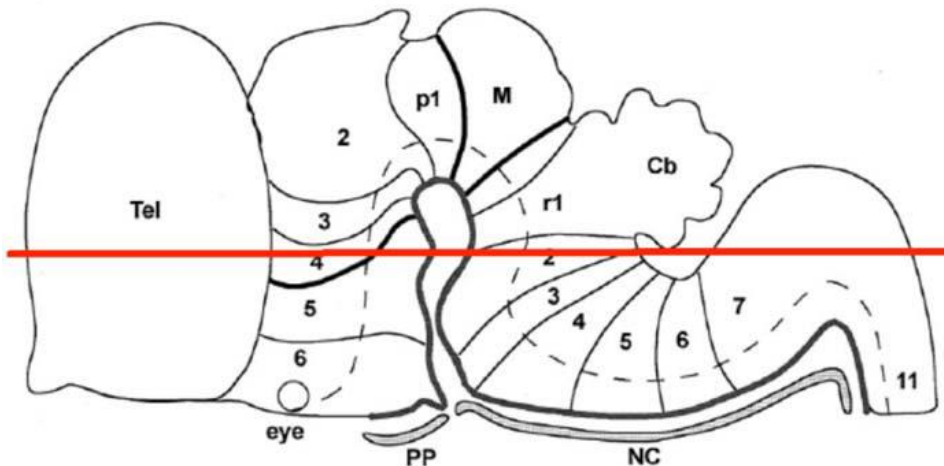
Developmental models of the CNS

Topology *vs* topography
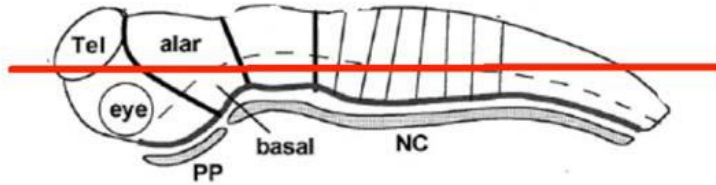
In early phase of development, the dorsoventral plane (red line) is nearly parallel to the alar-basal boundary
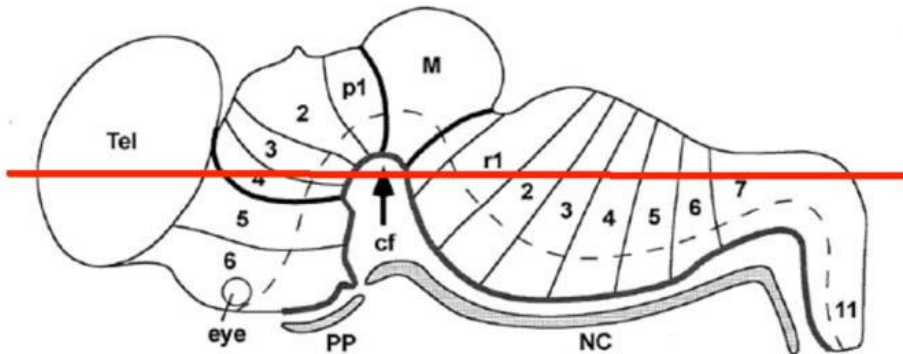
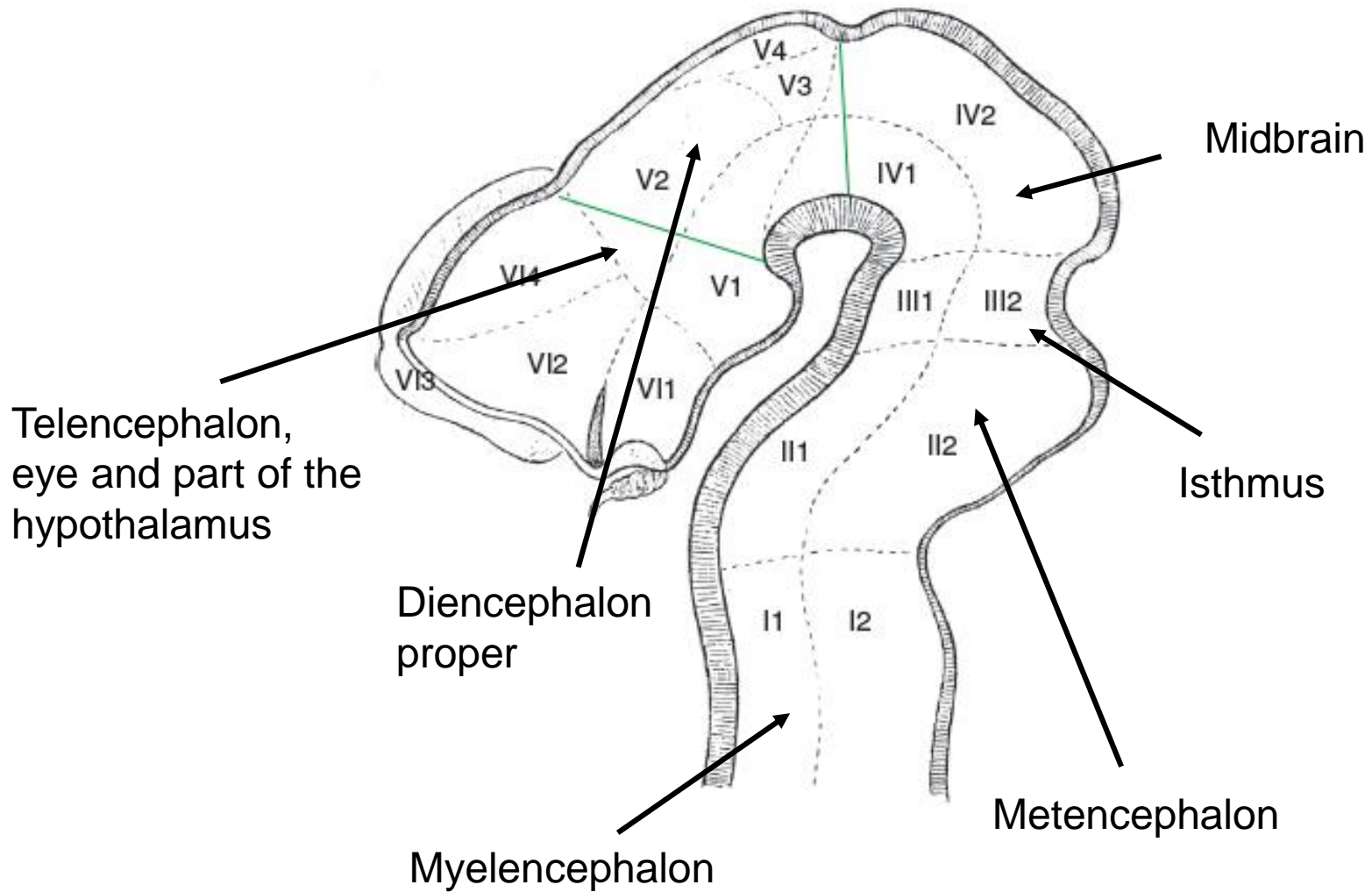In later phases of development, this relationship is no longer valid
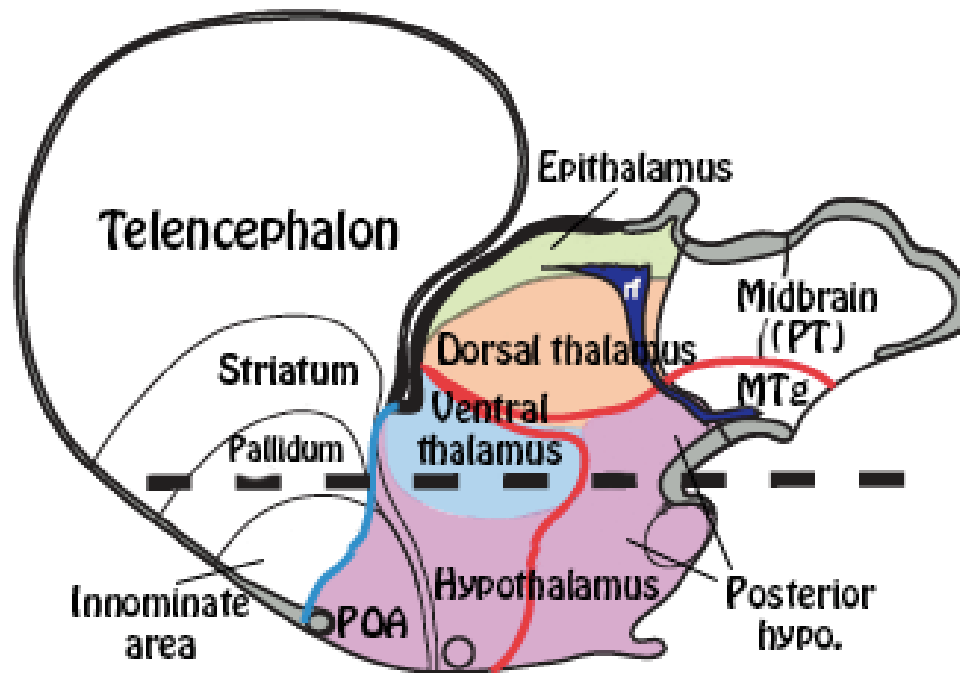
NC – notochord

