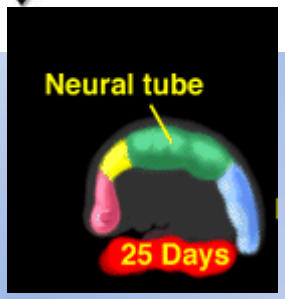
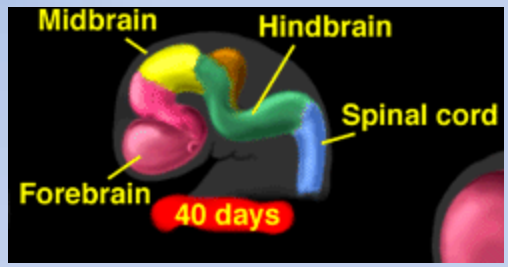
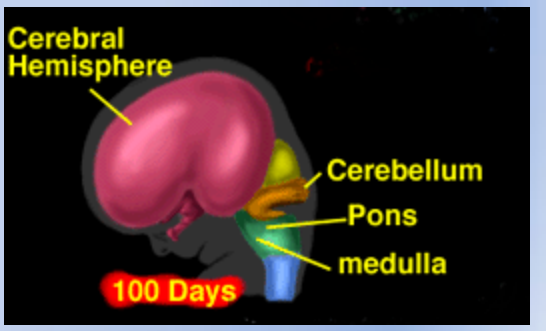




MSS Embriyolojisi

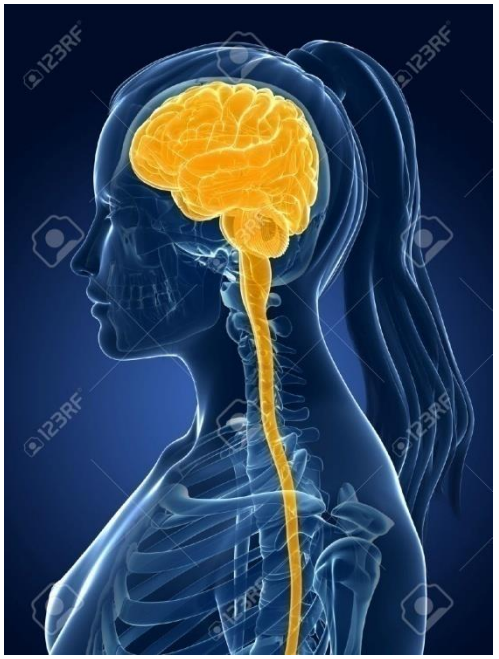


N. Cenk SAYIN

Trakya Üniversitesi Tıp Fakültesi

İstanbul-01/10/2017

Sinir sistemi



- Merkezi sinir sistemi (MSS): ensefalon+medulla spinalis

- Periferik sinir sistemi (PSS): MSS dışındaki nöronlar ve periferal yapılar, beyin ve medulla spinalisi bağlayan kranial ve spinal sinirler

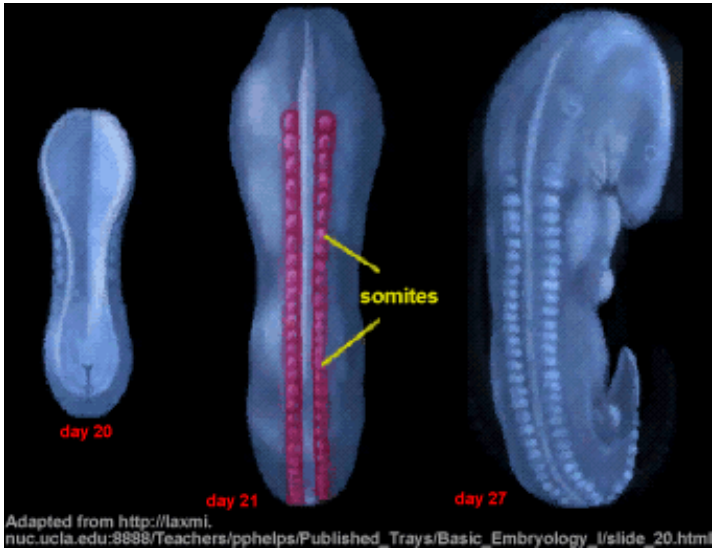
- Otonom sinir sistemi (OSS): Düz kas, kalp kası veya bez epitelini innerve eden MSS ve PSS nöronları

3. Hafta – Nörülasyon

Nörülasyon;

- Nöral tüpün oluşumudur

- **4. hafta** başında 4-6. somitlerin bulunduğu bölgede başlar

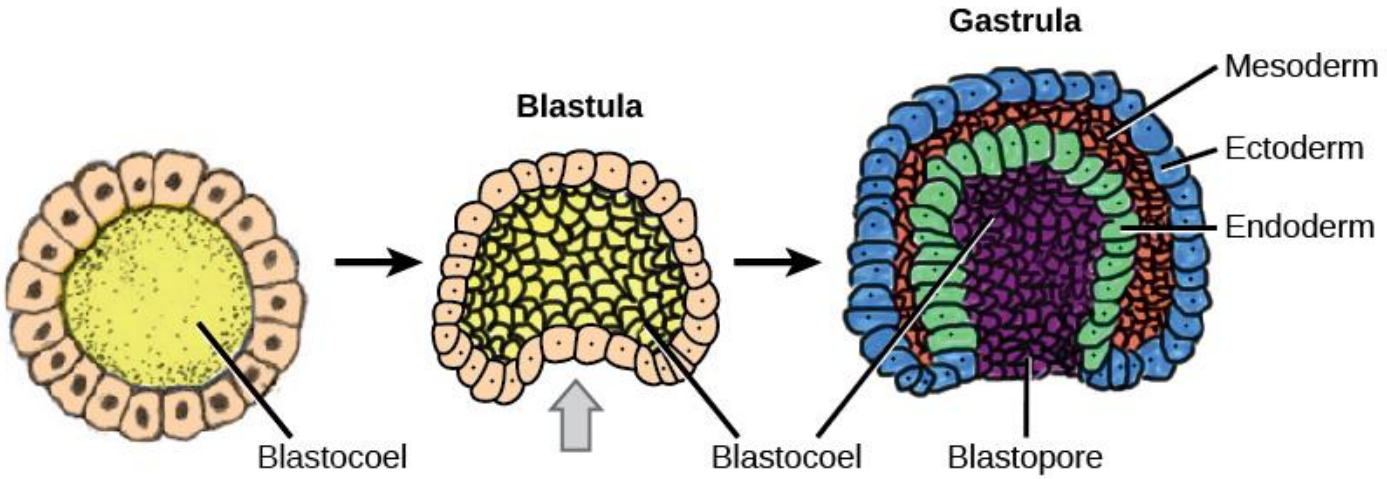


  - *Kranial 2/3:* beyin

  - *Kaudal 1/3:* medulla spinalis'i meydana getirir

3. hafta

- Mezoblastın ortaya çıkmasıyla embriyonal disk 3 tabakalı hale gelir (Bu dönemde embriyoya **trilaminar germ diski=gastrula**, olaya da **gastrulasyon** denir)

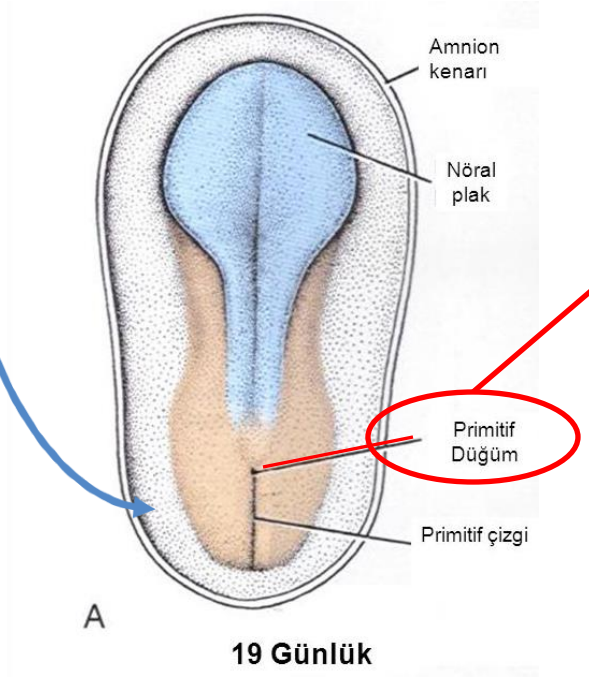


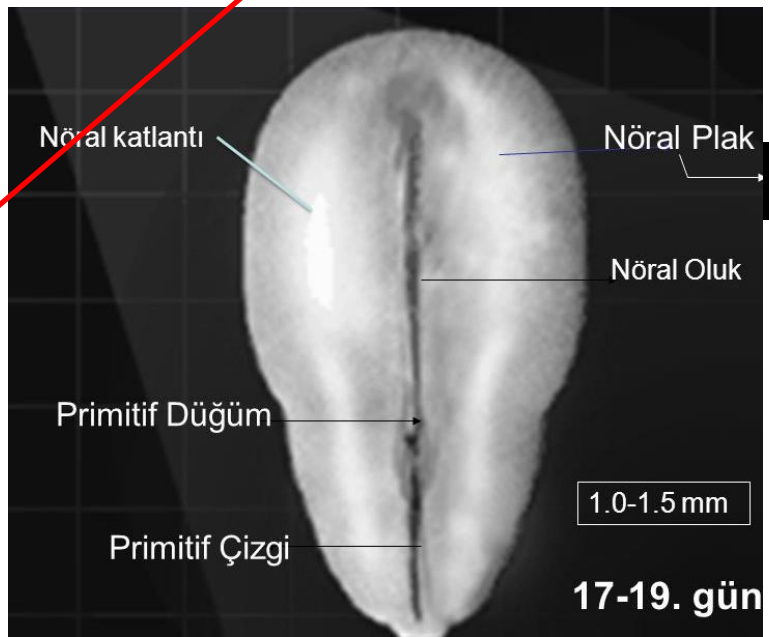
3 önemli olay:

- **Primitif çizginin oluşması**
- **Notokordun oluşması**
- **Üç germ tabakasının farklılaşması**

3. hafta-Primitif çizgi

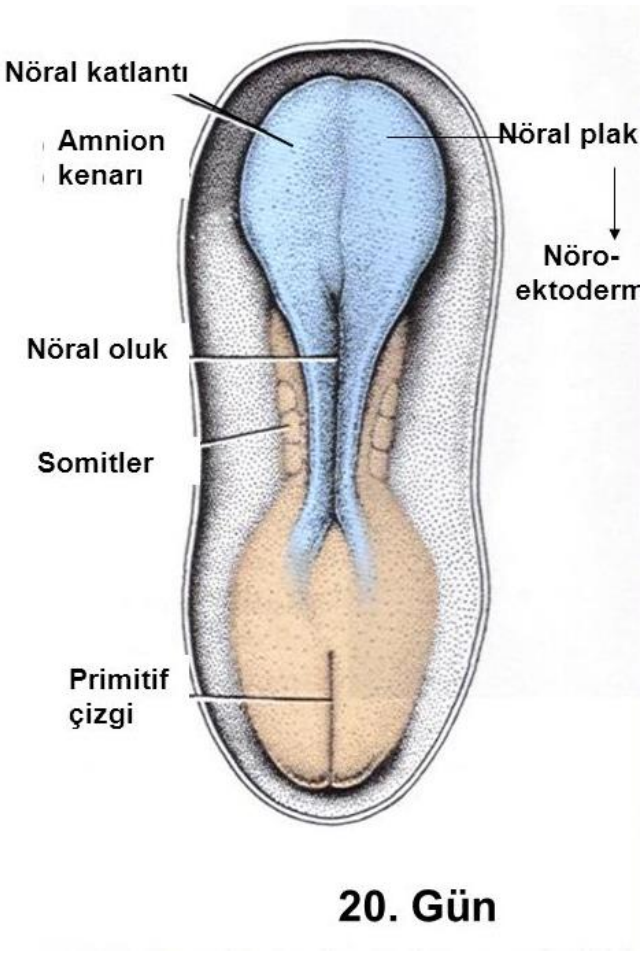
- 3. hafta başında, embriyonel diskin dorsal yüzünde, orta çizgi kaudalinde, kalın şişkin, çizgisel bir bant gözlenir
- **Epiblast** hücrelerinin çoğalarak toplanması ile oluşan bu çizgiye **primitif çizgi** denir.
- Primitif çizgi kaudal ucuna hücrelerin eklenmesi ile uzar, kranial ucunda hücre proliferasyonu ile **primitif düğüm** adını alır.





3. hafta-Primitif çizgi

- Kısa bir süre sonra bu çizginin ortası boyunca uzanan **primitif oluk (yarık)** belirir.

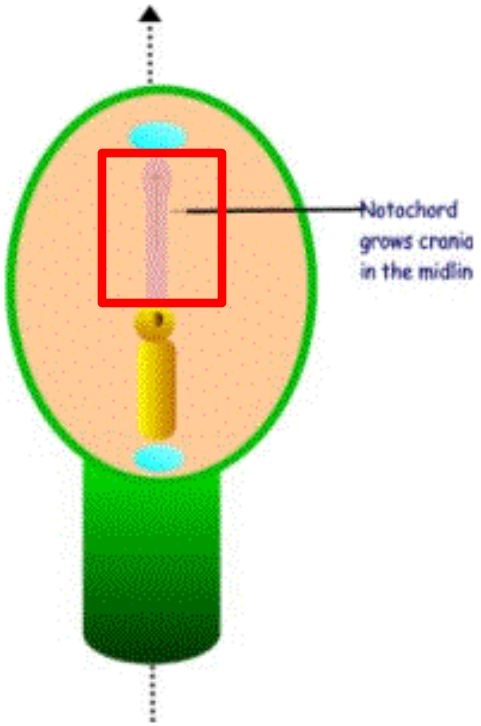


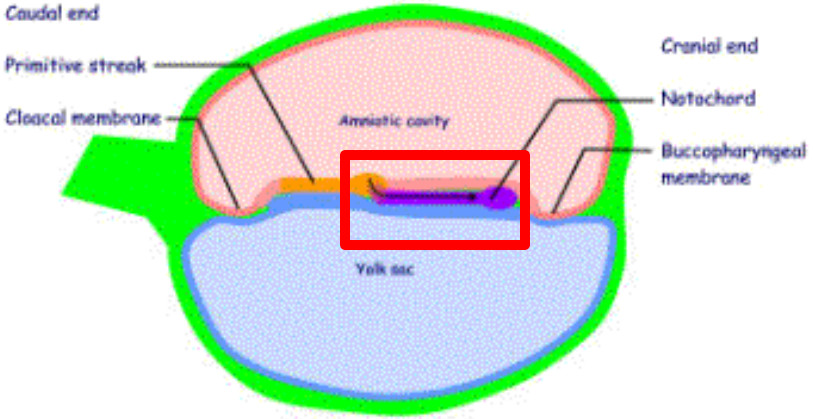
- **Sinir sistemi,** primitif çizginin ön kısmındaki **ektodermden (nöral plak)** gelişir (*23.gün*)
- ***Nöral plak;*** notokord ve paraaksiyal mezodermin ektodermi indüklemesiyle ortaya çıkar

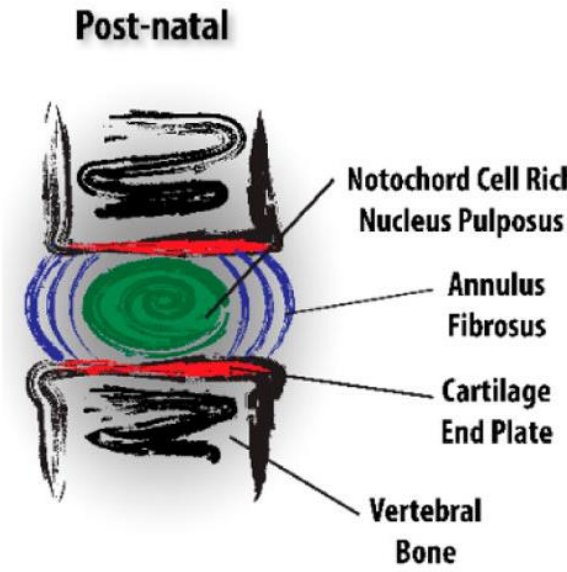
3. Hafta – Notokord

- **Notokord** hücresel bir kordon- embriyonun ilkel iskeletini meydana getirerek dik durmayı sağlar
- Kas-iskelet yapıları, MSS gelişimi için gerekli sinyalleri verir (erken embriyoda primer uyarandır)*

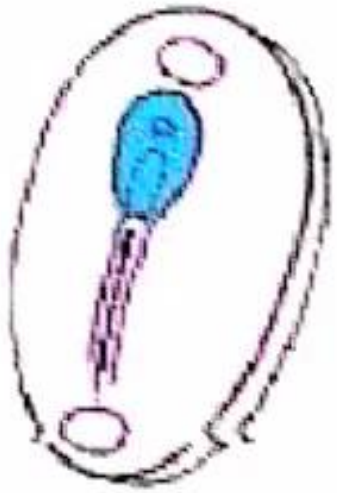
- Erişkinde→ İntervertebral disklerin yapısına katılır.