PP – prechordal plate

p1-6 prosomeres

r1-11 rhombomeres

Puelles, 2001

Neuromeric model by His 1895

Columnar model by Herrick

Four parts of diencephalon are distinguished in a dorsoventral sequence:

Epithalamus, dorsal thalamus, ventral thalamus, hypothalamus.

The new prosomeric model follows a longitudinal order (marked by the red line), and the parts do not fully coincide with those of Herrick

Abbreviations: MTg – mesencephalic tegmentum; POA – preoptic area; PT – pretectum; rf – roof plate

Adapted by Dong 2008

Hypothalamus – a modern interpretation

Correctly: „hypotelencephalon"?
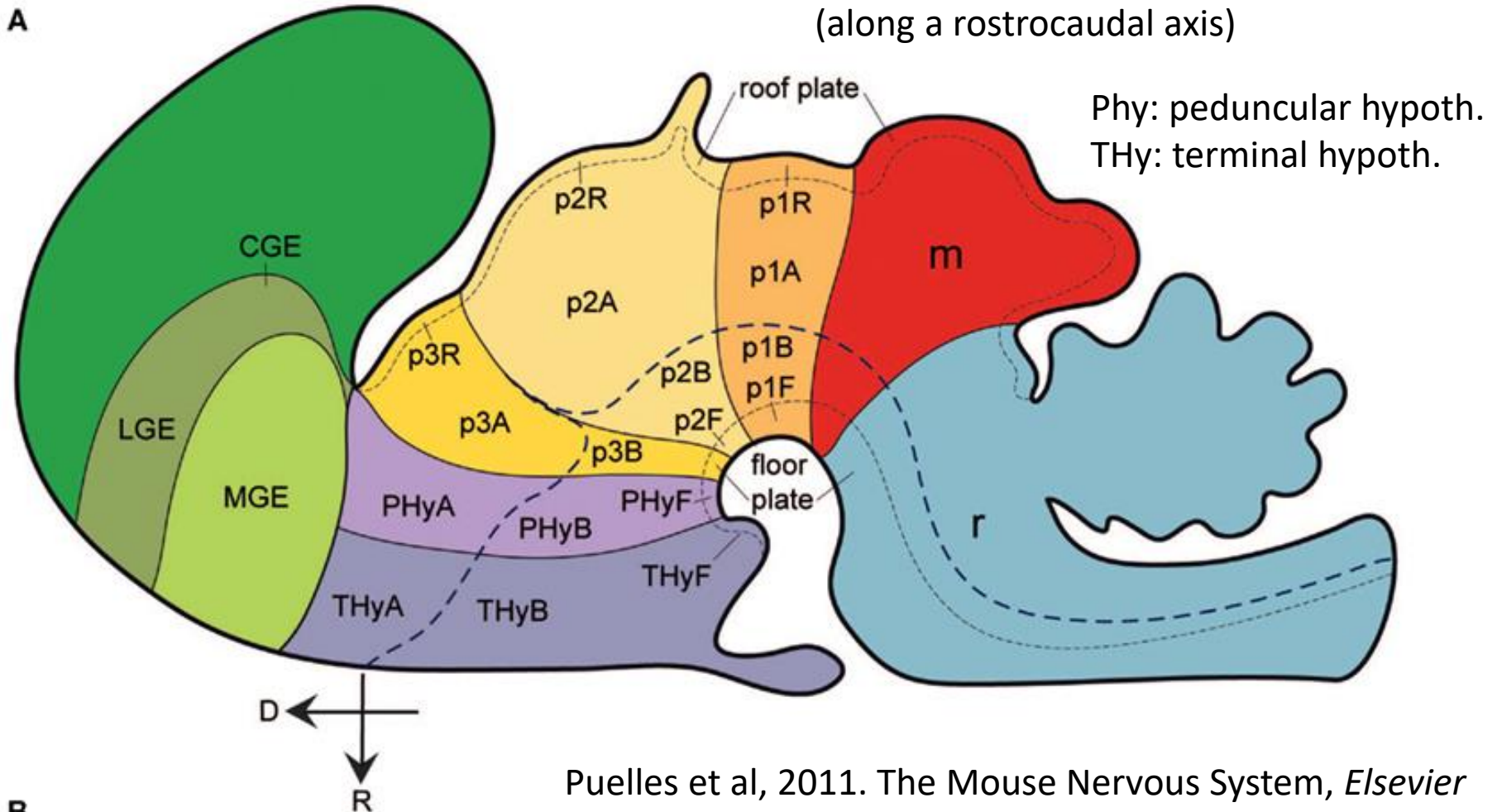Not part of diencephalon!
True diencephalic parts:
 pretectum, thalamus, prethalamus

His 1893 – floor plate theory
Ariens Kappers 1947 – prosencephalic model
Herrick – columnar organisation
(along a rostrocaudal axis)

Phy: peduncular hypoth.
THy: terminal hypoth.

Puelles et al, 2011. The Mouse Nervous System, *Elsevier*
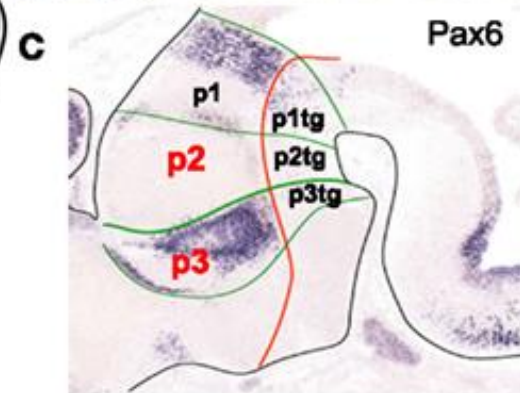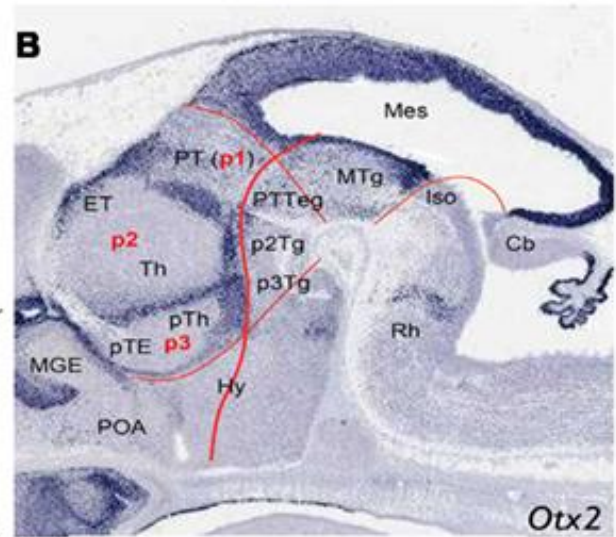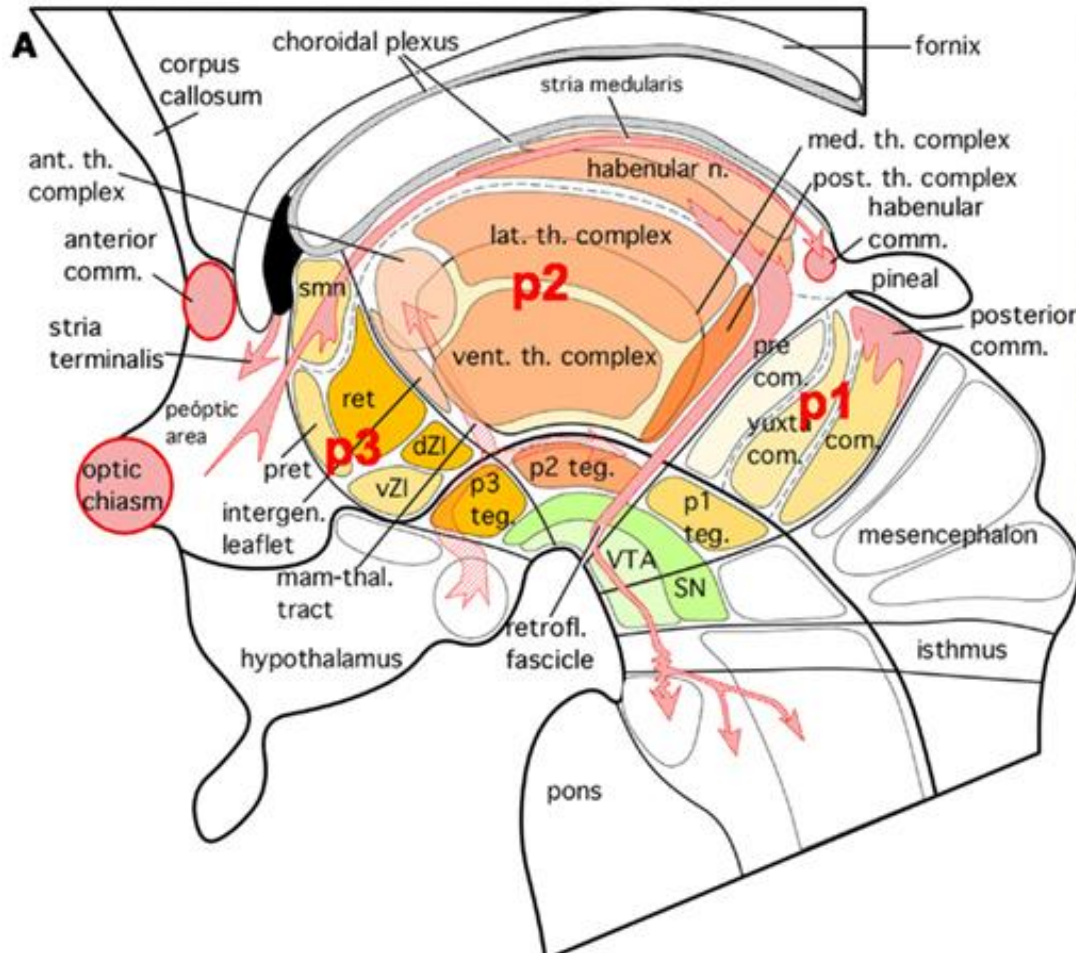
Thalamus, prethalamus
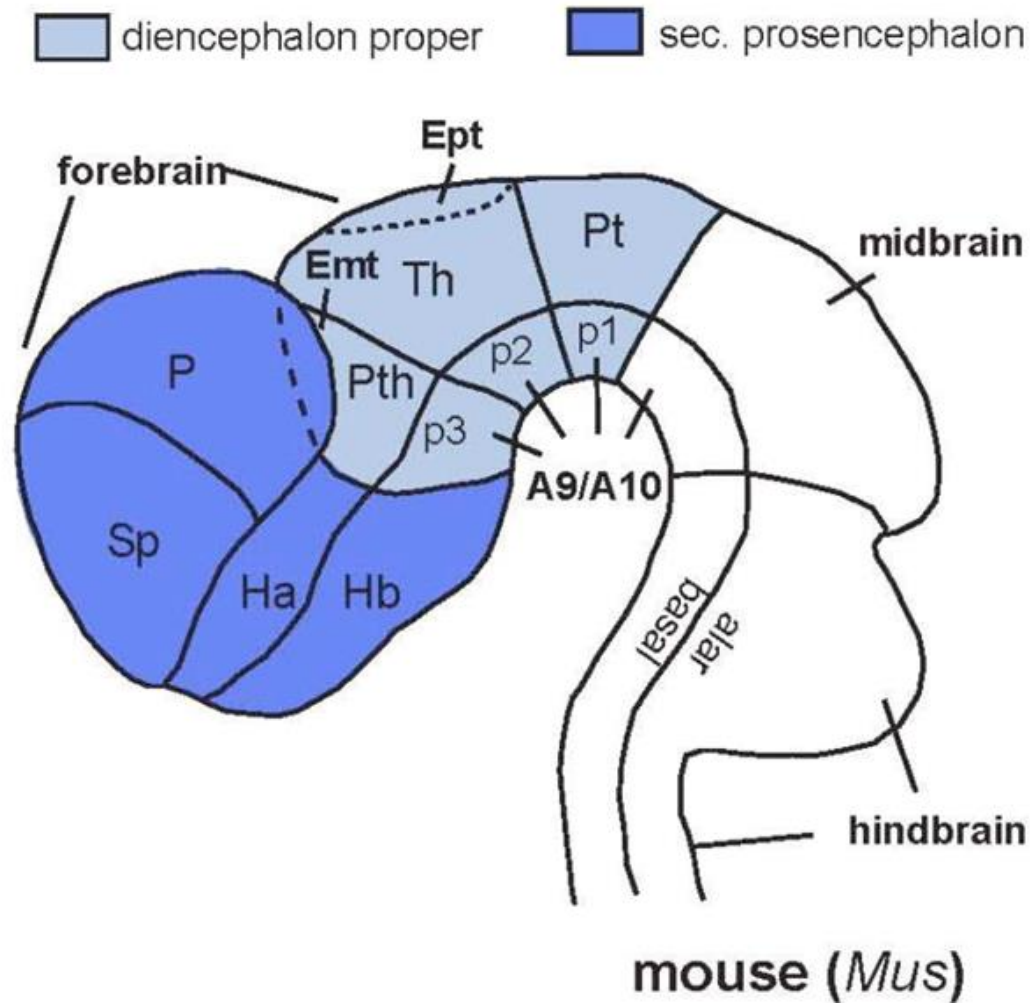
p1 – pretectum