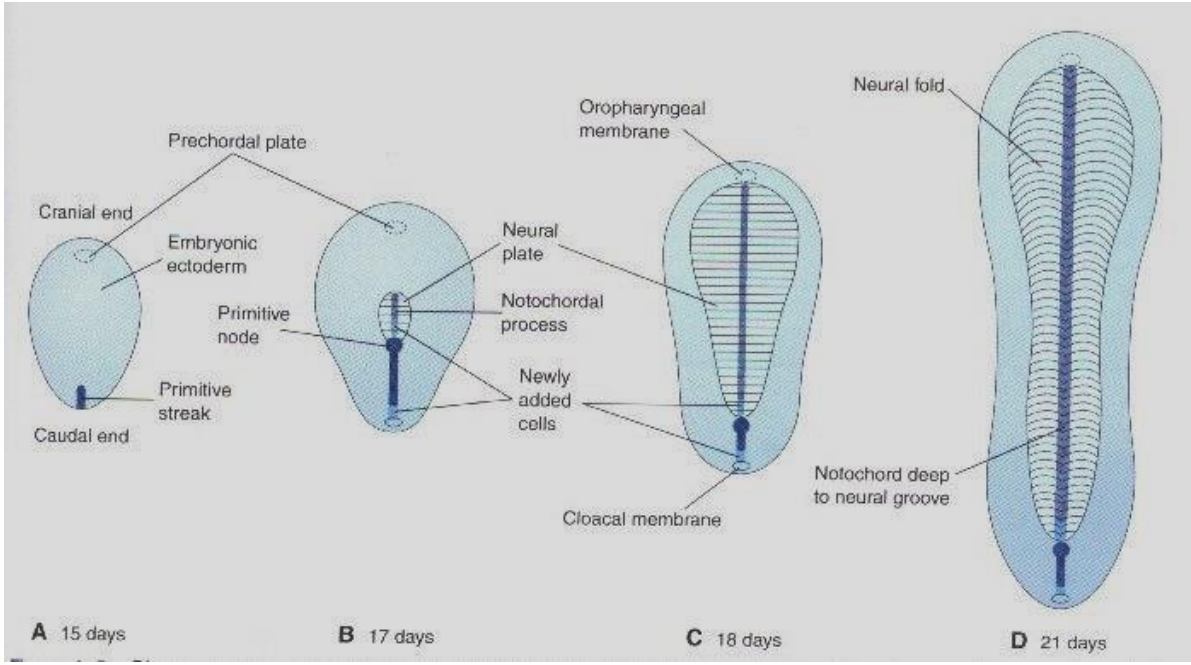






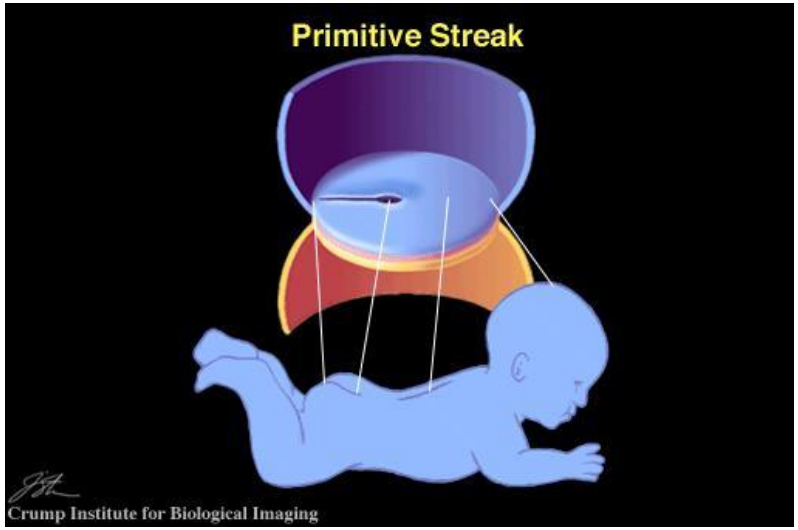
3. hafta





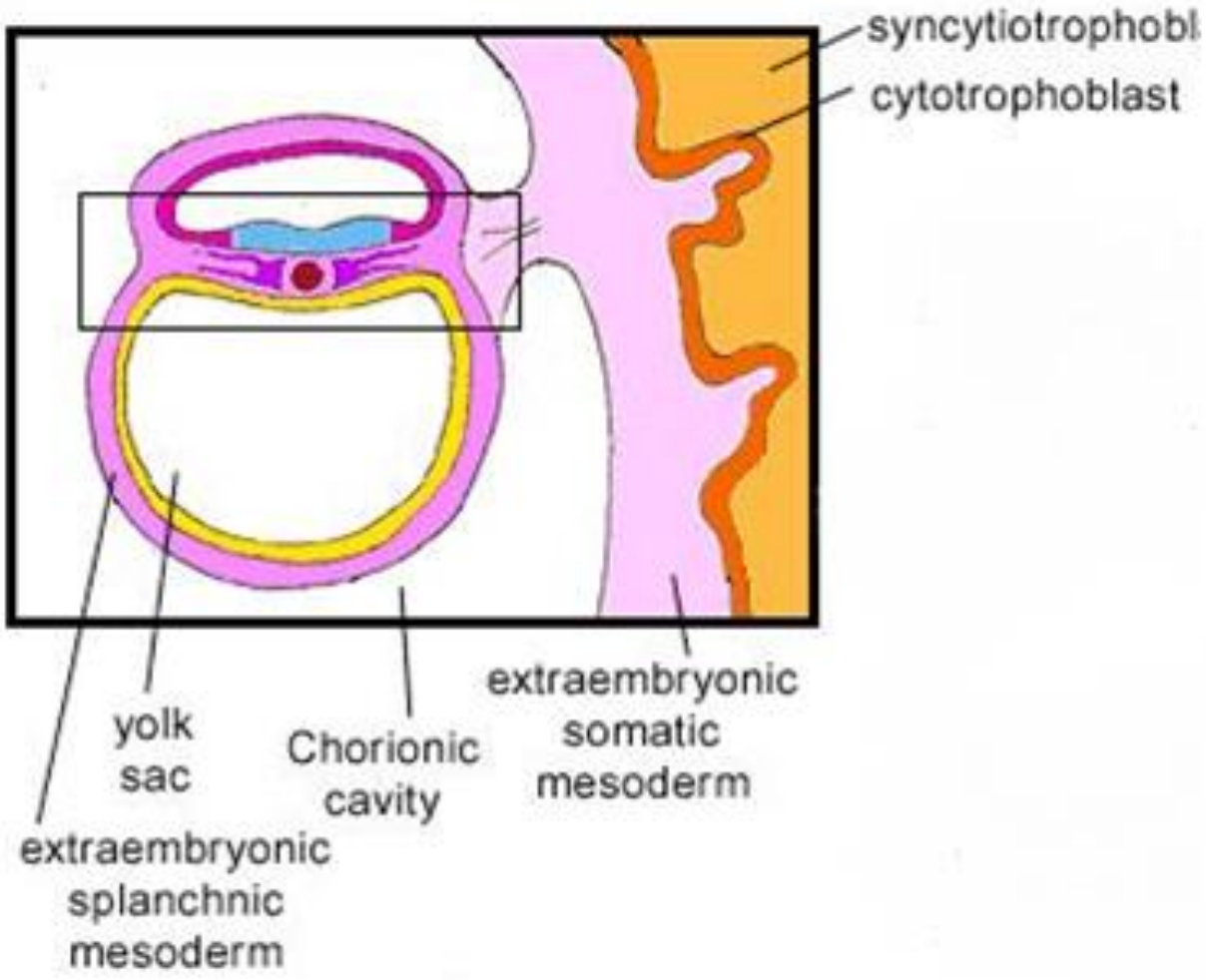
3. hafta-Primitif çizgi

- Primitif çizginin boyutu göreceli azalarak embriyonun sakrokoksigeal bölgesinde önemsiz bir yapı haline gelir
- Normal koşullarda: 4.haftanın sonunda kaybolur
- Primitif çizgi kalıntılarının varlığını sürdürmesi → "***sakrokoksigeal teratom***"



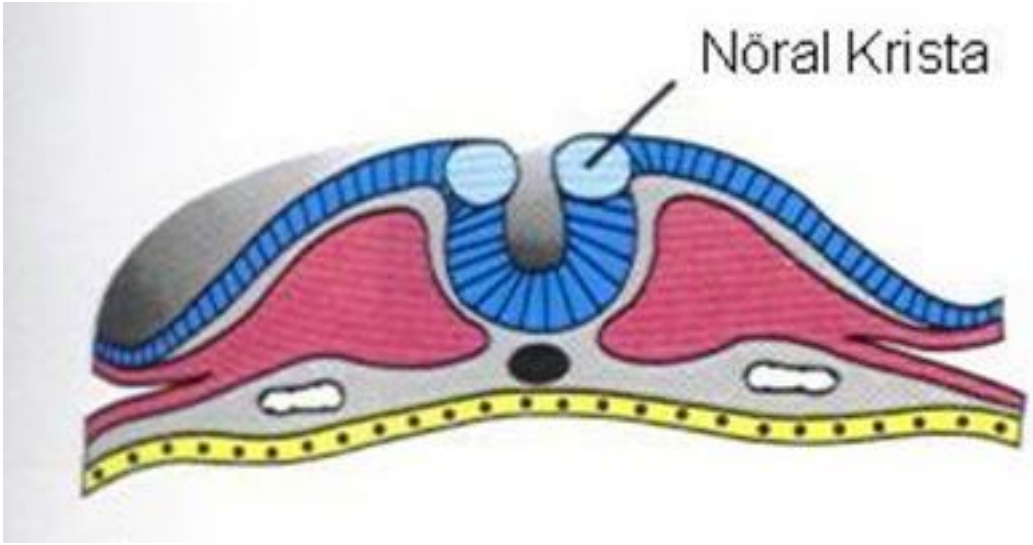
Nöral Tüp

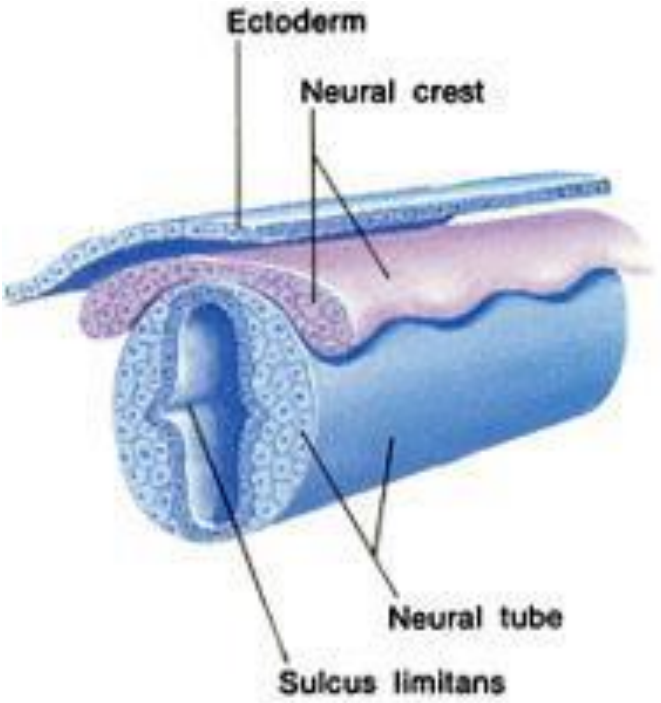
- **Nöral plak:** MSS ve medulla spinalis gelişir.



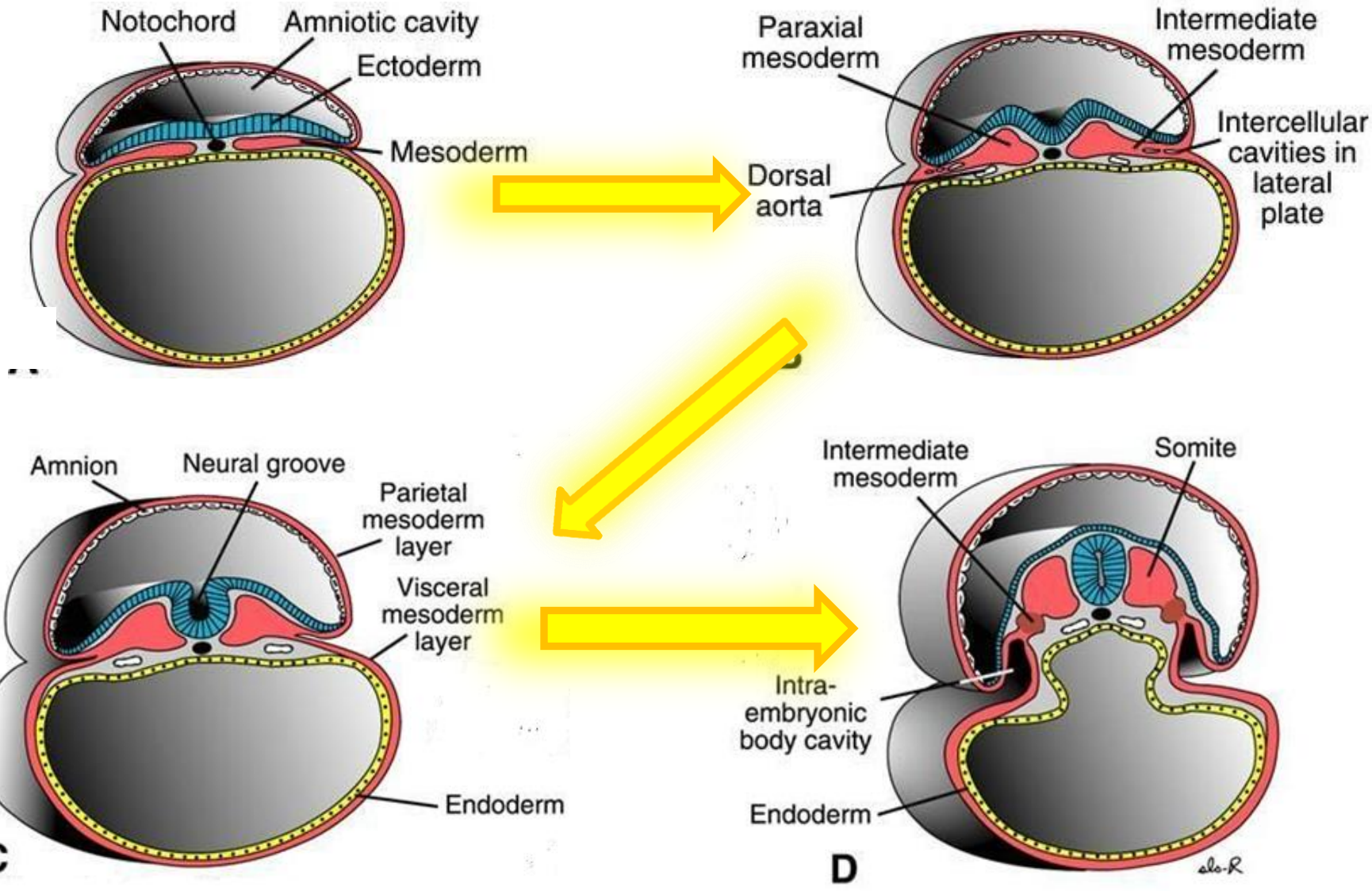
3. hafta-Nörülasyon

- Nöral tüp, yüzey ektoderminden ayrılınca; nöral tüpün her iki yanındaki hücreler dorsolaterale göç eder ve nöral tüp ile yüzey ektodermi arasında ***nöral krista***yı oluşturur





Nöral Tüp


Notochord
Amniotic cavity
Ectoderm
Mesoderm
Paraxial mesoderm
Intermediate mesoderm
Intercellular cavities in lateral plate
Dorsal aorta
Amnion
Neural groove
Parietal mesoderm layer
Visceral mesoderm layer
Endoderm
C
Intermediate mesoderm
Somite
Intra-embryonic body cavity
Endoderm
D

3. hafta-Nörülasyon

- **Nöral tüp**; Beyin + medulla spinalis

- **Nöral krista**; Periferik ve Otonom SS dahil kranial, spinal ve otonomik ganglionları oluşturan hücrelerin çoğunu meydana getirir.

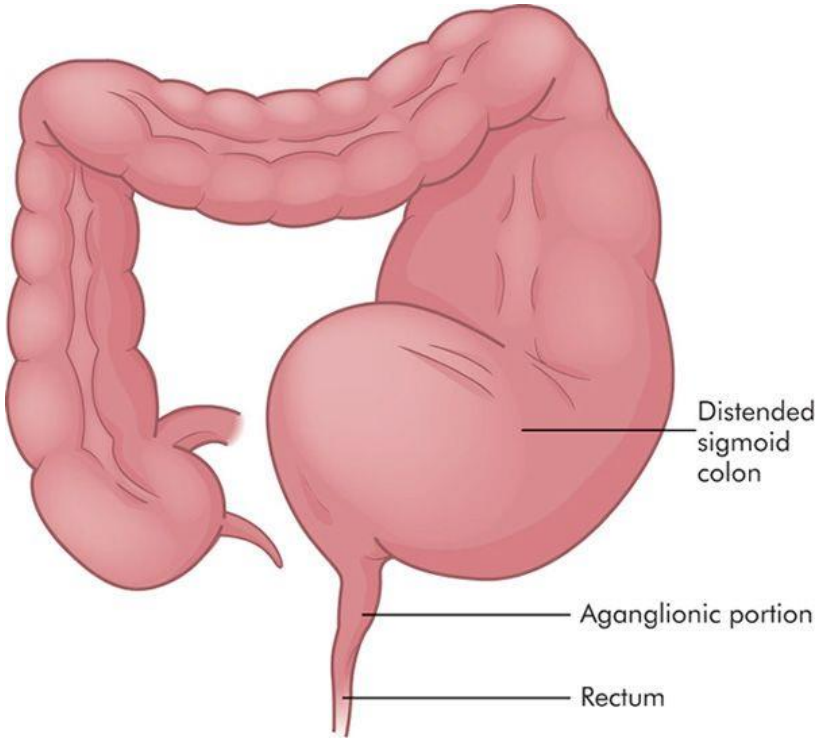
  – *Tiroid bezi C hücreleri, odontoblastlar, adrenal medulla, melanositler, yüz ve boyun derisi, yüz ve kafatasının kemik ve yumuşak dokuları* vb. yapıları da oluşturur.

Hirschsprung (Aganglionik megakolon)

- Konjenital megakolon

(Kolonun bir parçasının aşırı dilatasyonu)

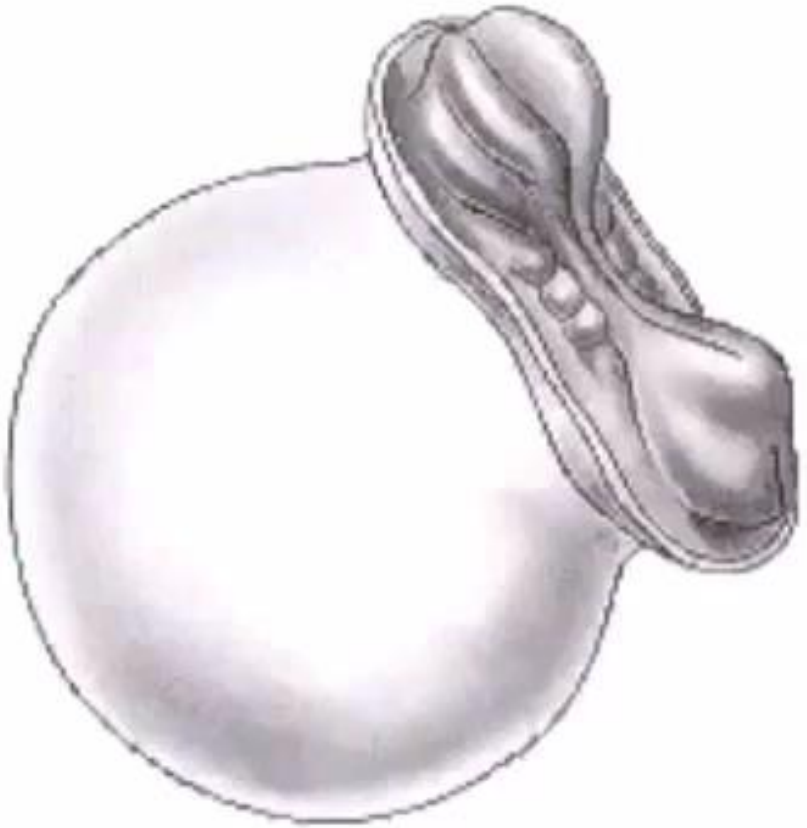
  - Dilatasyon → genişlemiş bağırsak parçasının distalinde plexus myentericus'ta **otonomik ganglion hücrelerinin olmaması**



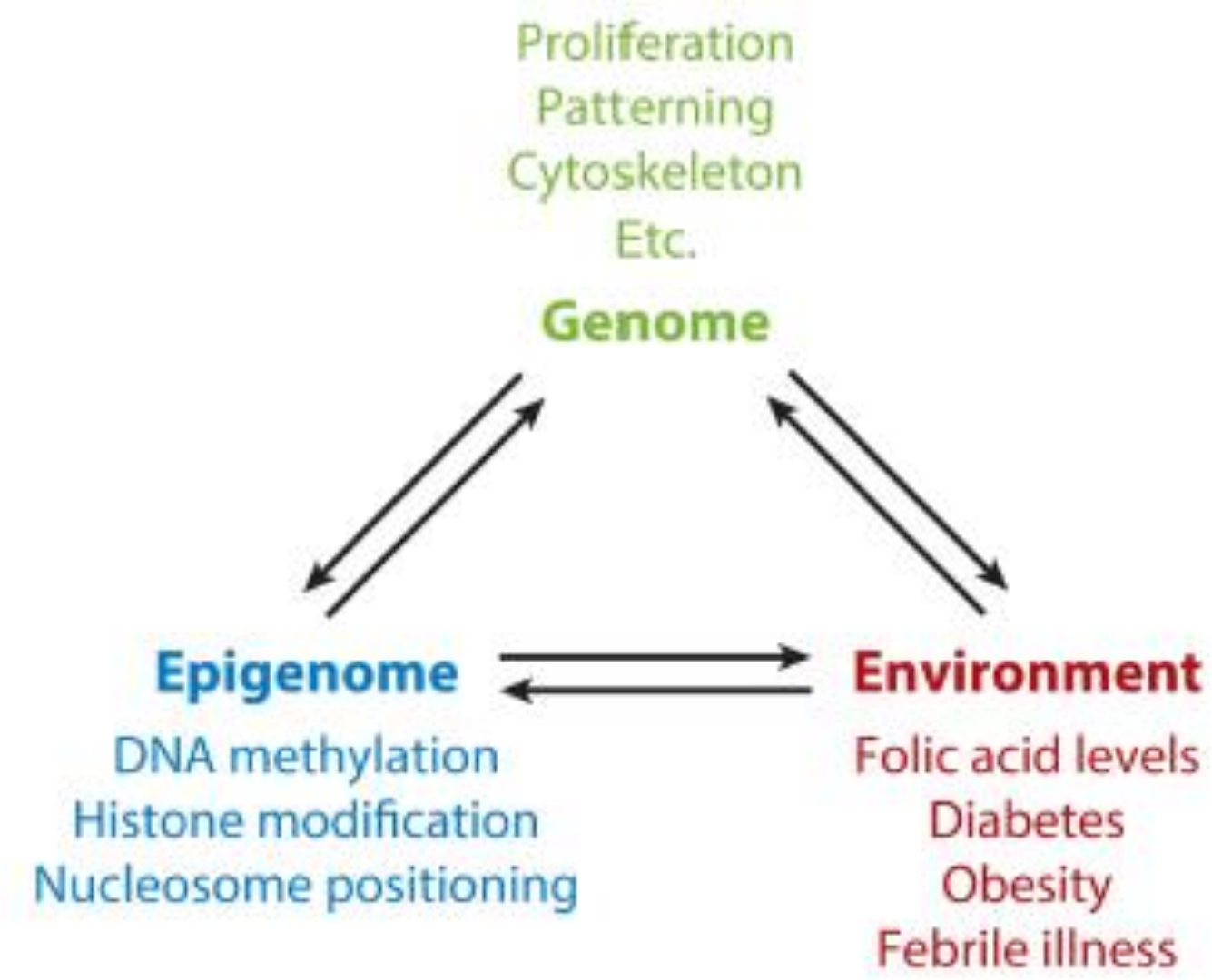
- *Kolon duvarına nöral krista hücreleri göç edemez ve parasempatik ganglion hücrelerine farklanamazlar*

3. hafta-Nörülasyon

- **Nöral tüp kapanması:**
  - **kranial** (anterior nöropor) *24. gün*
  - **kaudal** (posterior nöropor) *26.gün* kapanmasıyla sonlanır (Önce servikalde, sonra kaudal ve sefalik iki yönlü olacaktır)



Nöral Tüp


Proliferation
Patterning
Cytoskeleton
Etc.
Genome
Epigenome
DNA methylation
Histone modification
Nucleosome positioning
Environment
Folic acid levels
Diabetes
Obesity
Febrile illness

Nöral Tüp

Annu Rev Genet. 2014 ; 48: 583–611. doi:10.1146/annurev-genet-120213-092208.