⟵ Fasc. retroflexus

p2 – thalamus

⟵ Zona limitans

p3 - prethalamus

Zona limitans: Wnt8b required for activation of Shh →
Early subdivisions of prosencephalon: rostral
(secondary telencephalon) és caudal (diencephalon)

Development of prosencephalon

p1: pretectum (Pt); p2: thalamus (Th) and epithalamus (Ept); p3 prethalamus (Pth) and prethalamic eminence (Emt). The principal subdivisions of telencephalon: pallium (P) and subpallium (Sp). Rostral prosencephalic regions: hypothalamus, alar (Ha) and basal (Hb) and the subpallium. After Medina et al., 2011.

Development of prosencephalon
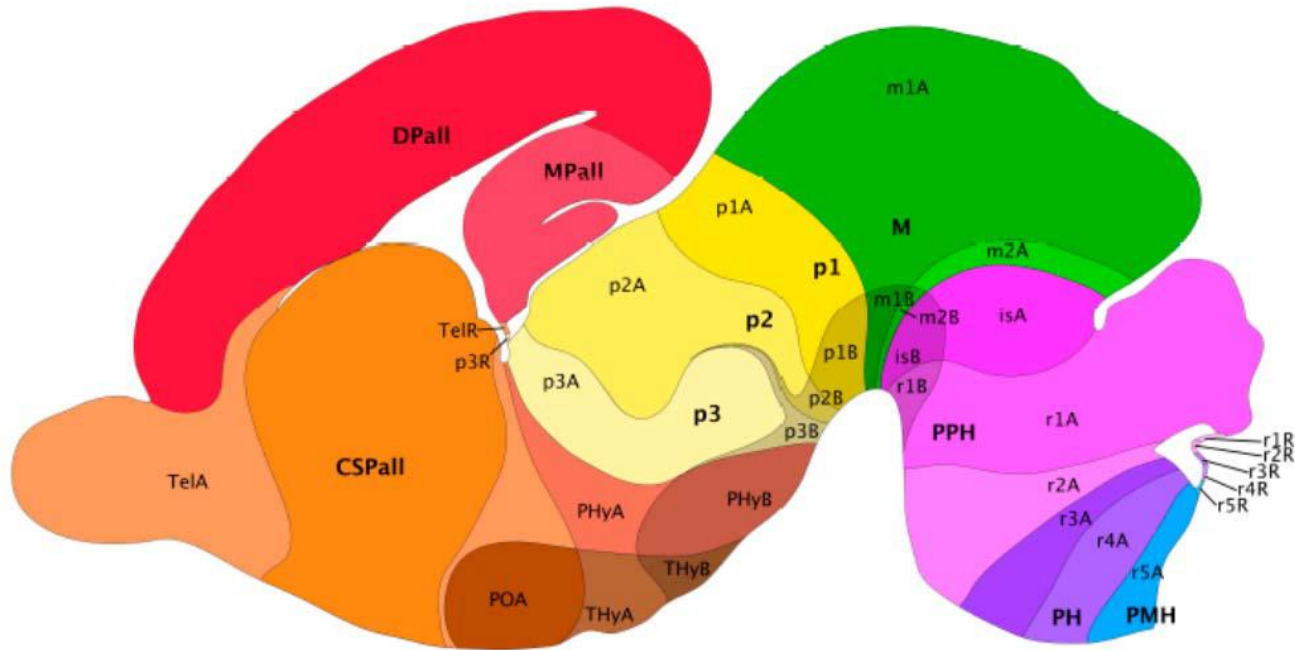
Abbrev: DPall, dorsal pallium; CSPall, central supallium

fi, fimbria; is, isthmus; M, mesencephalon; m1…2, mesomers 1…2; MPall, medial pallium; opt, optic tract; p1…3, prosomers 1…3; p2A, alar division of prosomer 2; p2B, basal division of prosomer 2; p3A, alar division of prosomer 3; p3B, basal division of prosomer 3; p3R, roof plate of prosomer 3; PH, pontine rhombencephalon; PHyA, alar division of peduncular hypothalamus; PHyB, basal division of peduncular hypothalamus; PMH, pontomedullary rhombencephalon; POA, preoptic area, alar plate; PPH, prepontine rhombencephalon; r1…5, rhombomers 1…5; TelR, roof plate of telencephalon; THyA, alar division of terminal hypothalamus; THyB, basal division of terminal hypothalamus.

http://developingmouse.brain-map.org

Pallium – cortical development

Pallium consists of:
• ventral pallium (olfactory bulb, olfactory cortex, VEP – ventr. endopiriform nucl.)
• lateral pallium (insula, claustrum)
• medial pallium (hippocampus)
• pallial amygdala
• dorsal pallium (all other cortical areas)
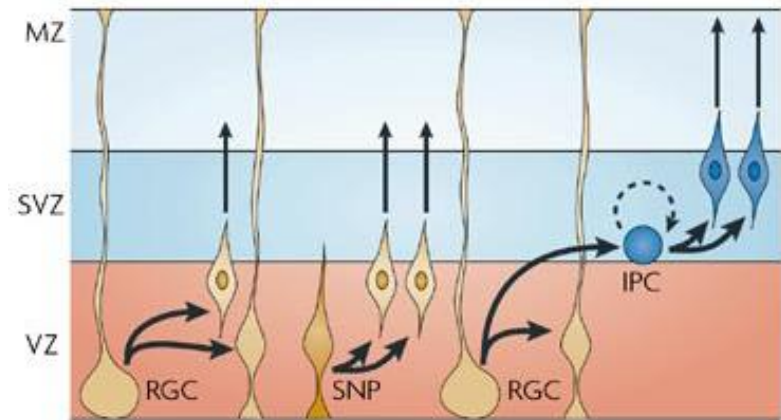
RGC: radialis glia, IPC: intermed. progenitor sejt

From neuroepithelial cells to complex cortical structures

1. Anatomical és functional modules (Waddingon 1956. 'Epigenetic landscape')
2. Cell proliferation (radial glia as neural progenitor – Dehay és Kennedy 2007)
3. Growing complexity – Radial and tangential migration - the majority of cortical GABAergic interneurons immigrates from basal ganglia; Cajal - Retzius cells derive from ventral pallidum and septum.

Developmental models of cortical areas:
1. protomap-model (Rakic 1988 – cortical arealization induced by intrinsinc molecular signals of cortex)
2. protocortex-model (O'Leary 1989, van der Loos és Woolsey 1973 – developmental signals provided by thalamocortical afferents)

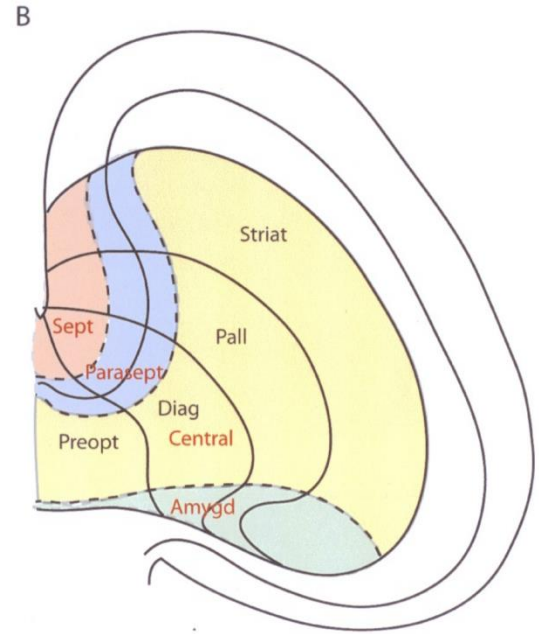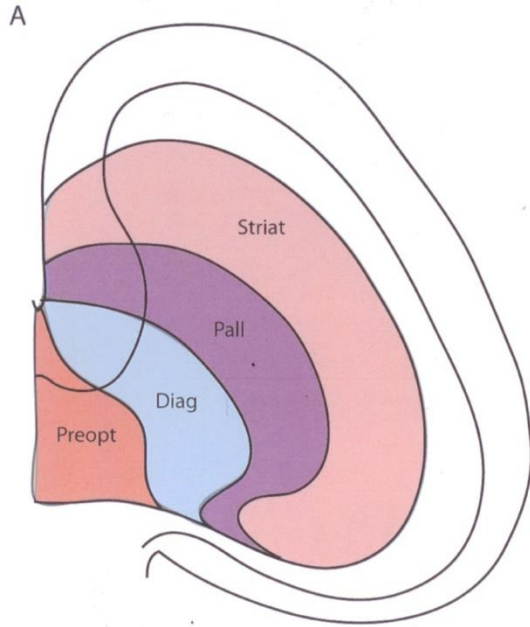# Divisions of pallium and subpallium in mammals and birds