Genetic, Epigenetic, and Environmental Contributions to Neural Tube Closure

Jonathan J. Wilde[1,2,*], **Juliette R. Petersen**[1,3,*], and **Lee Niswander**[1,*]

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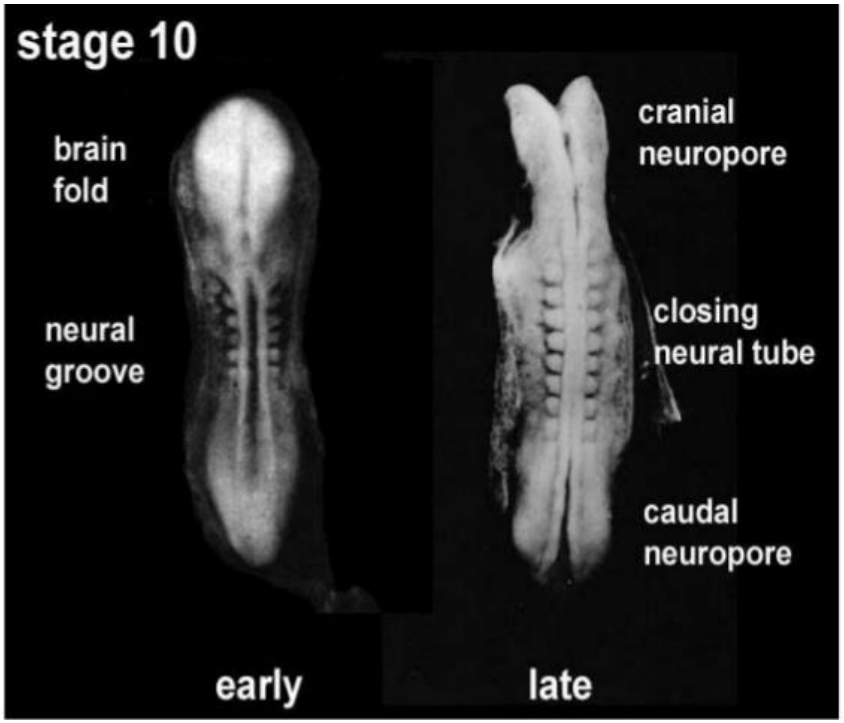
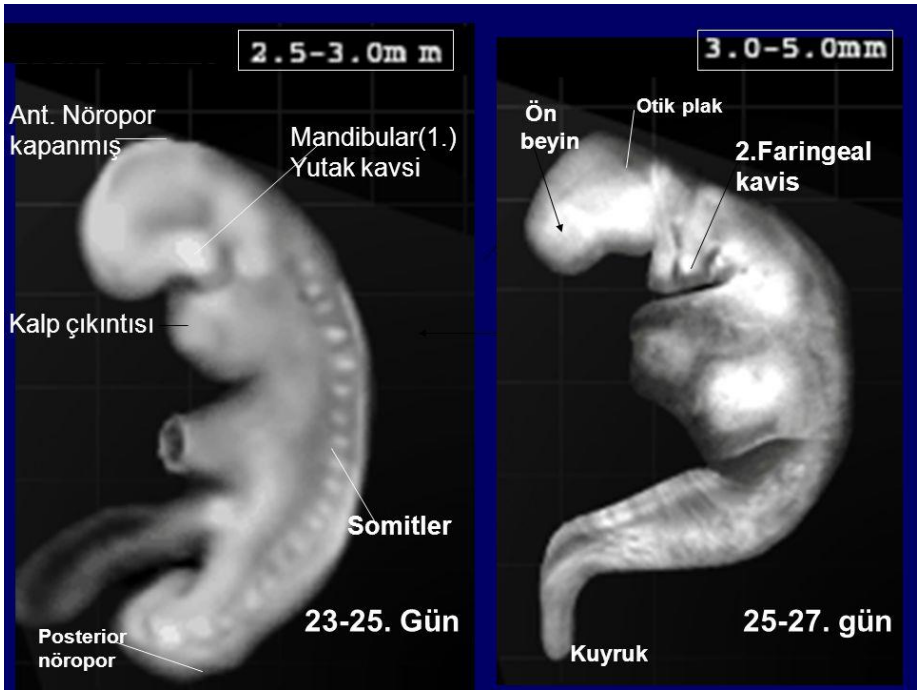
Epigenetic regulators required for neural tube closure

Gene	Protein	Function	Observed Neural Tube Defect
Ppm1g	PPM1G	Chromatin remodeling	Exencephaly
Dnmt3a	DNMT3A	DNA methylation	Exencephaly
Dnmt3b	DNMT3B	DNA methylation	Exencephaly
Dnmt3L	DNMT3L	DNA methylation	Exencephaly
CBP	CBP	Histone acetylation	Exencephaly
Kat2a	GCN5	Histone acetylation	Exencephaly
Ep300	p300	Histone acetylation	Exencephaly
Hdac4	HDAC4	Histone deacetylation	Exencephaly
Sirt1	SIRT1	Histone deacetylation	Exencephaly
Kdm2b	FBXL10	Histone demethylation	Exencephaly
Kdm6a	UTX	Histone demethylation	Exencephaly
Uty	UTY	Histone demethylation	Exencephaly
Alkbh1	ALKBH1	Histone methylation	Exencephaly
Jmj	JARID2/Jumonji	Histone methylation	Exencephaly
Cited2	CITED2	Co-regulator of CBP/p300	Exencephaly
Smarcc1	BAF155	Nucleosome remodeling	Exencephaly
Smarca4	BRG1	Nucleosome remodeling	Exencephaly
Cecr2	CECR2	Nucleosome remodeling	Exencephaly
mIR-124a	N/A	Nucleosome remodeling	Spina bifida
*mIR-9**	N/A	Nucleosome remodeling	Spina bifida
Nap1L2	NAP1L2	Nucleosome assembly	Exencephaly

Beyin Gelişimi

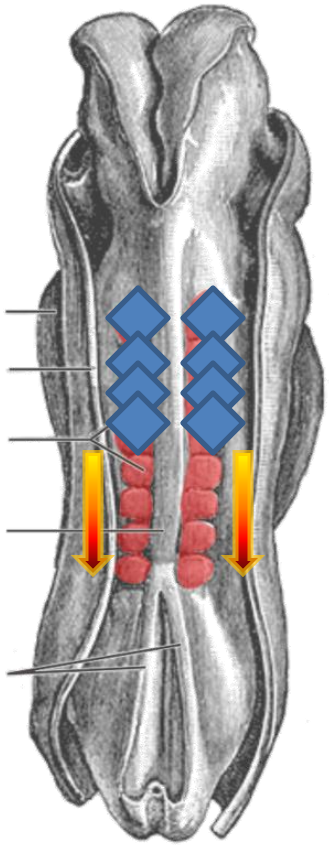
- Somitlerin **4. çifti kranialindeki** nöral tüp, beyni oluşturur……..

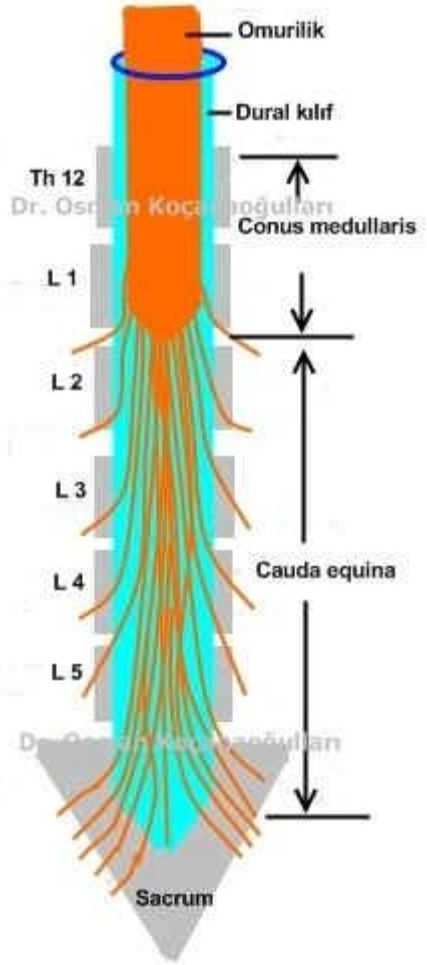




Medulla Spinalis Gelişimi

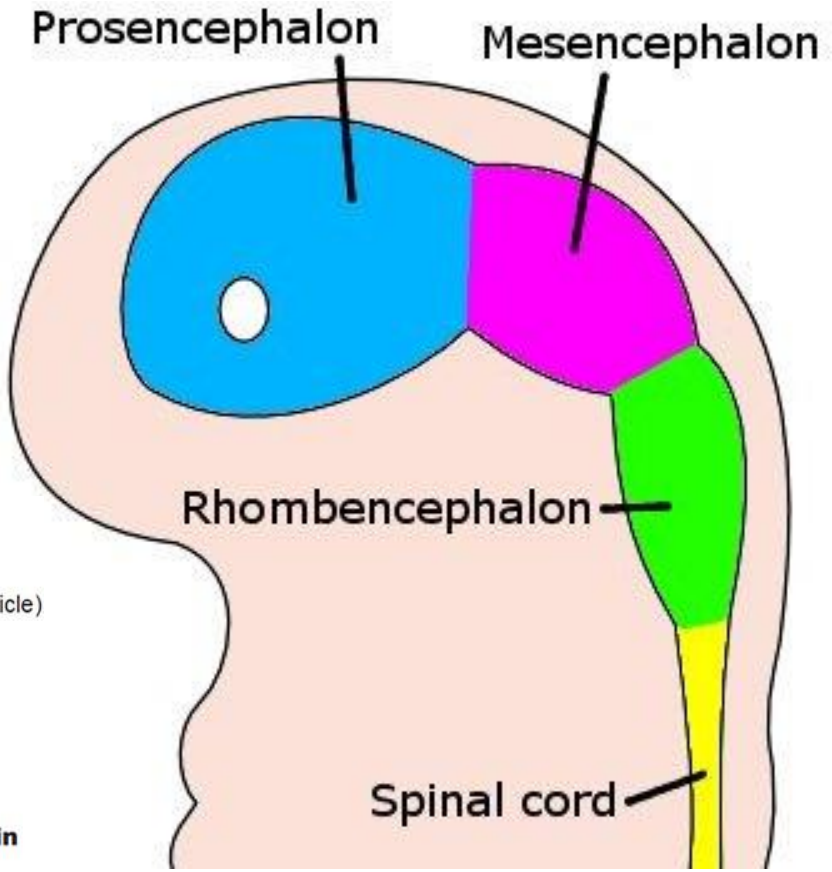
- *4. çift somit* kaudalinde kalan nöral tüp, medulla spinalis olarak gelişir

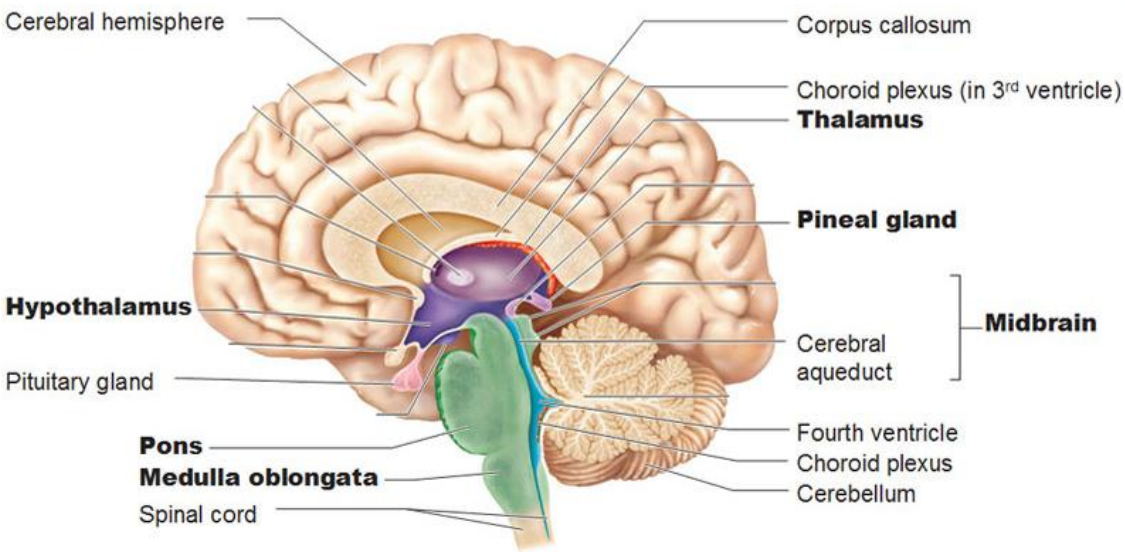




Beyin Gelişimi

- ***4. hf sonunda*** kranial bölgede rostral nöroporun kapanmasıyla beynin gelişeceği 3 ilkel beyin vezikülü oluşur:
  - Ön vezikül=prosencephalon
  - Orta vezikül=mesencephalon
  - Arka vezikül=rhombencephalon





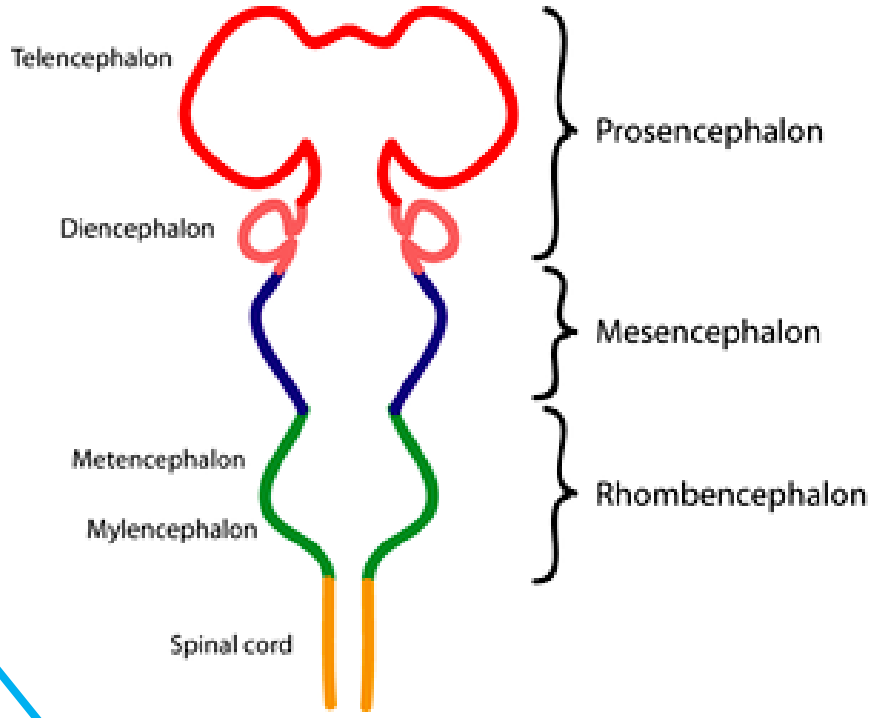
Beyin Gelişimi

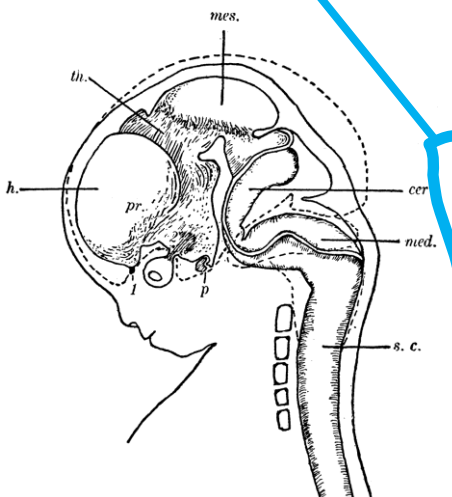
5. hafta

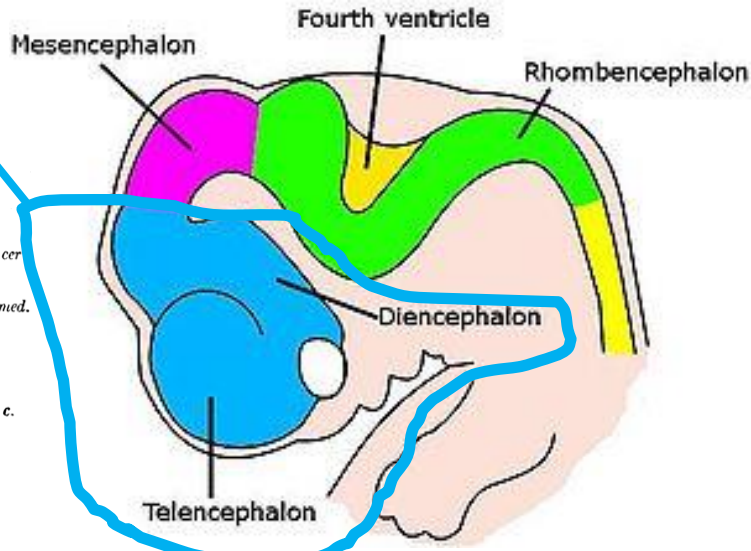
Prosencephalon
telencephalon
+ diencephalon

Mezensefalon
bölünmez!!!...

Rhombencephalon
metencephalon+
myelencephalon







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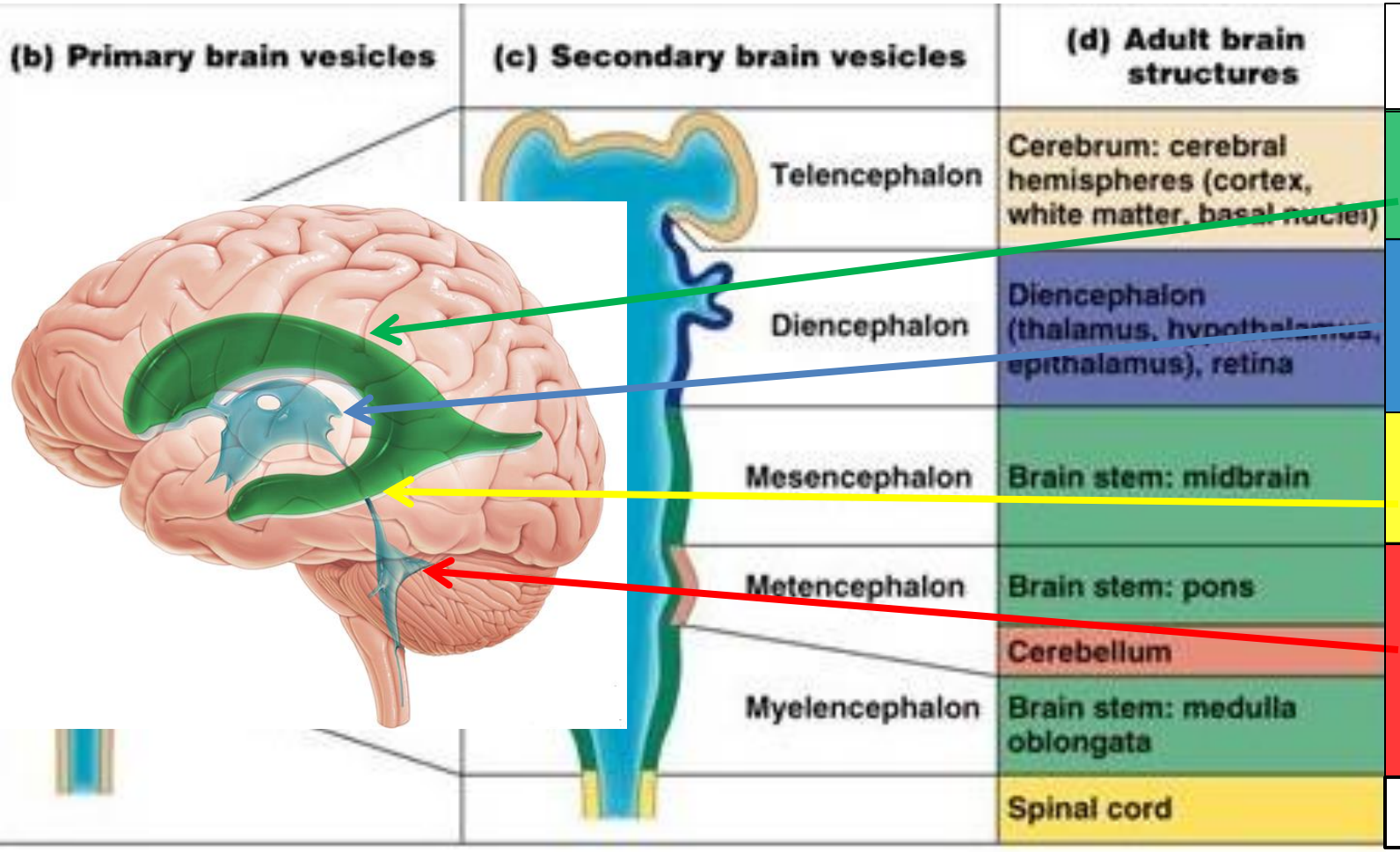