Mammal — Bird

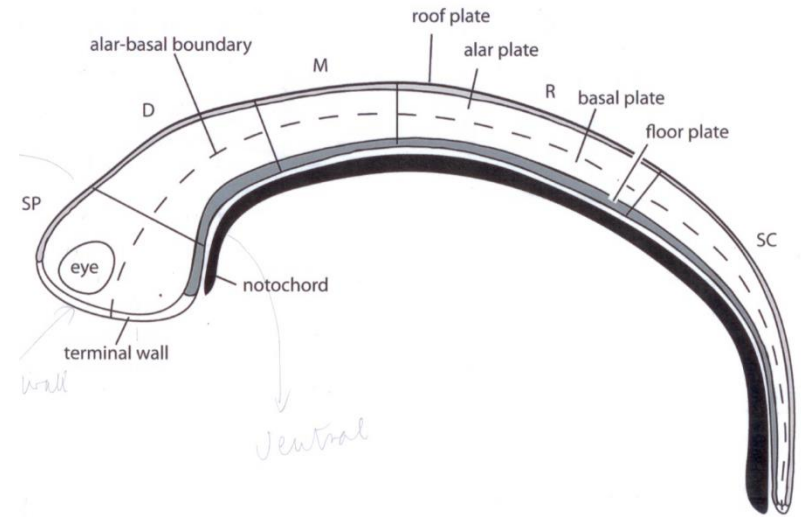|		
Tbr-1	Tbr-1 and Emx-1	Dlx-2
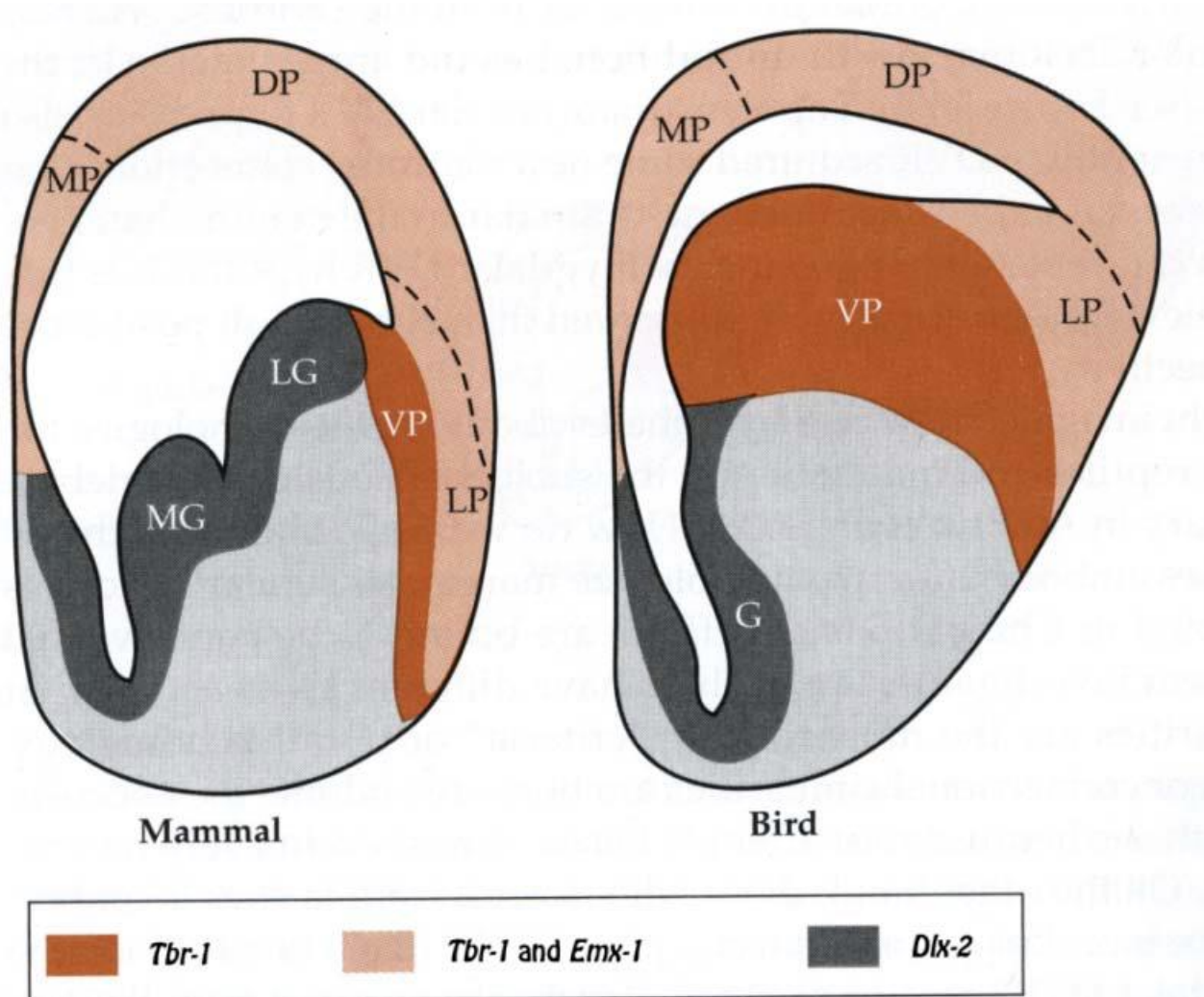
Pallium - subpallium
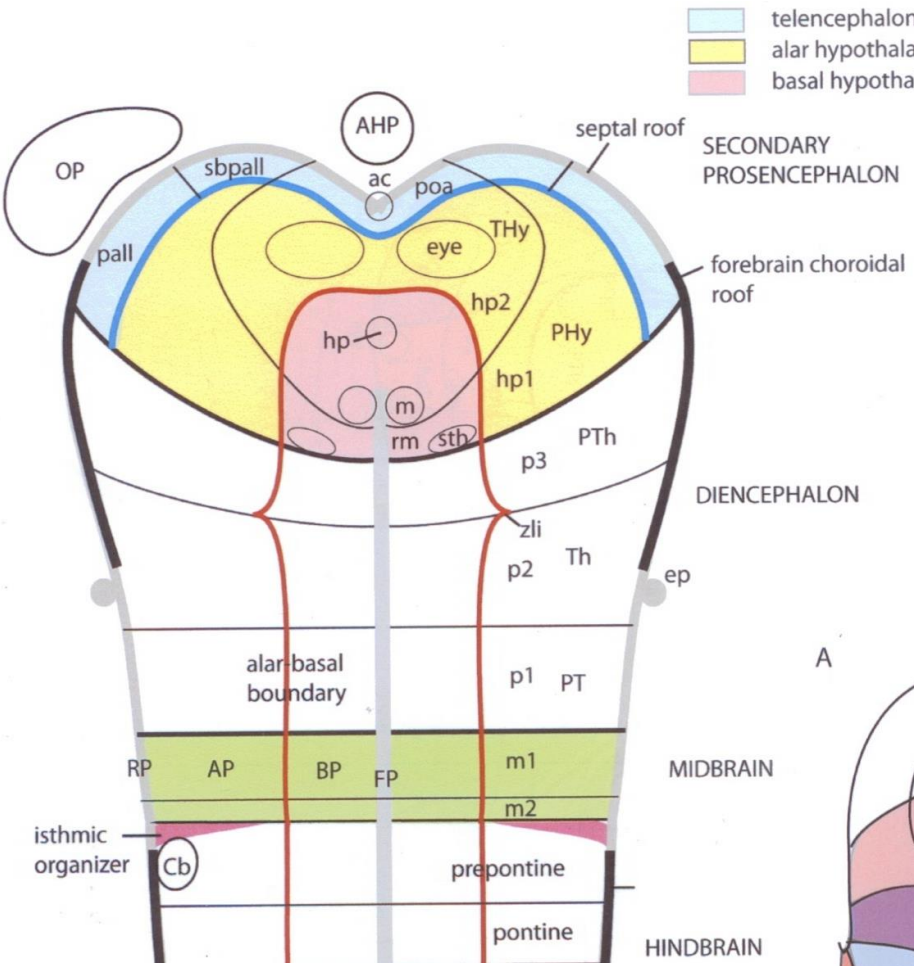
Subpallium: rostral to telencephalon, bordering on the hypothalamus

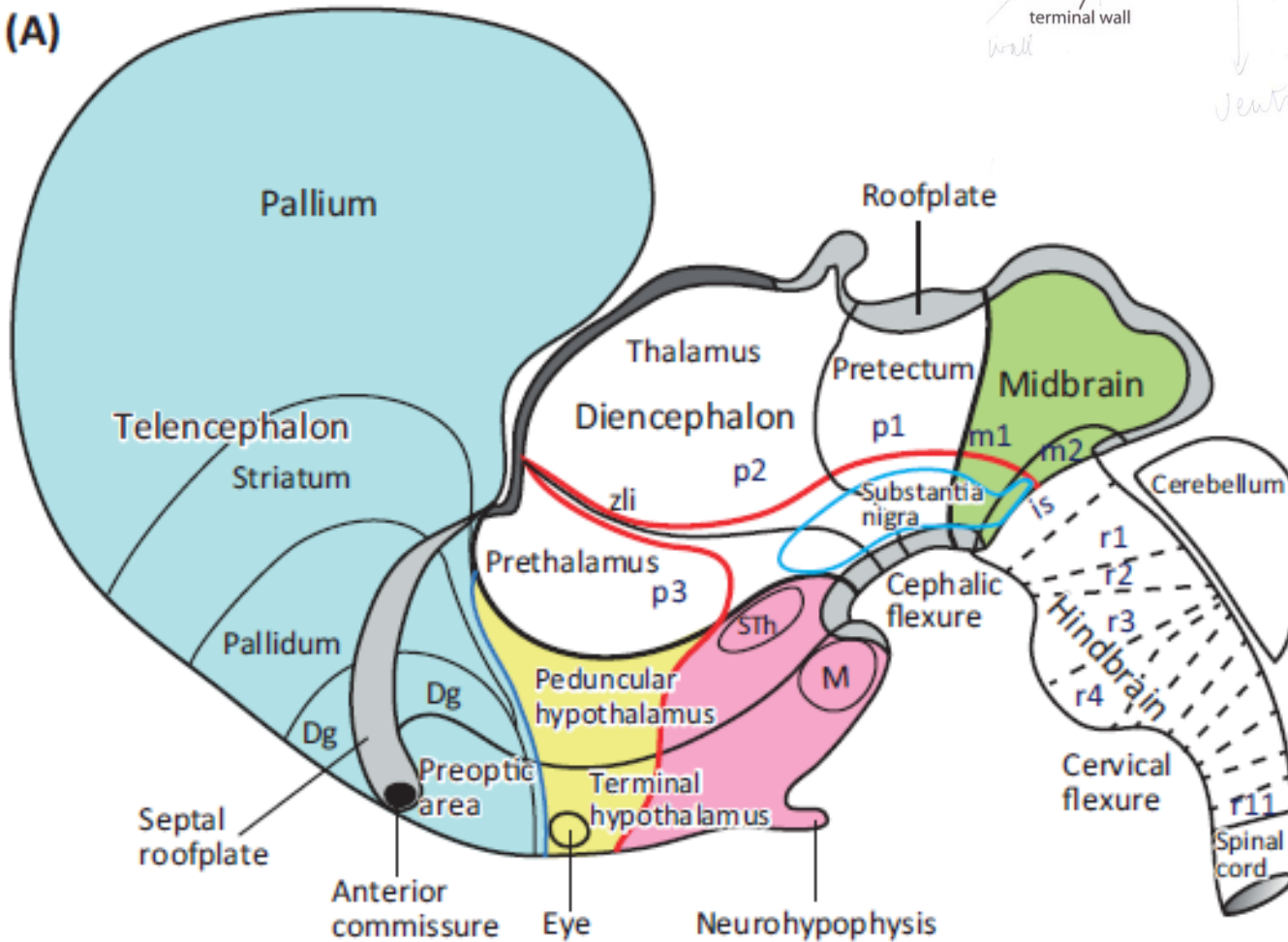**Preoptic area**: the rostralmost region of telencephalon

Scheme of segmental development

(based on mouse model)

Puelles et al, Trends in Neurosci, 2013.

Ventral surface of diencephalon, Hypothalamus

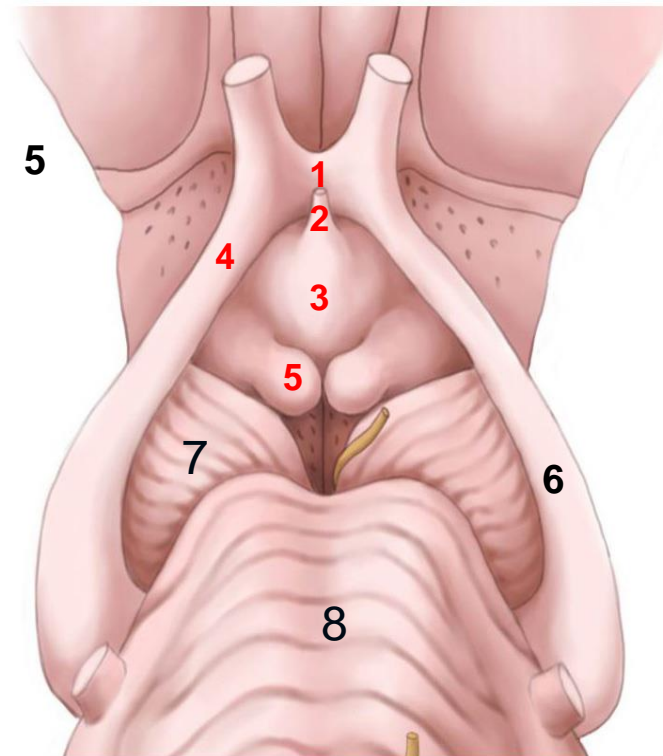1. optic chiasm

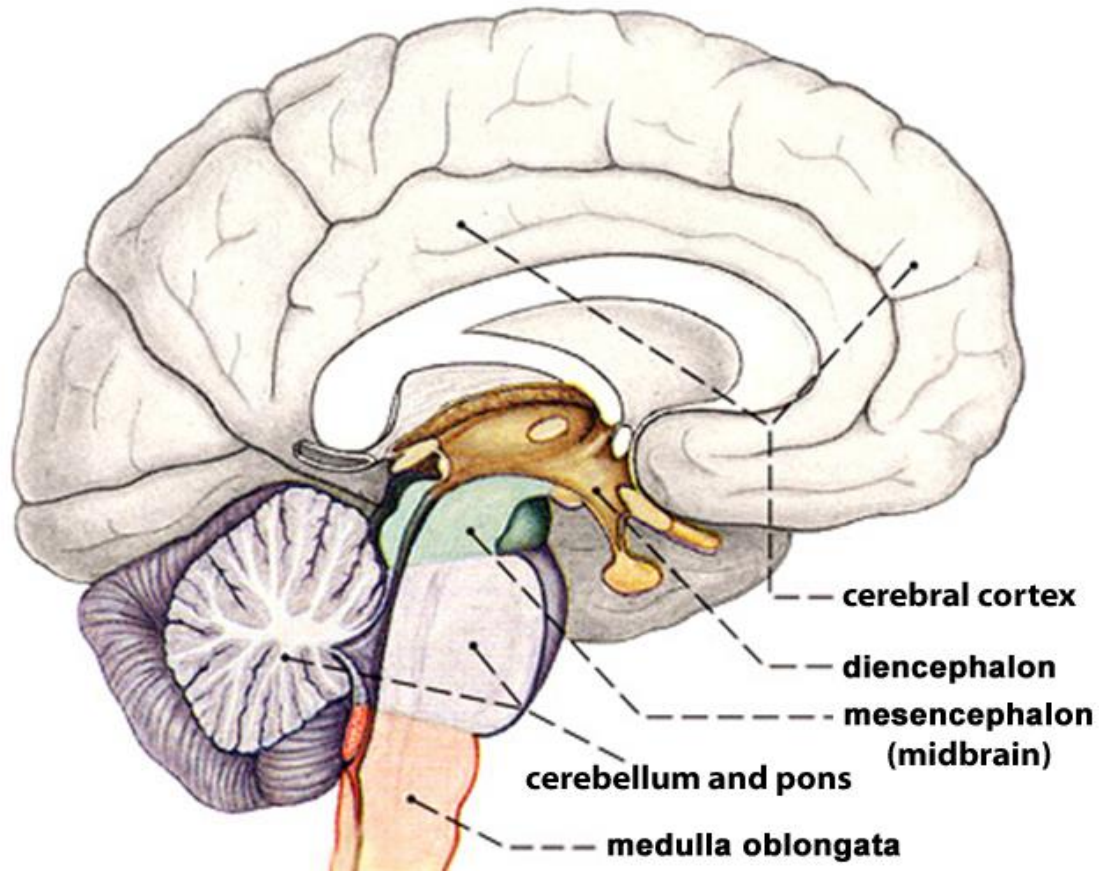2. infundibulum

3. tuber cinereum

4. optic tract

5. mamillary body

7. cerebral peduncle

8. pons

Position of diencephalon

cerebral cortex
diencephalon
mesencephalon (midbrain)
cerebellum and pons
medulla oblongata