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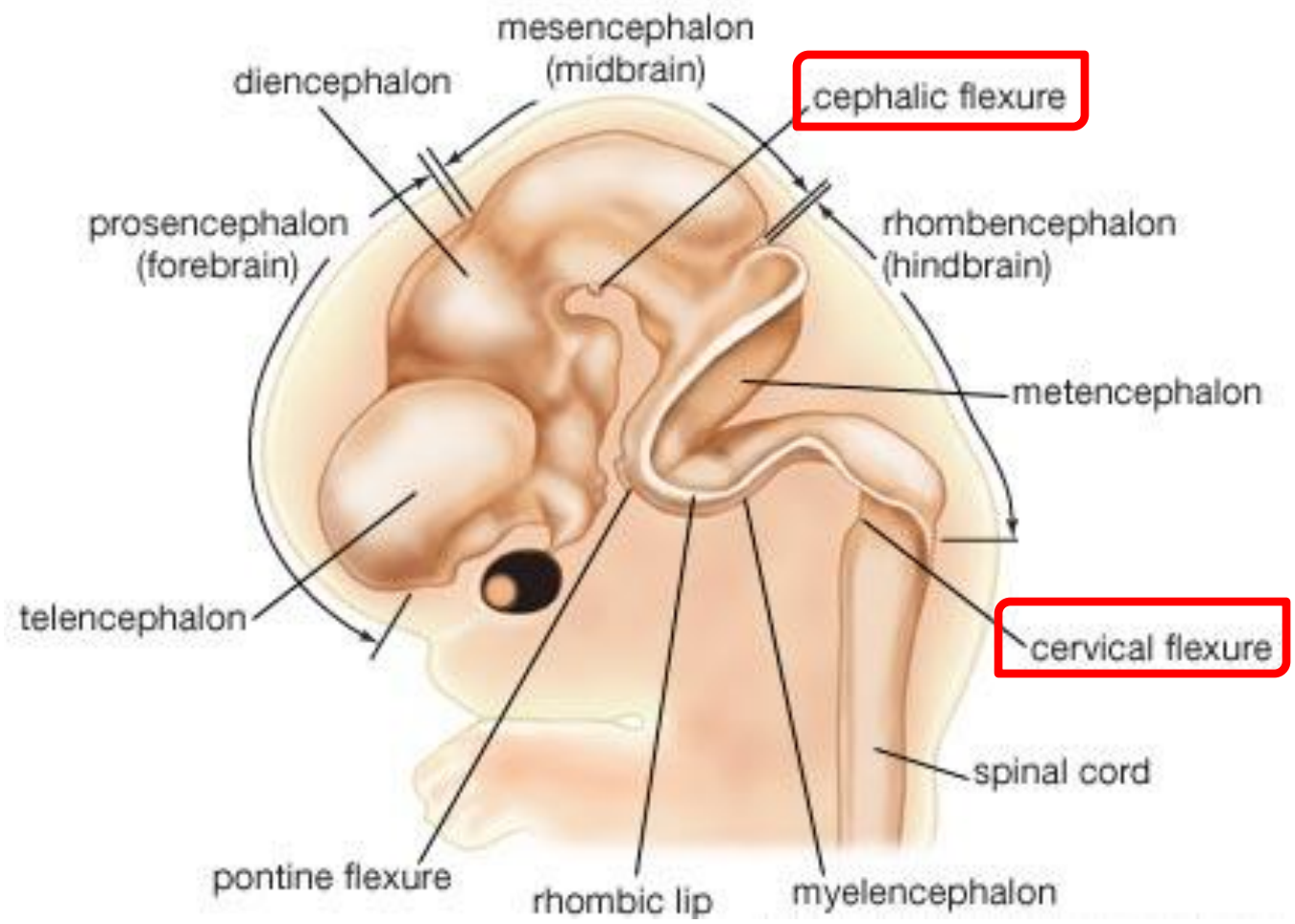
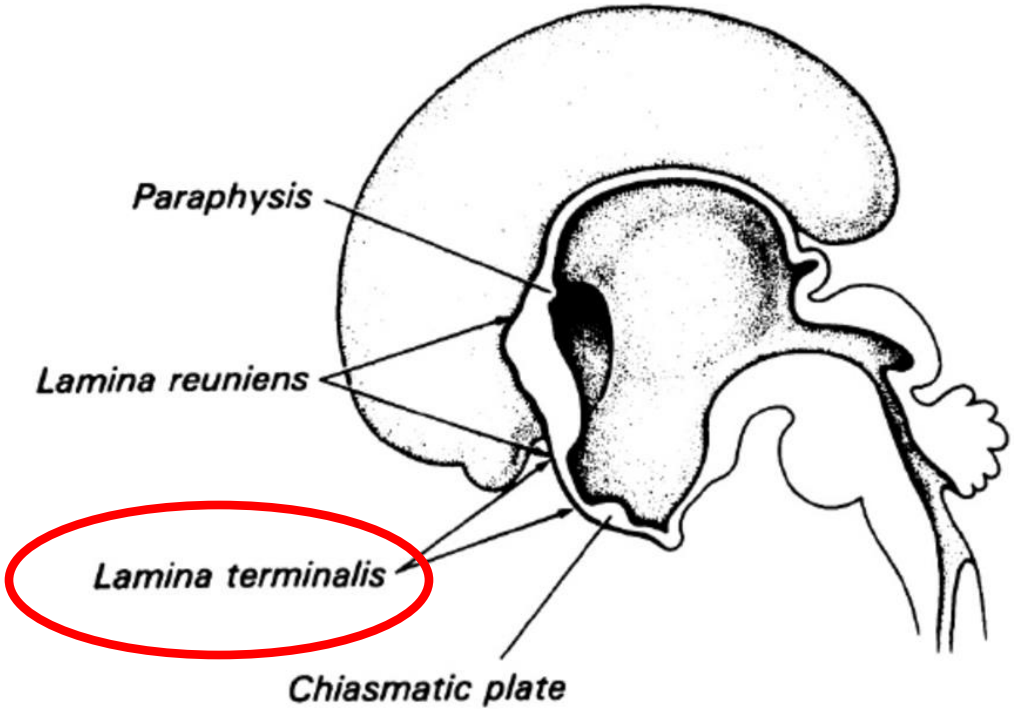
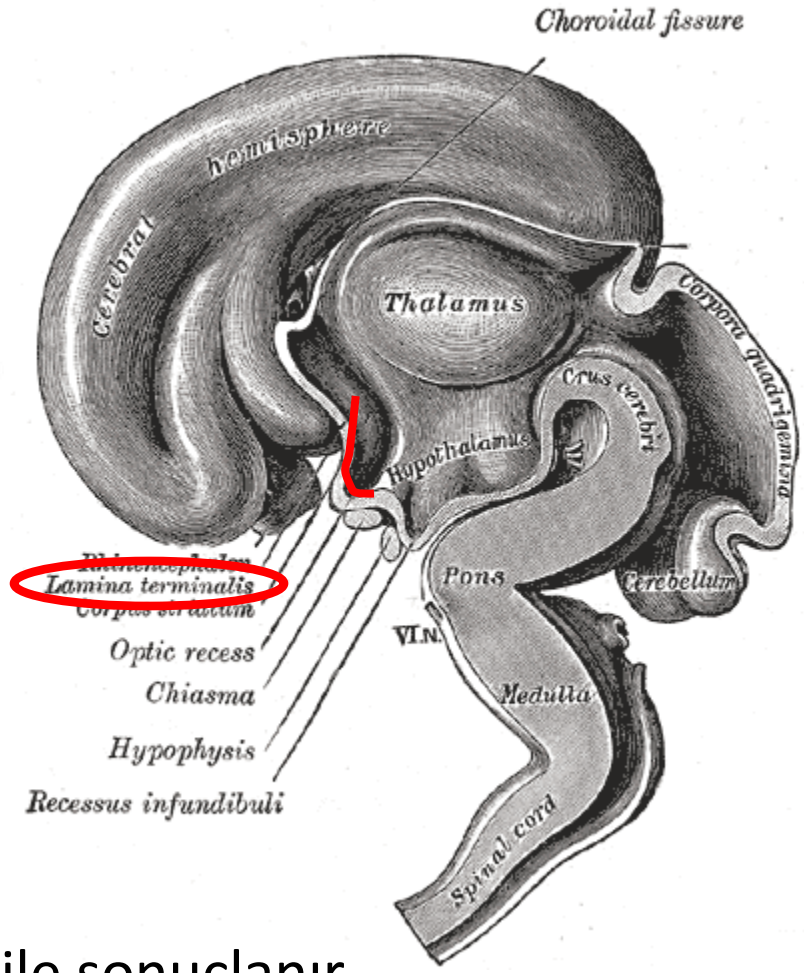


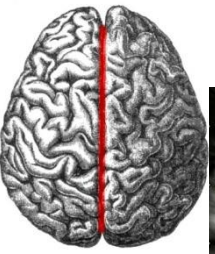
Beyin Gelişimi

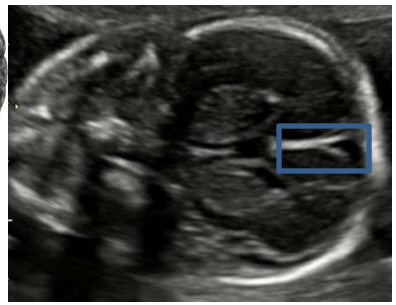


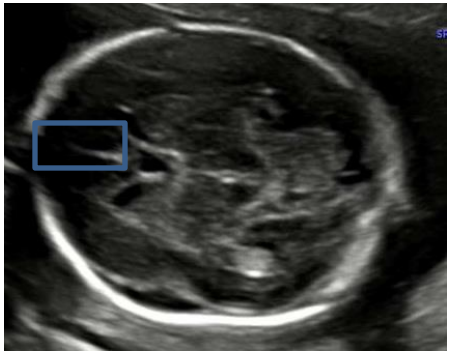


- Nöral tüpün rostral ucu
- Hatalı kapanması anensefali gelişimi ile sonuçlanır

Beyin Gelişimi







Ventral indüksiyon: Beynin 2 hemisfere ayrılması

Interhemisferik fissür ~10. haftada oluşur

Dural tabaka: 6. hf da oluşur

Primitif ventr medial duvarı kan damarından psödostratifiye epitelle kaplı **choroid pleksuslar** gelişir.

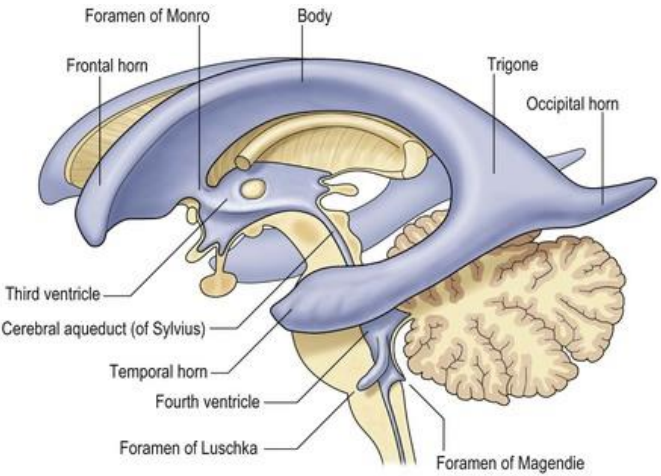
Erken gebelikte choroidde yüksek glikojen içeriği→ büyüyen beyin için enerji kaynağı – 19. hf sonrası CSF üretimi

Lat. Ventr: *13-14 hf* görünür, gebelik hf ilerledikçe dramatik olarak değişir

<16. hf primitif lat.ventr geniş görünürler

Gebelik hf ile dramatik değişmeye karşın atrial genişlik *14-40 hf* **<10mm**

USG ile MRI arası *1-2mm uyumsuzluk* beklenebilir

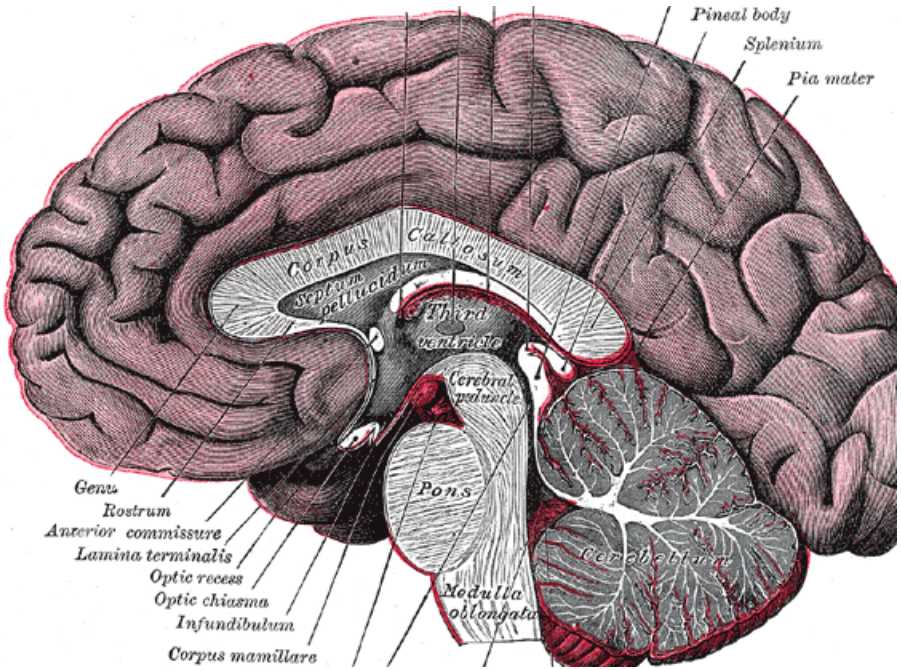


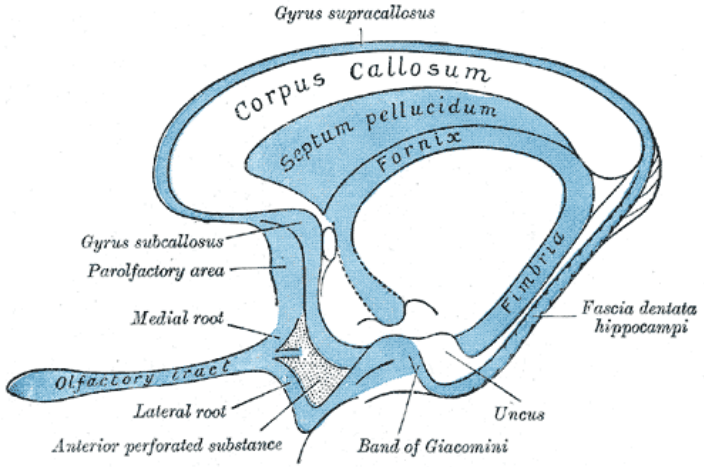
Beyin Gelişimi

CSP: 2 ince translusen membran - C. Callosum önünden başlayıp fornix'in üst yüzeyinin altına uzanan, yanda lateral ventr iç duvarları ile sınırlı

10-12.hf gelişmeye başlar - ***17. hf*** erişkin şeklini alır

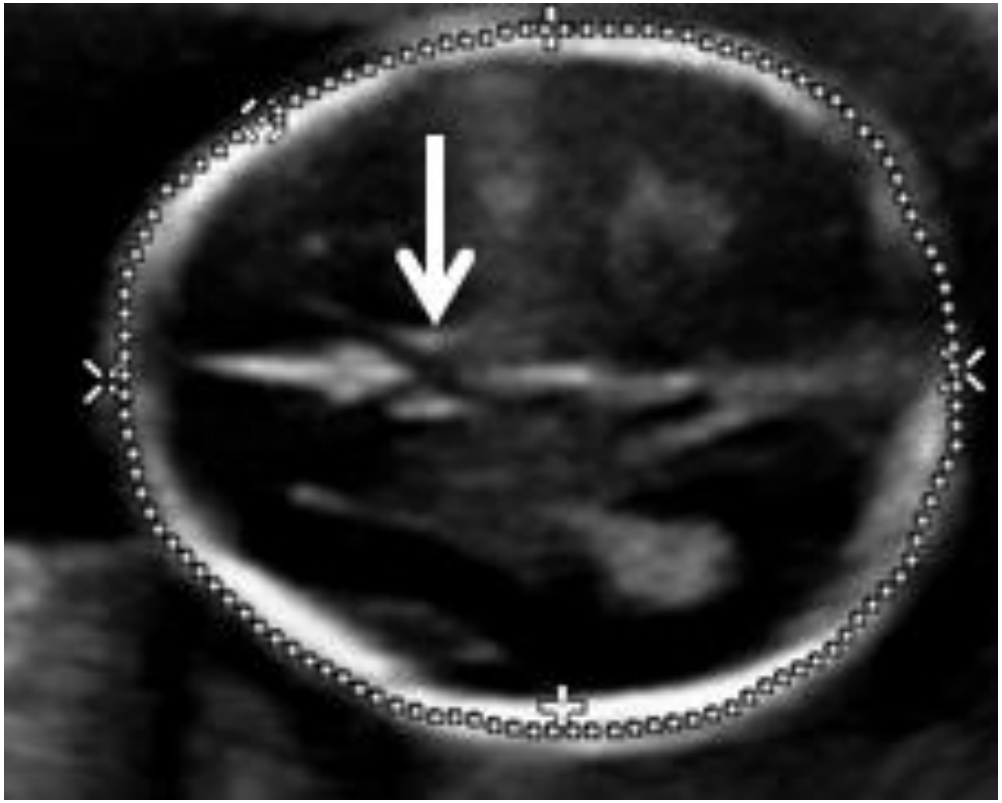
<18hf belirgin değildir Çap: *2-10mm*



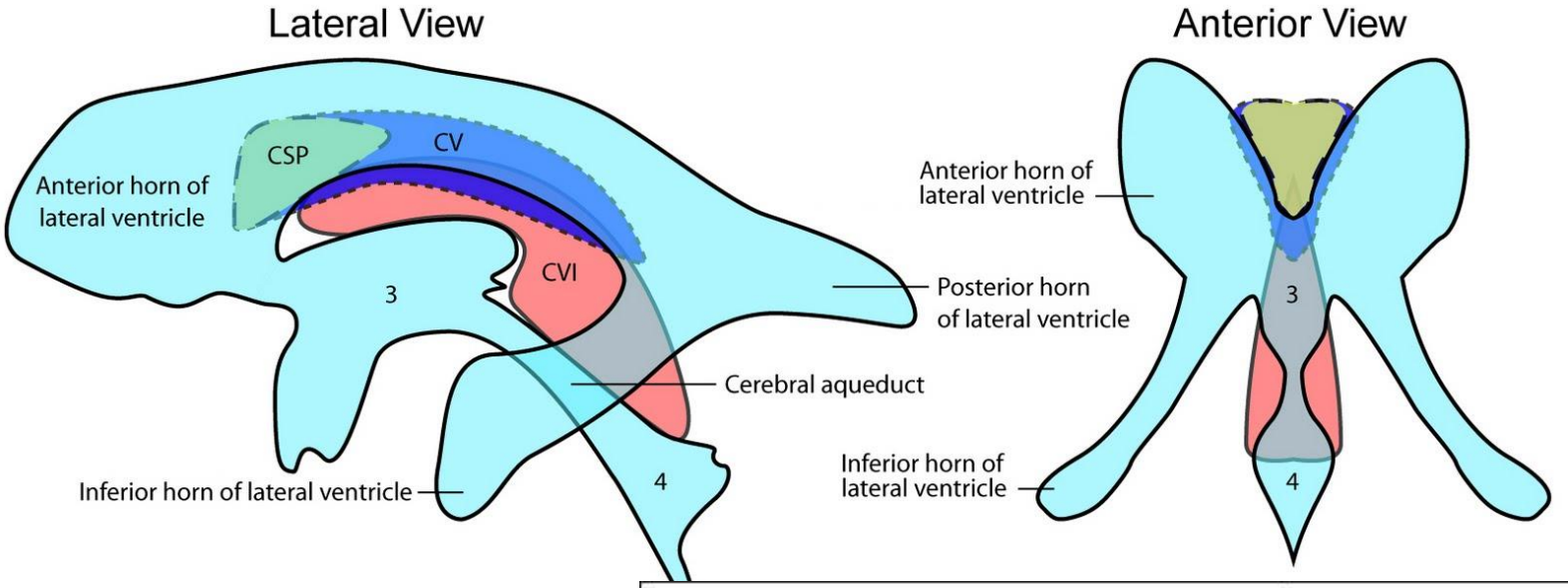


Beyin Gelişimi

CSP



Beyin Gelişimi



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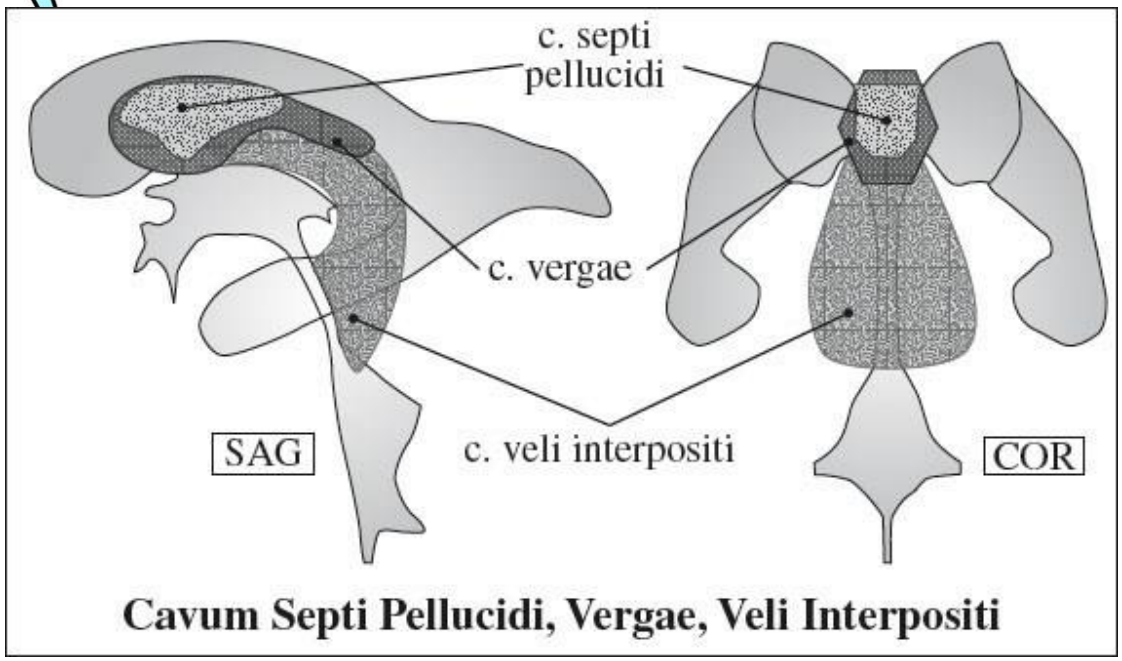
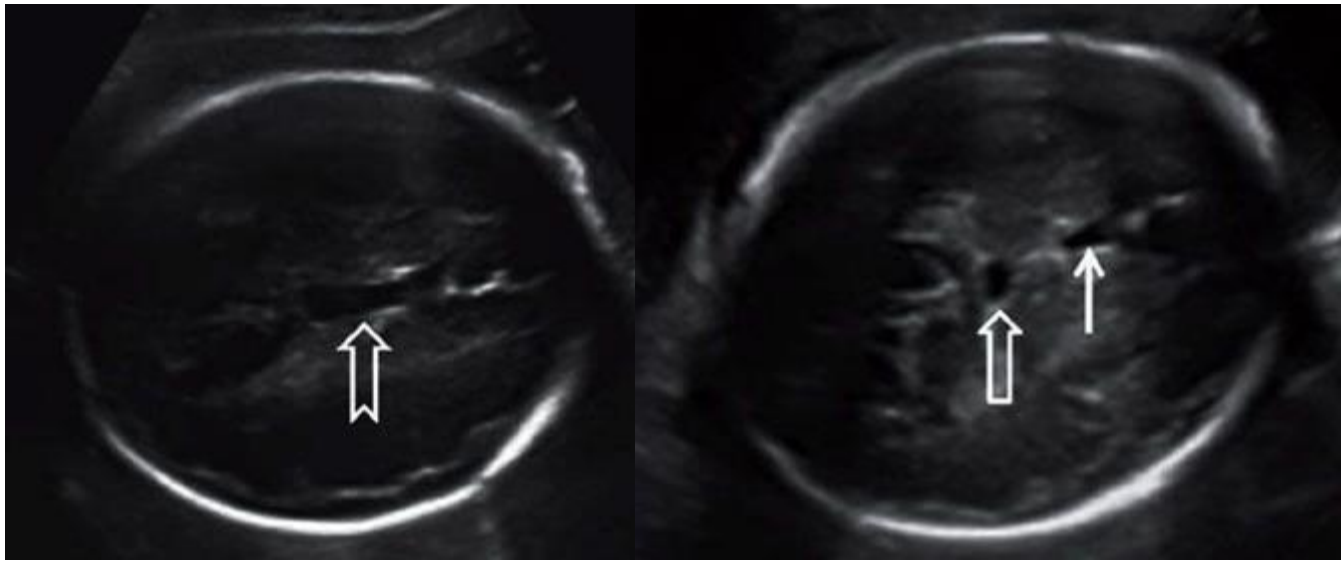


Beyin Gelişimi

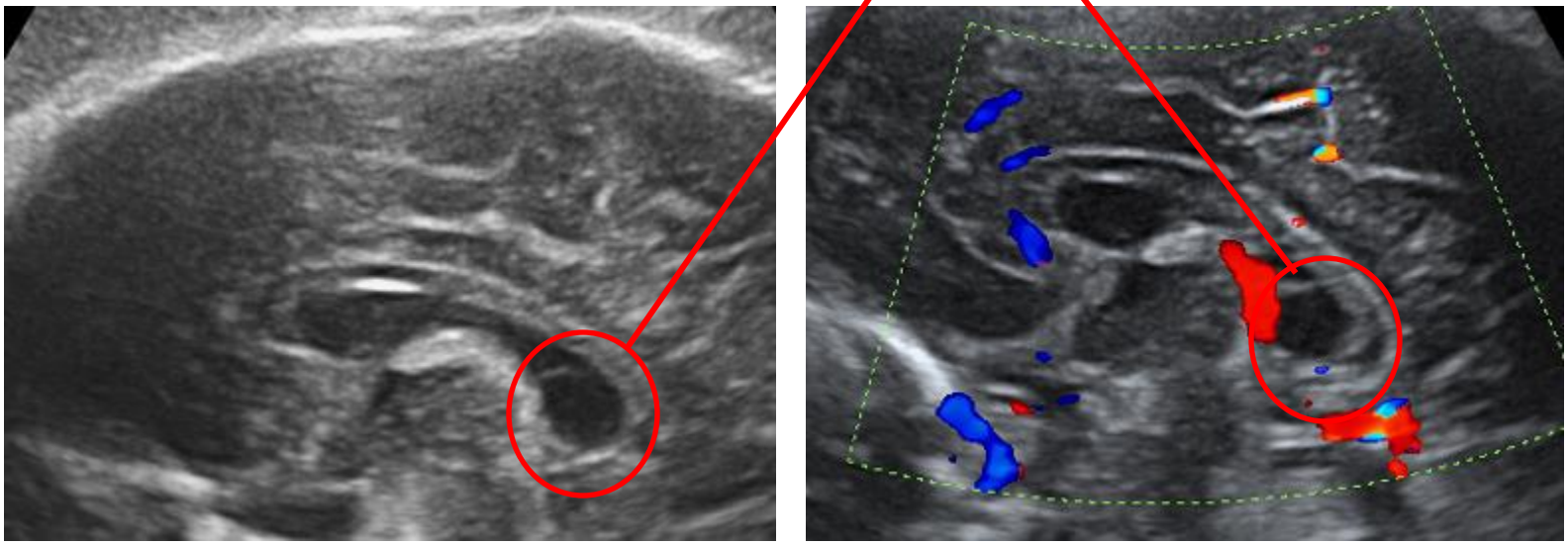
Cavum vergae:

CSP içinde bir kavite

Foramen Monroe'nun posteriorunda – forniksler tarafından oluşturulan dikey sütunların düzlemi

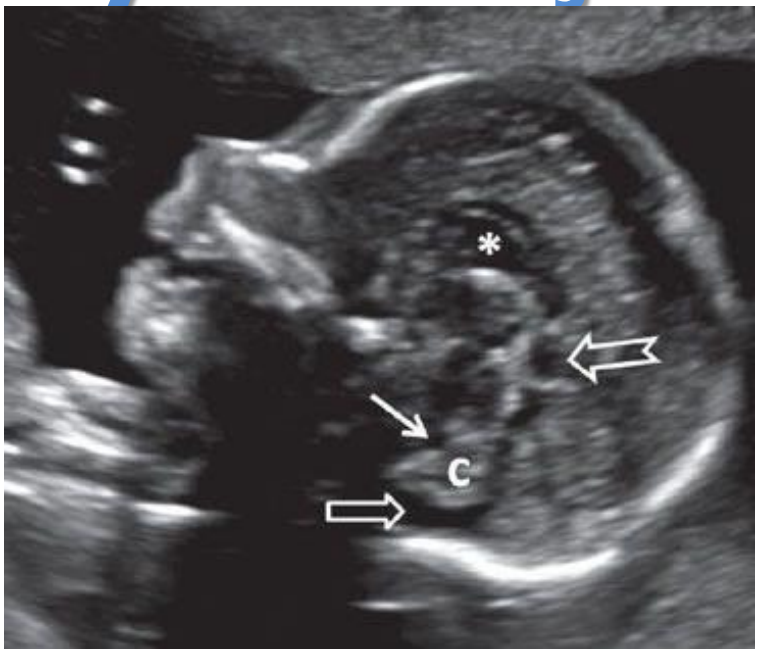


Sıklıkla 40.Hf birleşir

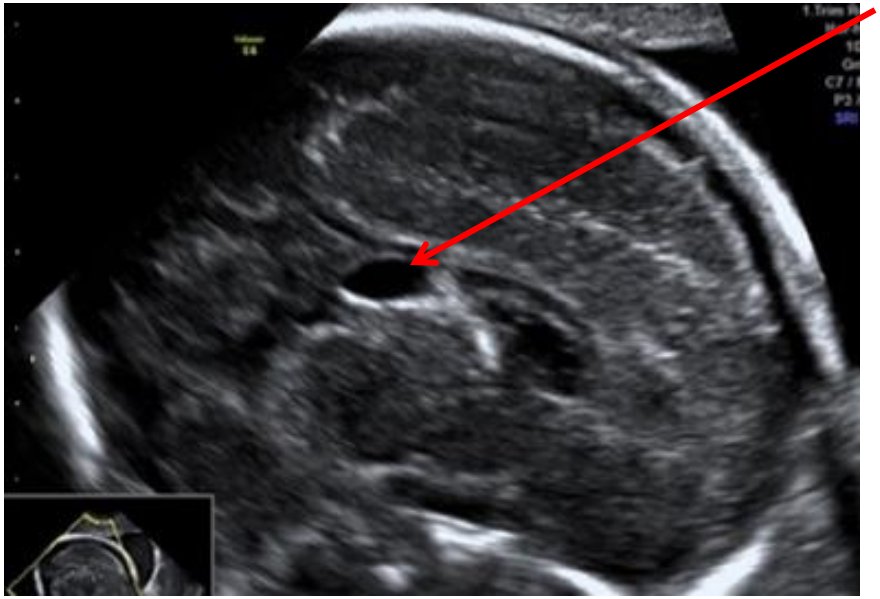


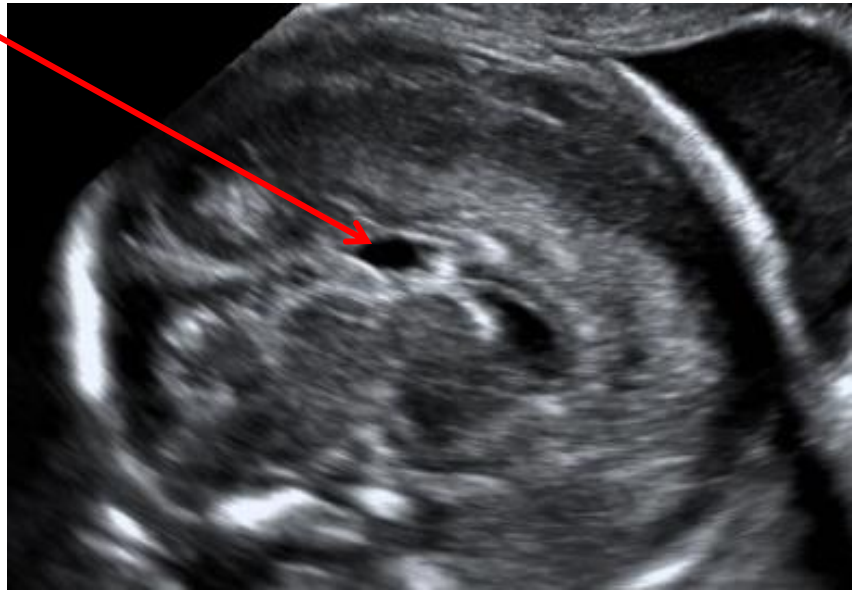
Beyin Gelişimi

Cavum Veli Interpositum

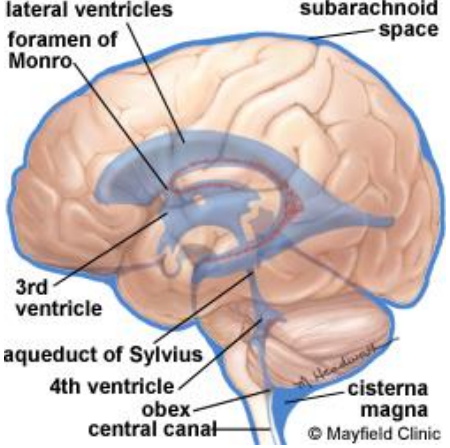


CVI





Beyin Gelişimi



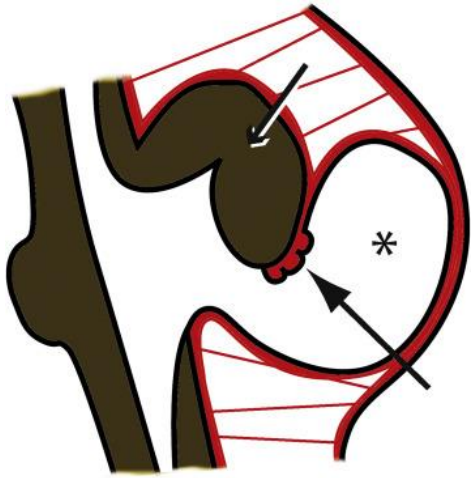
- **3.ventr:** geç 1. trim de görünebilir

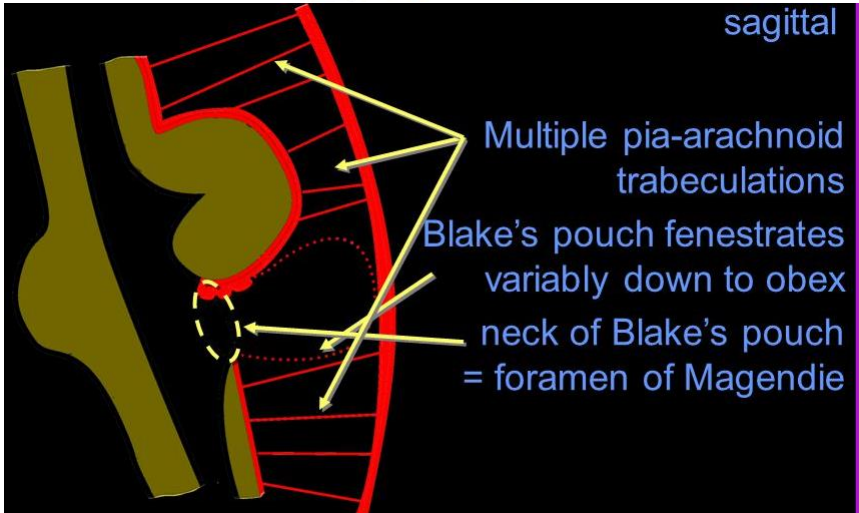
  Transvers boyut<4mm

- **4.ventr:** arka beyindeki santral kanalın fokal dilatasyonuyla olur. Bu vezikülün alt tavanı kaudal-dorsale dönerek "Blake pouch"u oluşturur.

  "Blake pouch" obex'e doğru fenestre → ***foramen Magendie*** (7-8.hf)

  (For. Lushka daha geç oluşur)

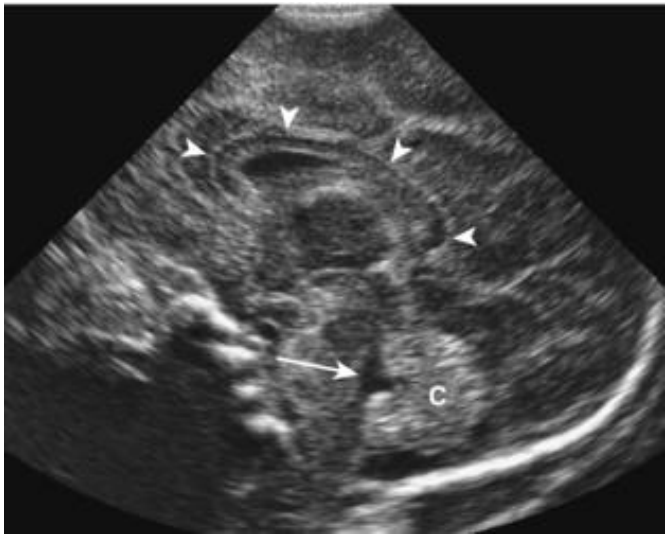




Beyin Gelişimi

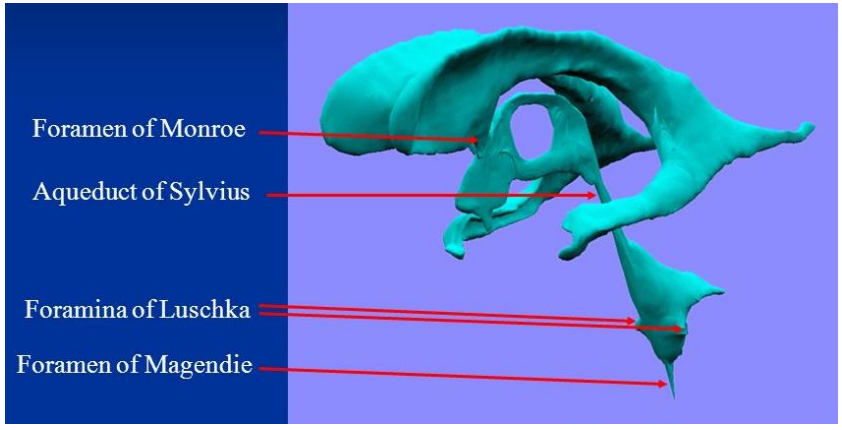
4.ventr: 14-16 hf genişler ve 22-23. hf'da normal boyutuna gelir. Cisterna Magna'daki septalar Blake pouch duvarlarının kalıntılarıdır