Diencephalon, aspect from the third ventricle

Levels of diencephalon
(classic description)

- **Thalamus**

- **Epithalamus**

- **Metathalamus**

- **Subthalamus**

- **Hypothalamus**

1 – fornix
2 – commissura ant.
3 – thalamus
4 – tela choroidea ventriculi tertii
5 – corpus callosum
6 – commissura habenularum
7 – pars tecta columnae fornicis
8 – adhaesio interthalamica
9 – foramen interventriculare (Monroi)
10 – corpus mammillare
11 – chiasma opticum
12 – corpus pineale
13 – commissura posterior
14 – septum pellucidum
15 – lamina tecti

The walls of third ventricle

Lateral: thalamus, hypothalamus

Anterior: column of fornix, ant commissure,

                lamina rostralis, lamina terminalis

Posterior   epithalamus

Inferior: hypothalamus (optic chiasm,

                infundibulum, mamillary body,

                 cerebral peduncle

Superior: tela choroidea of third ventricle
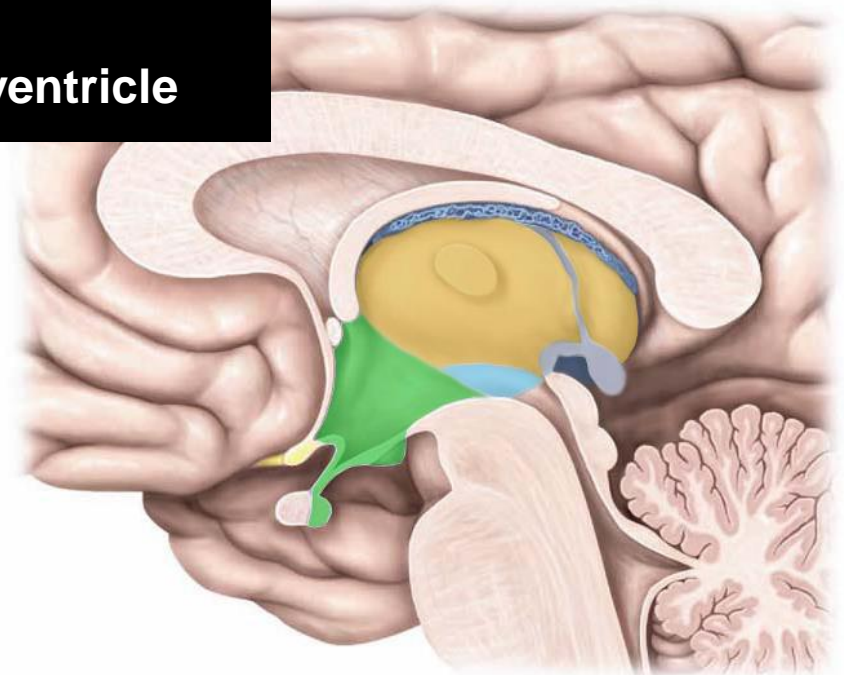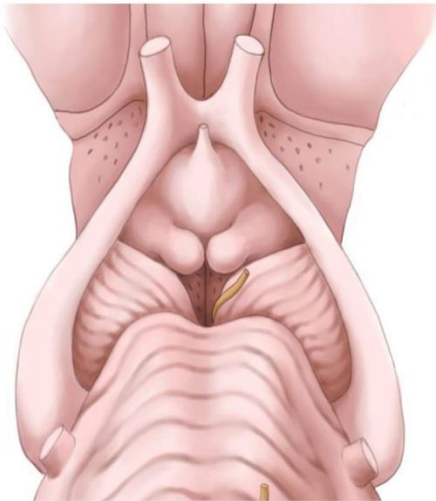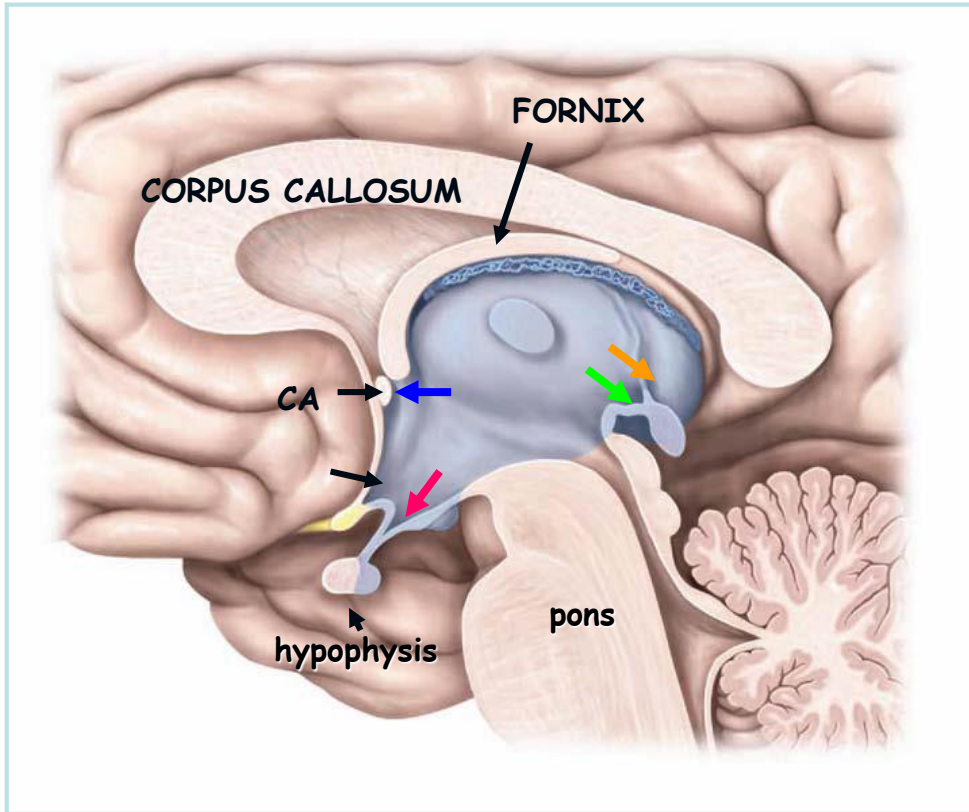
The recesses of third ventricle

Triangular recess

optic recess

infundibular recess

suprapineal recess

pineal recess