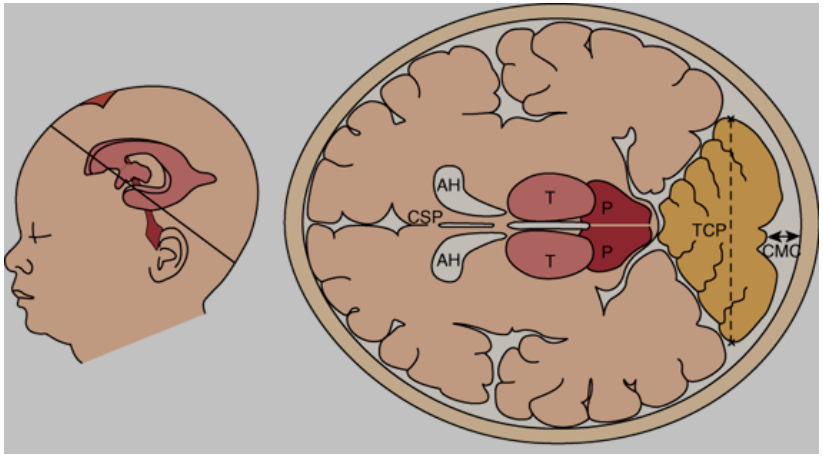
Sagital planda 4.ventr AP çapı <7mm

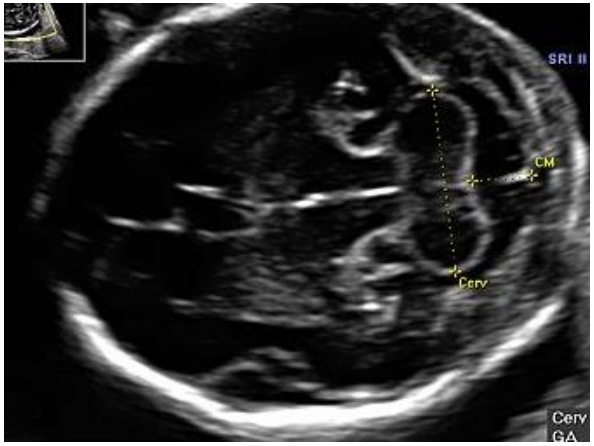


CM

2 – 10 mm





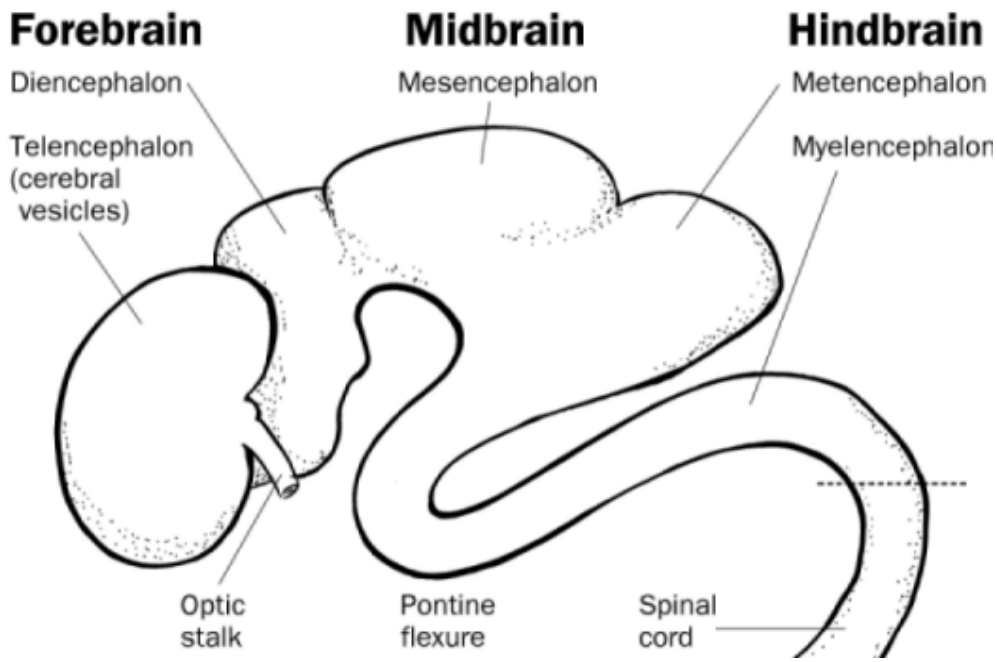


Beyin Gelişimi

- **Serebral parankim:** 2 tip nöronal migrasyon
  - Dairesel – teğetsel

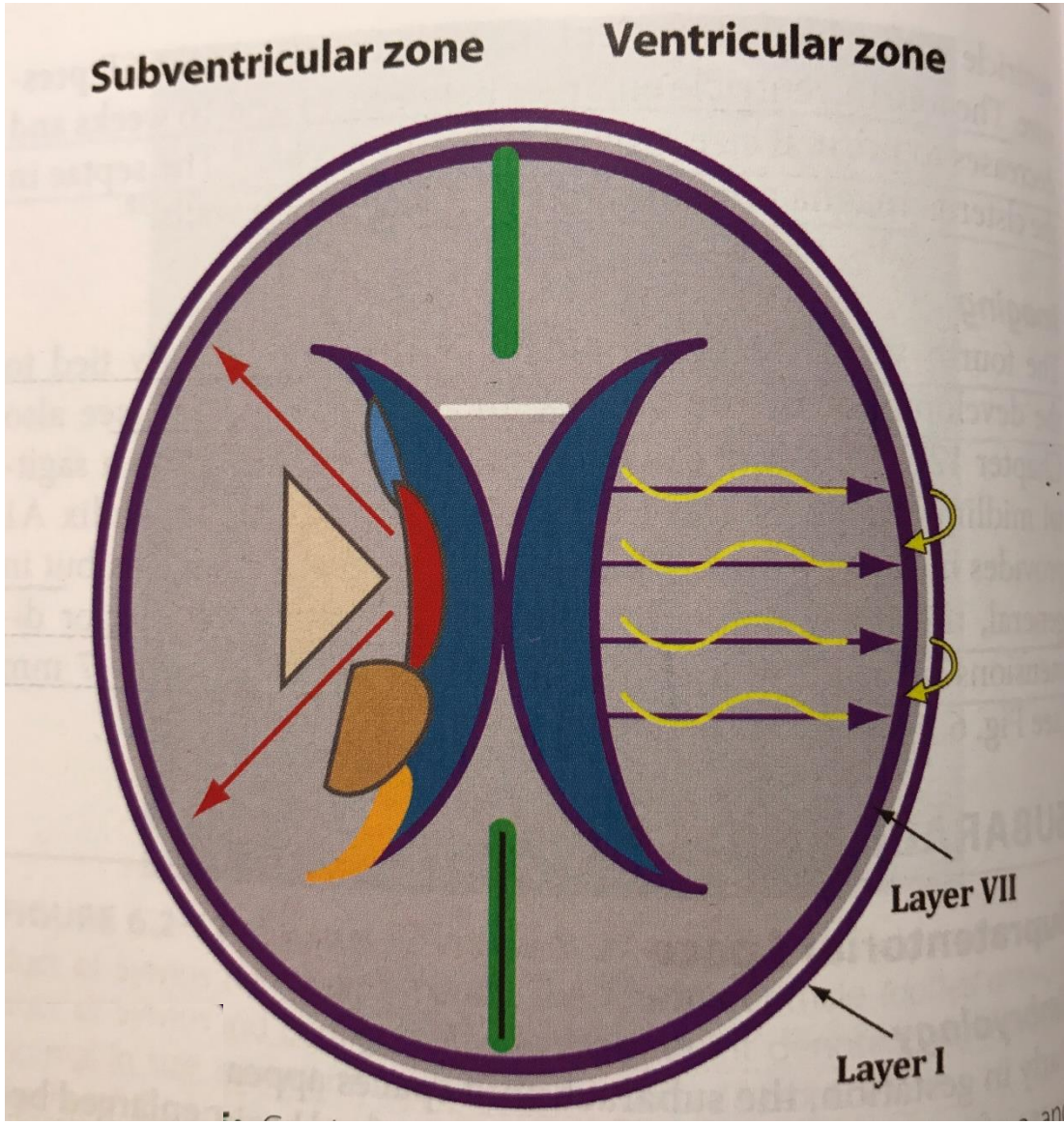
8 – 24 hf: kortikal nöronal migrasyon

24 hf – term: nöronal organizasyon + maturasyon

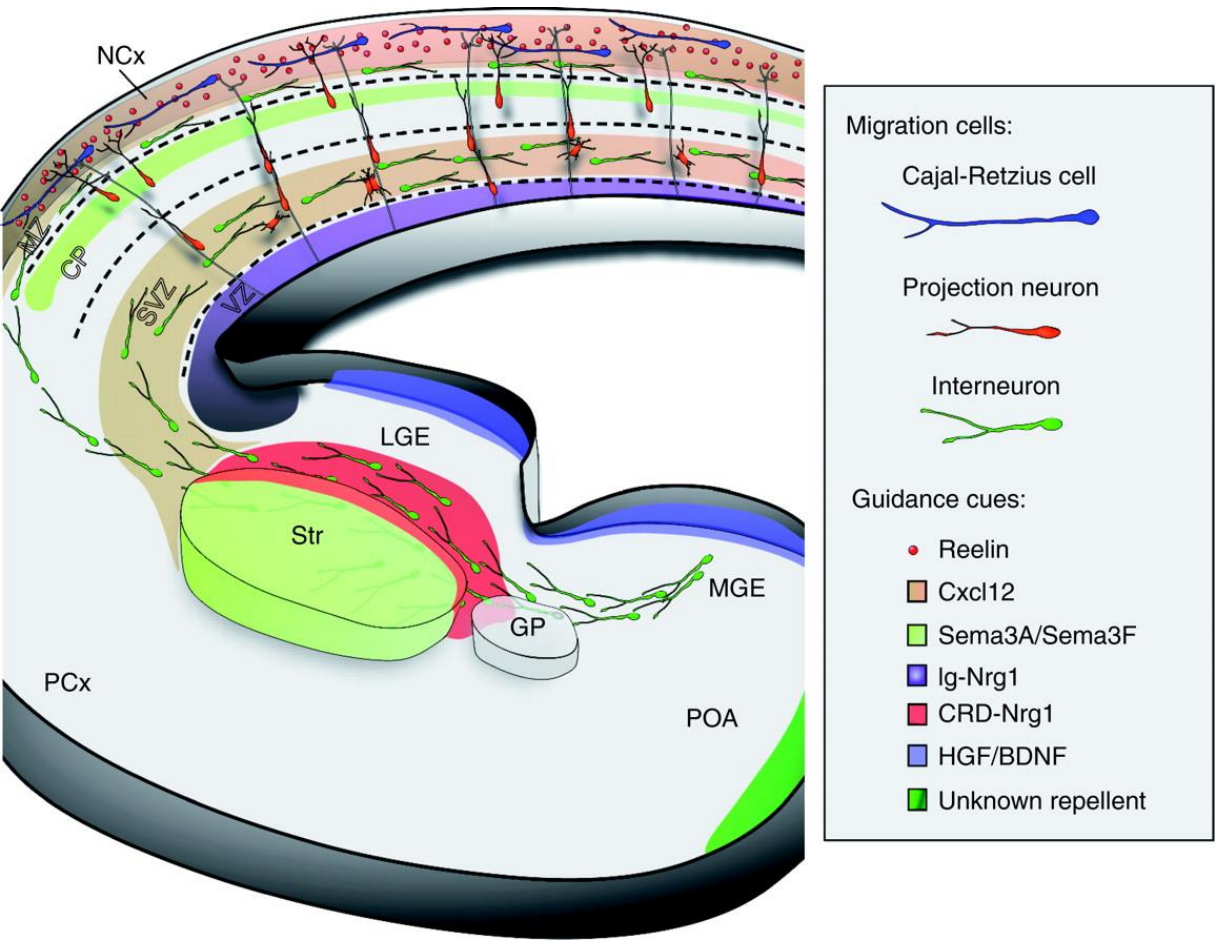


Beyin Gelişimi

- Serebral vezikül başta primitif germinal matrix (**ventriküler zon**) denilen tek tabaka nöroepitelyal hc içerir.
- 5hf'da hücresel proliferasyon ve migrasyonla önbeyin 2 tabaka hc'den oluşur. Bu zamanda "***preplate***" olarak bilinen yüzeyel ve derin nöroepitelyal tabaka vardır.
- Preplate'in oluşumu nörogenesis'in başlangıcıdır.
- Bu hücreler bazal telensefalondan teğetsel olarak piamatere doğru göçlerini nöral tüp kapanmadan tamamlar



Beyin Gelişimi



(CP) cortical plate; (GP) globus pallidum; (IZ) intermediate zone; (MZ) marginal zone; (NCx) neocortex; (PCx) piriform cortex; (Str) striatum; (SVZ/VZ) subventricular/ventricular zones

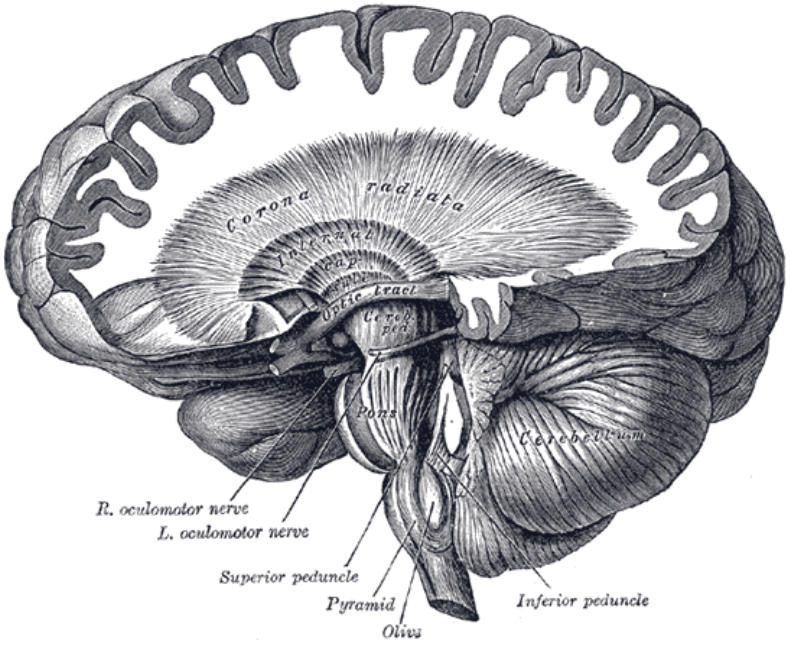
Telencephalon'da nöronal migrasyon:

(Koronal kesit) ***Medial ganglionic eminence (MGE)***'den doğan internöronlar teğetsel şekilde subpallidumdan kortekse doğru göç ediyorlar.

Beyin Gelişimi

Beyaz madde

24 – 34 hf: corona radiata gelisir



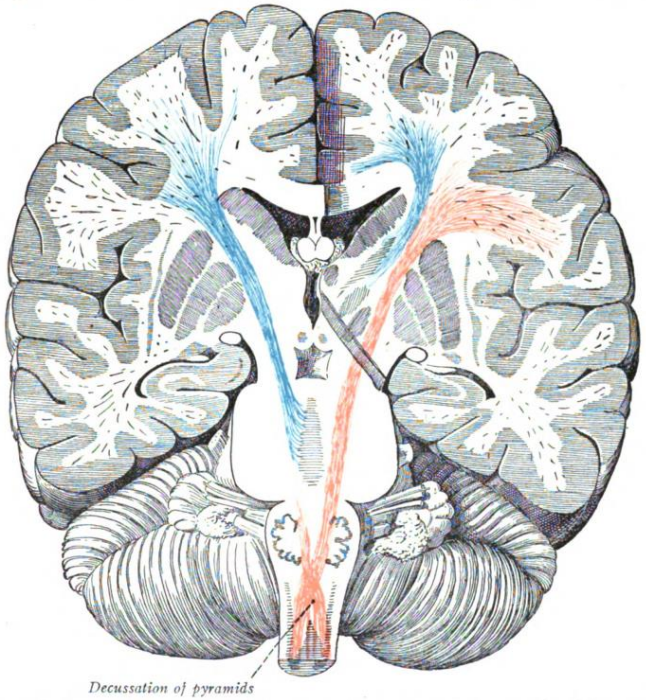
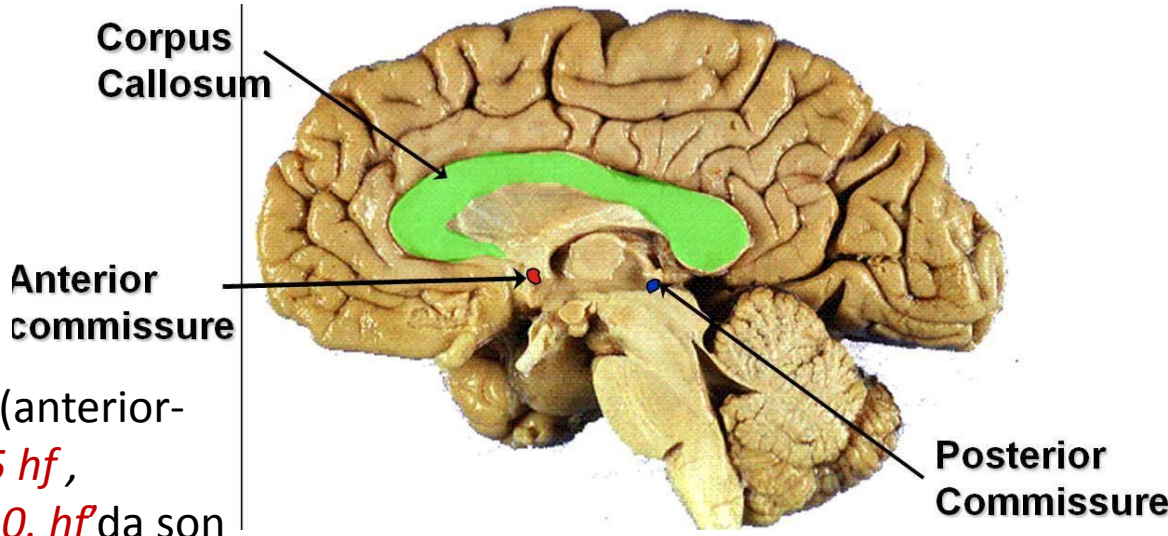


FIG. 675.—Certain tracts of the brain, particularly of the corona radiata, introduced into an outline of Fig. 642.
The pyramidal tracts are red; the cerebropontile and central tegmental tracts are blue.

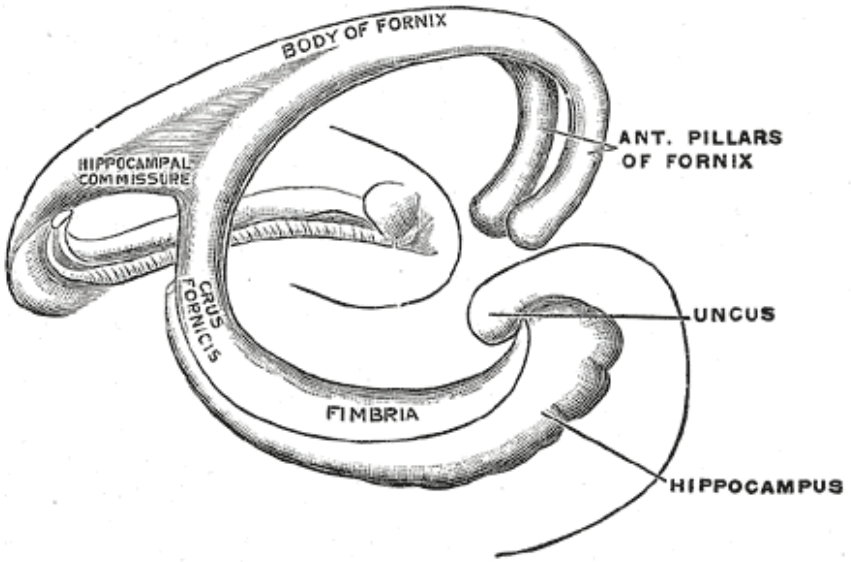
28 – 40 hf: Beyaz madde (corona radiata dahil) genişler

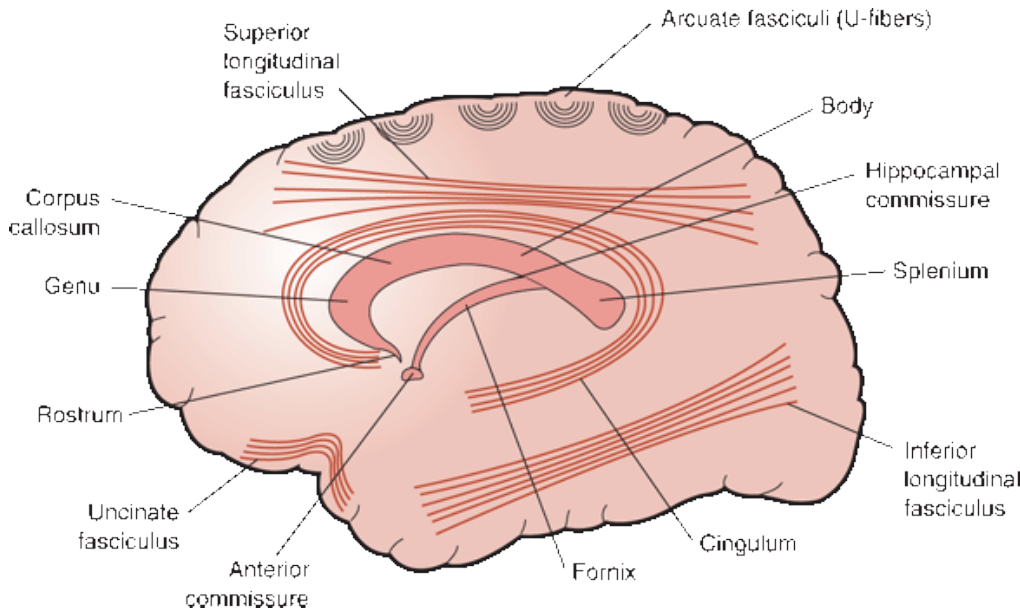
Beyin Gelişimi

3 ana kommissür:
Anterior: 8 – 9 hf
Hippokampal ve Posterior: 9 – 11 hf
C.Callosum: 10 hf gelişim başlar,



C.Callosum 2 bağımsız parça şeklinde (anterior-posterior) büyür. Anterior parça *14-15 hf* , posterior *18-19hf*'da ayırd edilebilir. *20. hf*'da son şeklini alır (erişkin şeklinin %5'i)





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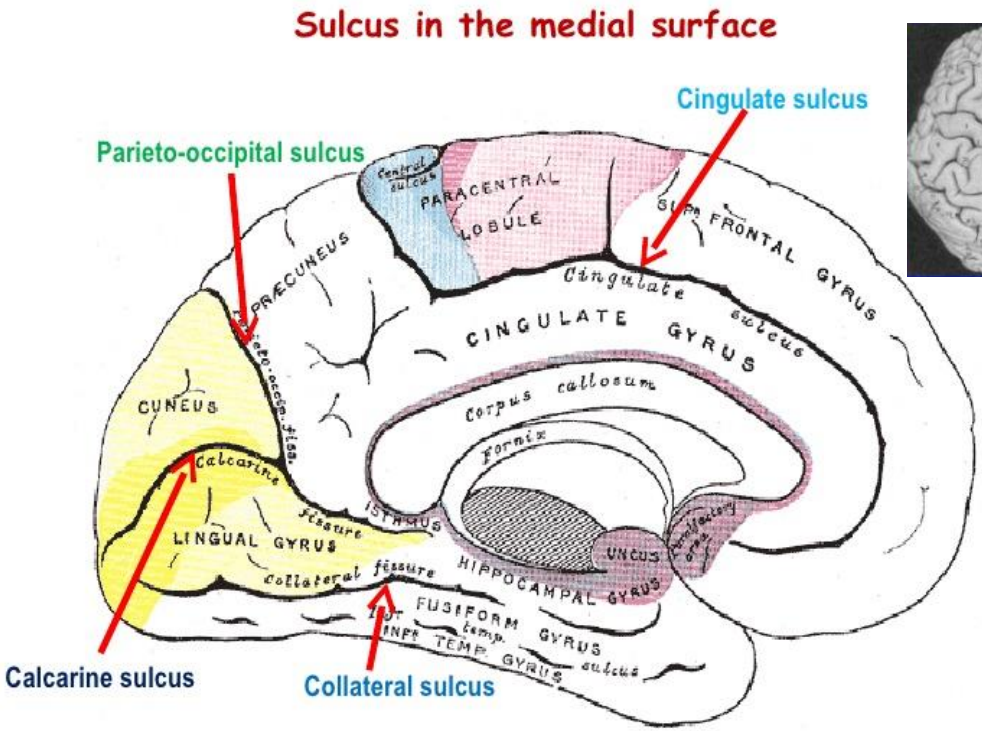

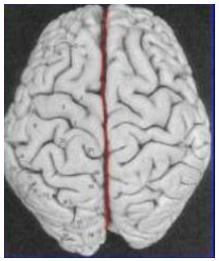

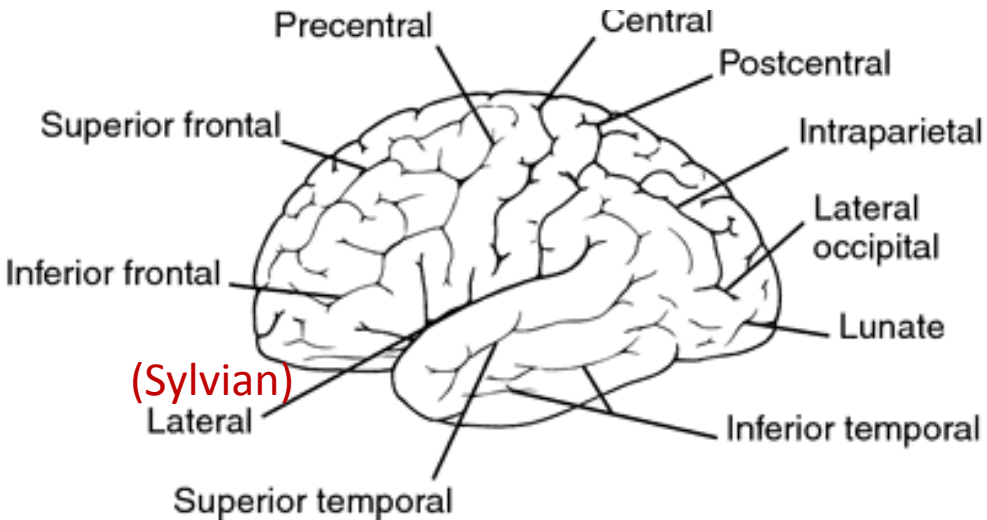

Fetal Sulkasyon	
14 – 15	Interhemisferik
16	Sylvian
22 – 23	Callosal Parieto-occipital Hippokampal
24 – 25	Calcarine Cingular
26	Central Collateral
27	Precentral Superior temporal
28	Postcentral Intraparietal
29	Superior frontal Inferior frontal
33 – 34	Inferior temporal Occipitotemporal

Ultrasound Obstet Gynecol 2006; 27: 494–502
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.2757

Sonographic developmental milestones of the fetal cerebral cortex: a longitudinal study

B. COHEN-SACHER*, T. LERMAN-SAGIE†, D. LEV‡ and G. MALINGER*

**Department of Obstetrics and Gynecology, Fetal Neurology Clinic, †Pediatric Neurology Unit and ‡Genetics Institute, The Edith Wolfson Medical Center, Holon and Sackler School of Medicine, Tel Aviv University, Tel-Aviv, Israel*

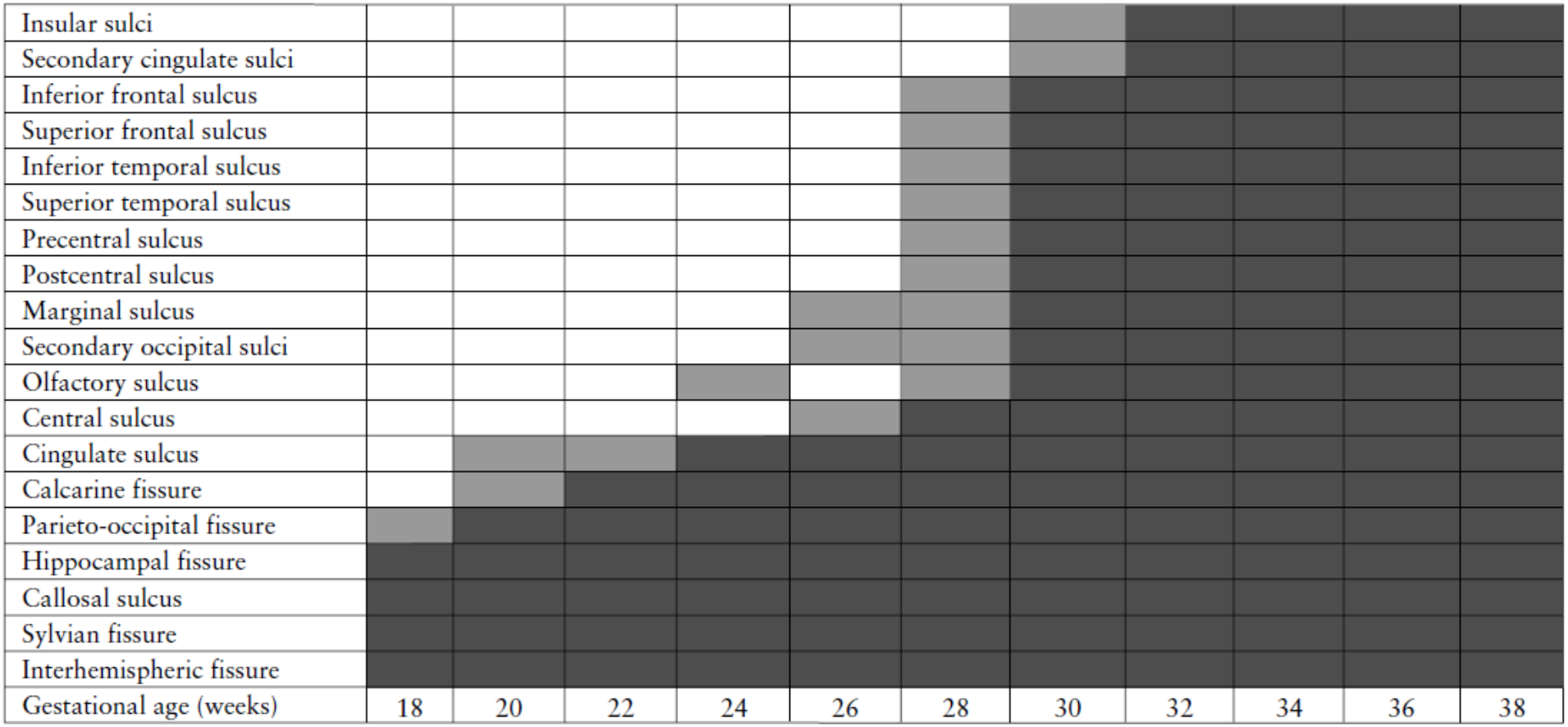

Figure 1 Detectability of sulci and gyri according to gestational age. We considered a particular structure to be present when it was seen in more than 75% of the fetuses (■) detectable if it was observed in 25–75% of the examinations (▩) and absent when it was not observed in at least 25% of the examinations (□).

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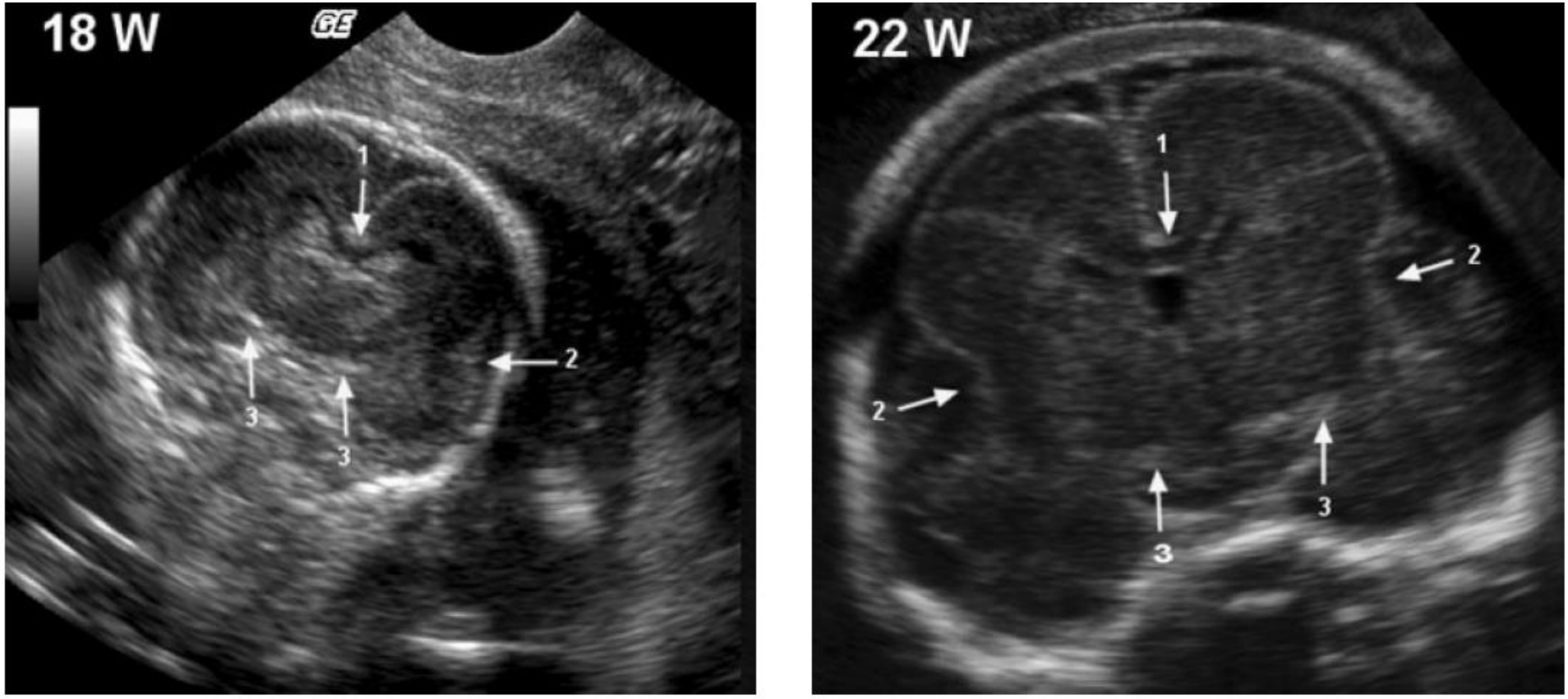

Figure 2 Ultrasound images showing coronal planes at 18 and 22 gestational weeks. Callosal sulcus (1), Sylvian fissure (2), hippocampal fissure (3). W, weeks.

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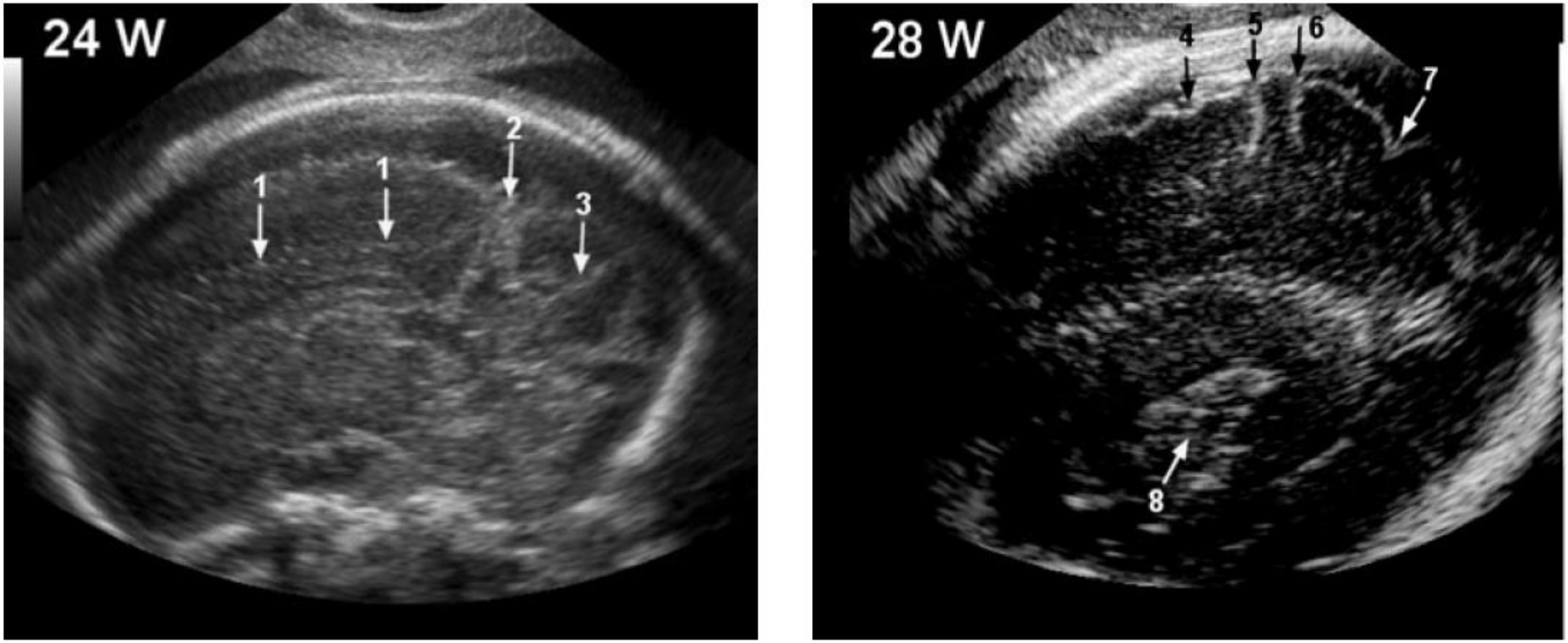
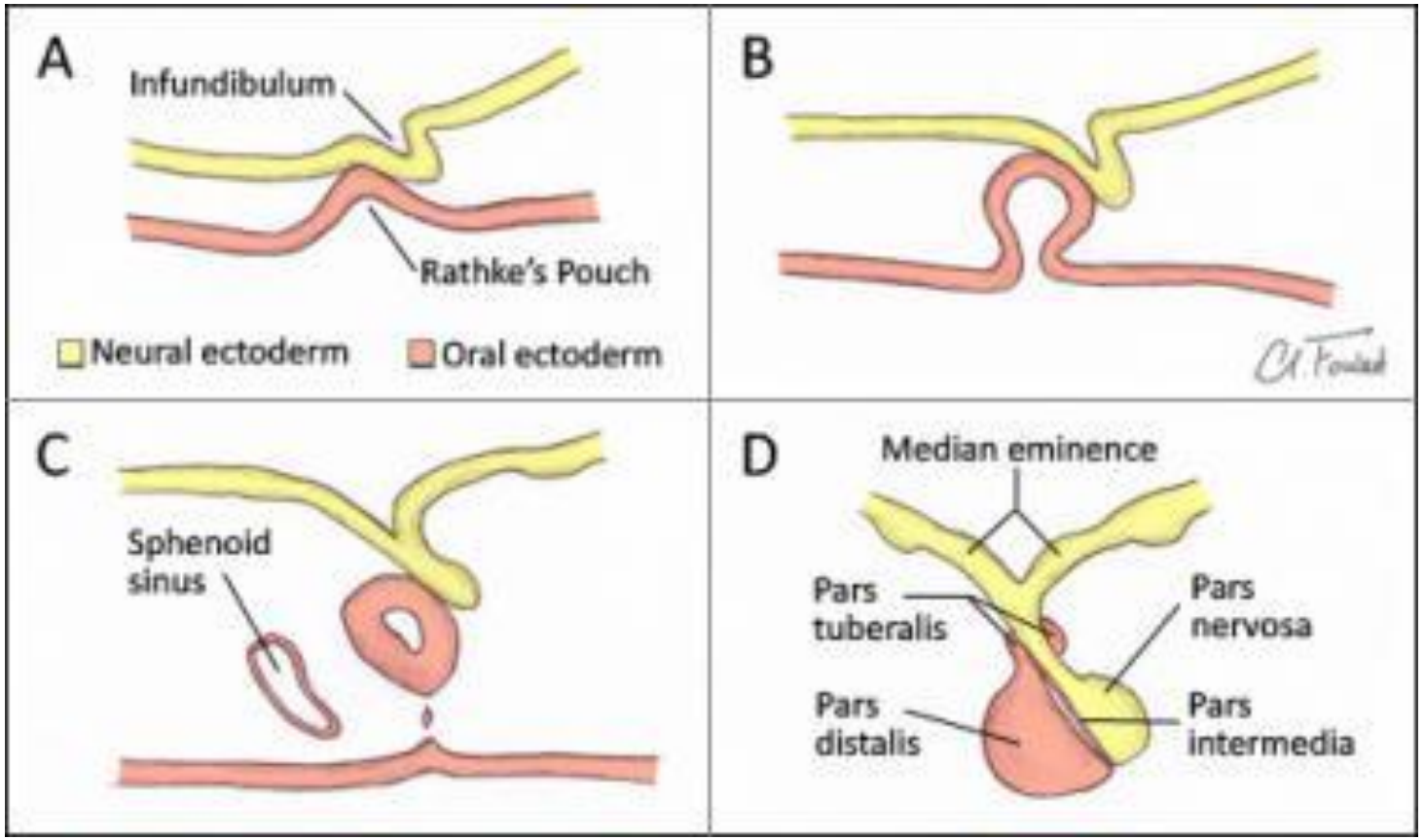


Figure 3 Ultrasound images showing sagittal planes at 24 and 28 gestational weeks. Note that the section at 24 weeks is close to the midline and at 28 weeks, periventricular. Cingulate sulcus (1), parieto-occipital fissure (2), calcarine sulcus (3), precentral sulcus (4), central sulcus (5), postcentral sulcus (6), marginal sulcus (7), Sylvian fissure (8). W, weeks.

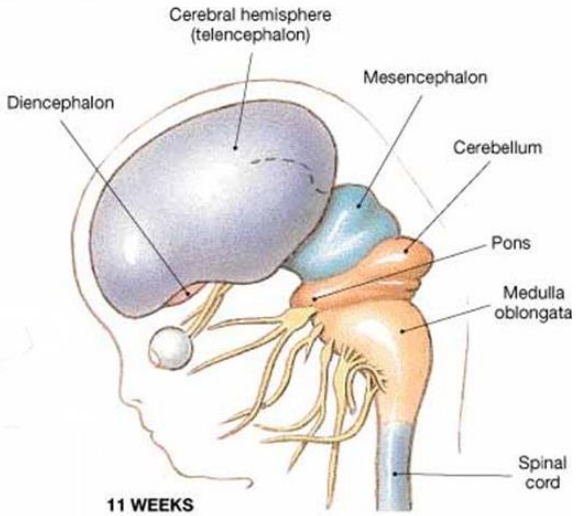
Hipofiz

- **Adenohipofiz:** *Rathke poşu* da denen Stomodeumun ektodermal tavanından yukarı doğru çıkıntı
  - 6. haftada oral kaviteyle bağlantı kaybolur.
- **Nörohipofiz:** *Diencephalon*'un nöroektoderminden aşağıya doğru çıkıntı

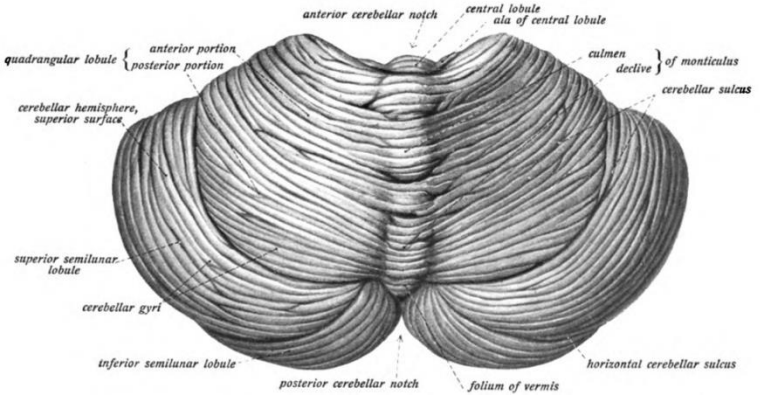


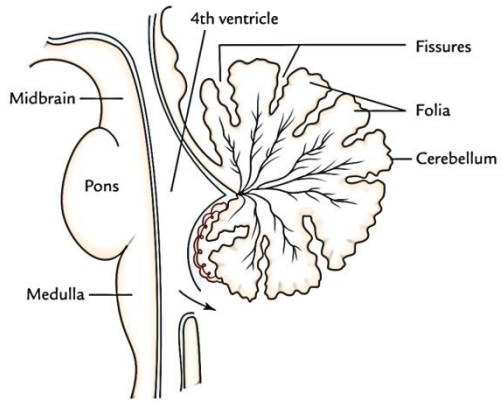
Serebellum

- İlk gelişmeye başlayanlardan, maturasyonu en son tamamlanan yapı
- Serebellar hemisferler metensefalon, vermis kısmen mesensefalon kökenli.
- Vermis oluşumu ***9.hf*** başlar



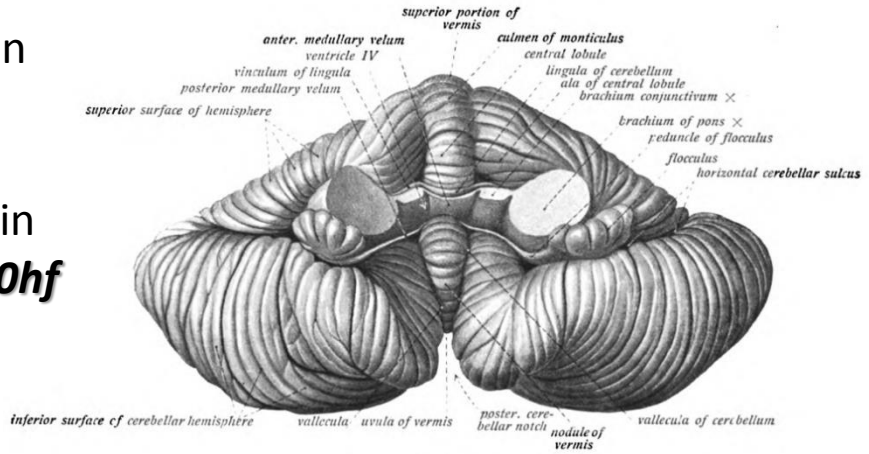
Serebellar fissürler:
20 – 30 hf





9 vermian subdivision
14.hf bulunmakta

Vermian hemisferlerin yapraksı yapısı: ***27-30hf***



Serebellum

Vermis → superiordan inferiora doğru gelişir

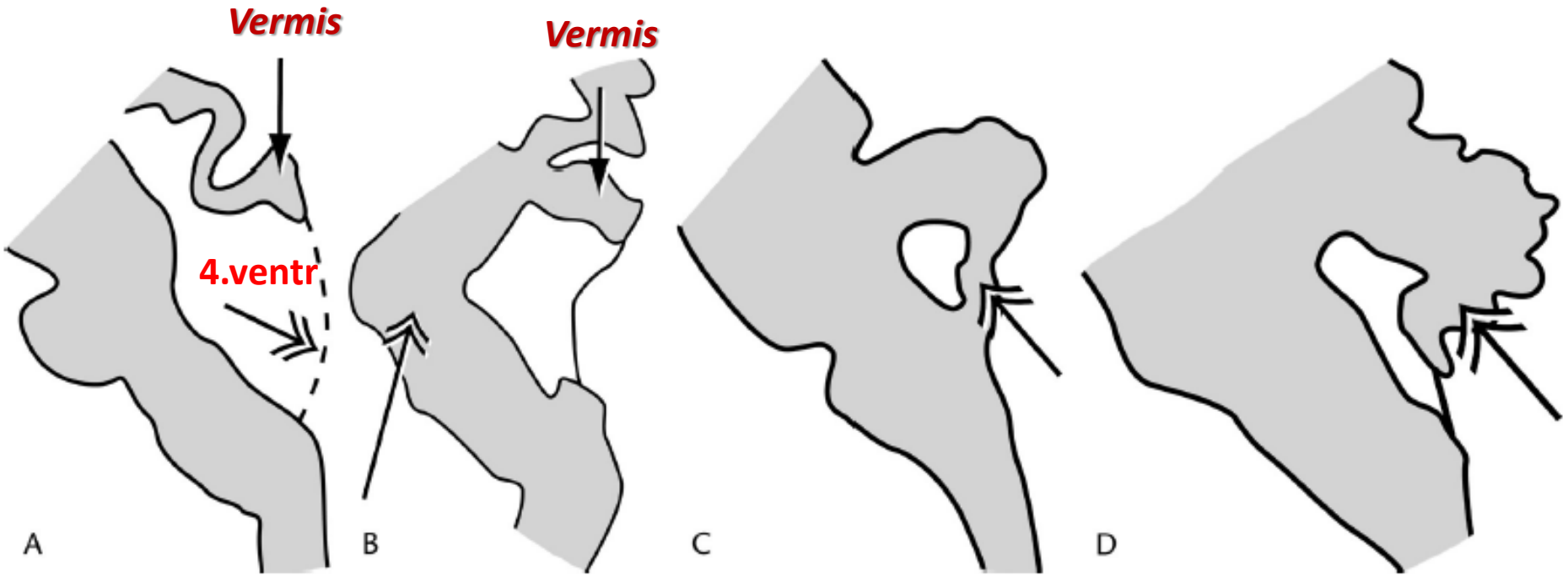
The Fetal Cerebellar Vermis

Assessment for Abnormal Development by Ultrasonography and Magnetic Resonance Imaging

Ashley J. Robinson, MB, ChB,† Susan Blaser, MD,† Ants Toi, MD,‡ David Chitayat, MD,§ William Halliday, MD,|| Sophie Pantazi, MD,‡ Munire Gundogan, MD,†¶ Suzanne Laughlin, MD,† and Greg Ryan, MB#*

(*Ultrasound Quarterly* 2007;23:211–223)

11-12 hf *13-14 hf* *16 hf* *18 hf*

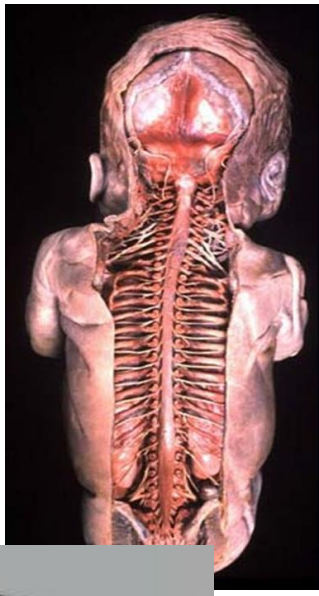


Myelinasyon

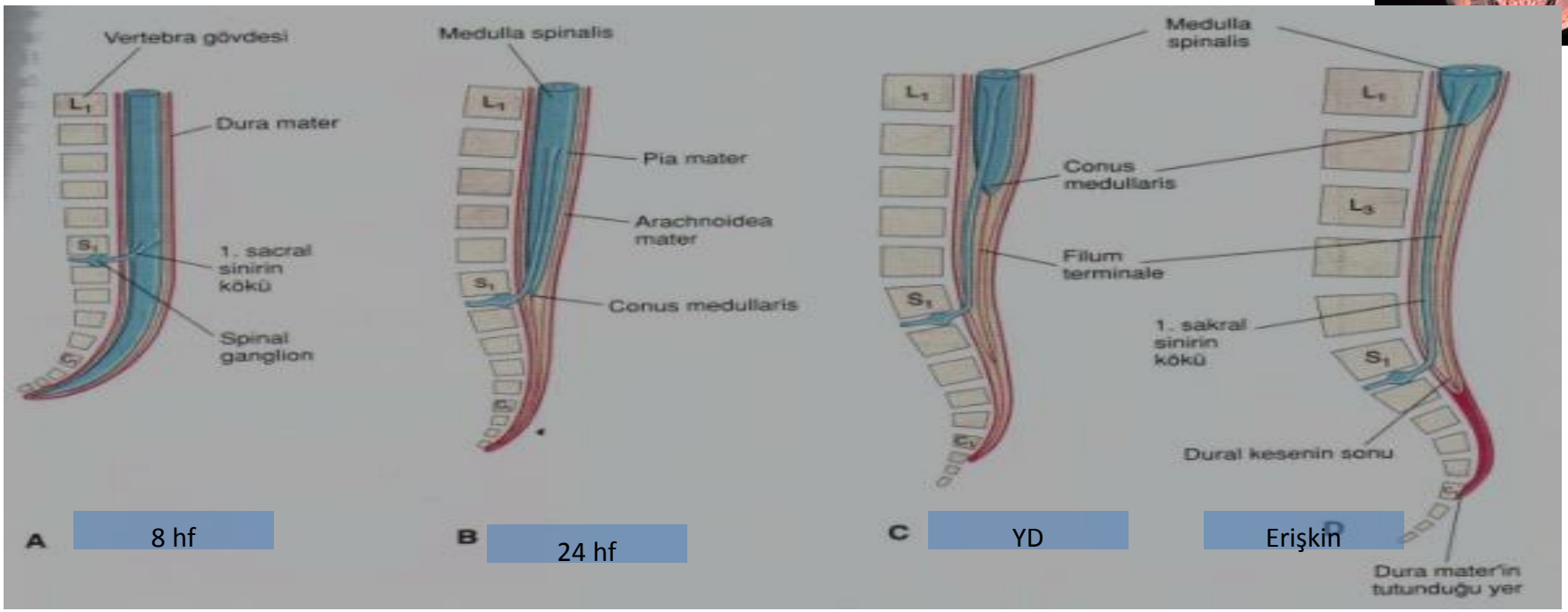
- Oligodendrositlerin proliferasyonu, astrositlerin nöronal destek ve bağlantı için çoğalmaları ile gerçekleşen bir süreç

- *12 – 13 hf* 'da **spinal kordda başlar**, daha sonra beyin sapı ile kranial yönde devam eder
- *28 – 29 hf* inf ve sup. serebellar pedünküller
- *32. hf* mesensefalon
- *32 – 33 hf* colliculus, putamen, ventrolateral thalami
- *35. hf* optik trakt
- *38 – 40 hf* **sup. vermis**

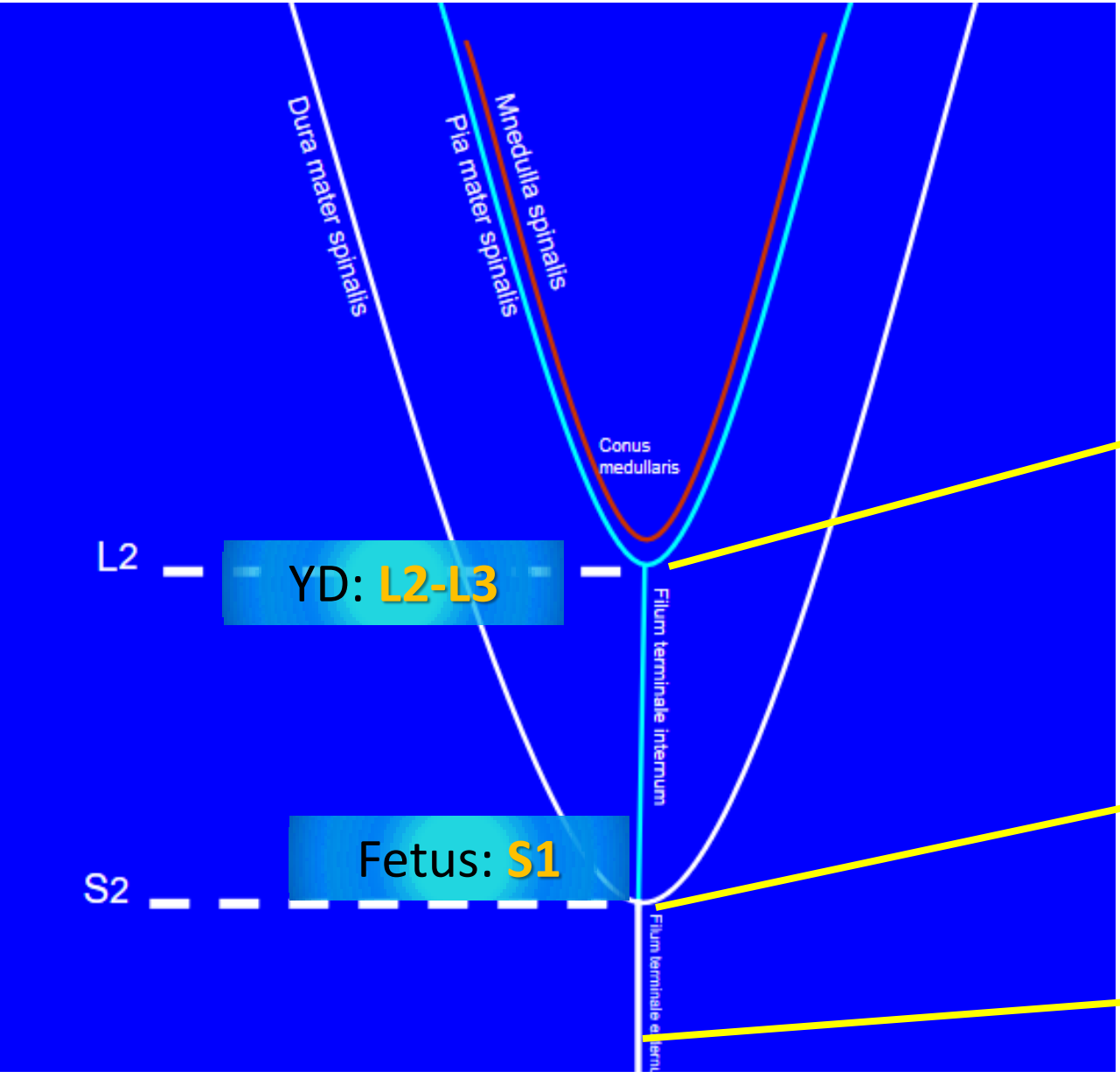
Medulla Spinalis Gelişimi



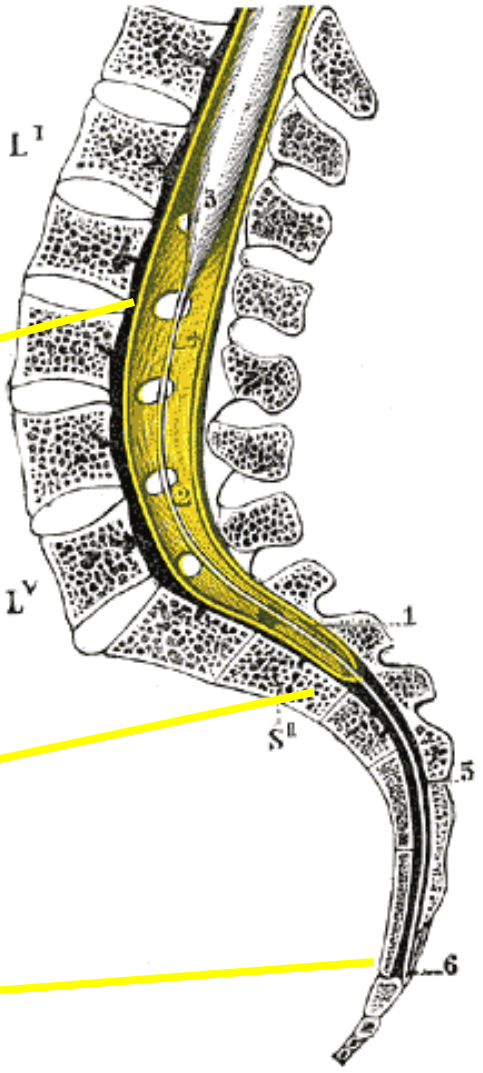
- Medulla spinalis(MS) intrauterin hayatta kanalın içini tamamen doldurur
- Columna vertebralis ve MS farklı büyüme hızı gösterirler→
  MS kanala göre daha kısa kalır



Medulla Spinalis Gelişimi



Eriskin Form

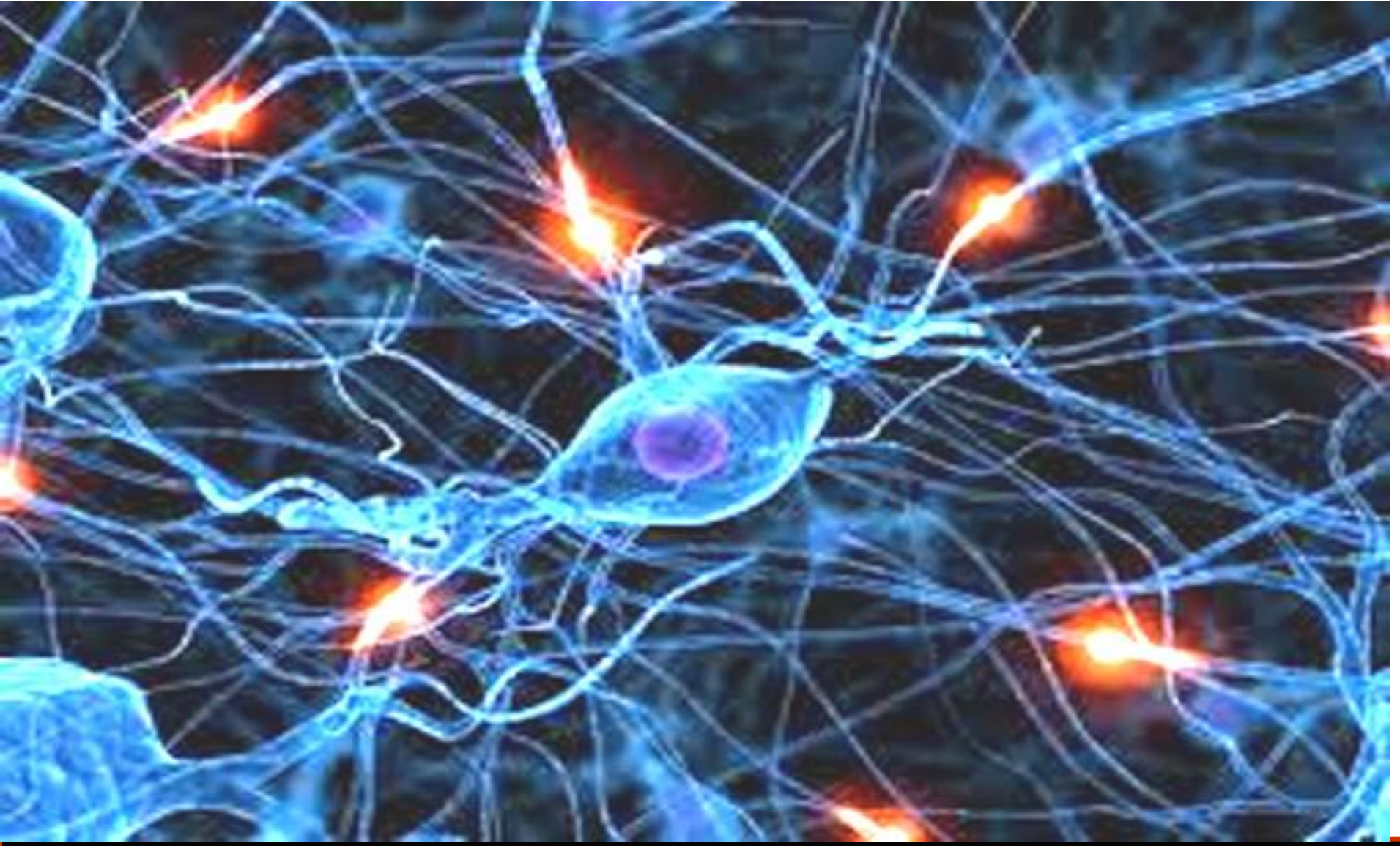


Embriyonik Gelişim Evreleri	
Primer nörülasyon	3-5 hf
Anterior nöropor kapanması	24.Gün
Posterior nöropor kapanması	26.Gün
Prosensefalon/rhombensefalon gelişimi	4-5 hf
Ventral indüksiyon	5-6 hf
Orta hat/kommisürler	8-20 hf
Anterior komissür	8-9 hf
Hippokampal	9-11 hf
Septum pellicidum	10-17 hf
Corpus callosum	10-17 hf
Nöronal gelişim, proliferasyon, migrasyon	
Serebral	5-24 hf
Ventriküler zon	5-14 hf
Subventriküler zon	14-24 hf
Serebellar; ventriküler, rhombic	8 hf – postnatal
Nöronal organizasyon	24 hf – postnatal
Miyelinasyon	20 hf – postnatal

Sinir sistemi

Embriyoloji ??

Anatomi ??



Beynimiz, onu anlayabileceğimiz kadar basit olsaydı, bizler muhtemelen onu anlayamayacak kadar basit olacaktık .... Jostein Gaarder