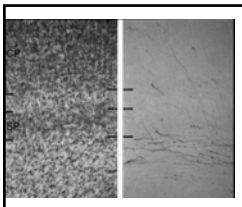
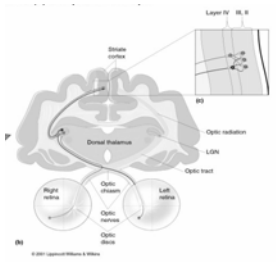
chapter 23

- THE CHANGING BRAIN
- WHEN DOES IT END???
- IS IT **GENETICS OR ENVIRONMENT**??

chapter 23



- how does the brain get connected?



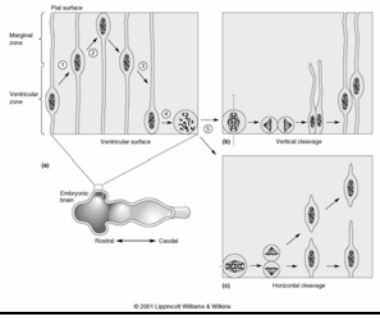
retinotopic

- Operation of the brain
  - Precise interconnections among 100 billion neurons
- Brain development
  - Connections formed and modified
- Wiring in brain
  - Correct pathways and targets
  - Fine tuning

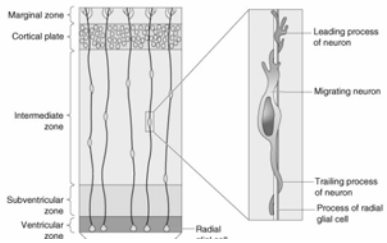
neurogenesis (birthday)

follows vertical cleavage (symmetric) and horizontal cleavage (asymmetric)

250,000/min



migration of "neuroblasts" extracellular molecular factors & radial glia

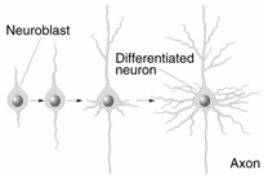


BUT ALSO MOVE LATERAL

differentiation of neuroblasts into neurons

- may actually begin as cells divide
- somewhat sealed upon arrival in brain region
- also requires environmental factors

we now know some "undifferentiated" cells remain in ventricular zones OF ADULTS!!!



new adult neurons

- song-learning centers of canaries
- hippocampus of rats
- lateral ventricle (ventricular zone) in monkeys

- hippocampus of humans??!!

- why do we care???????

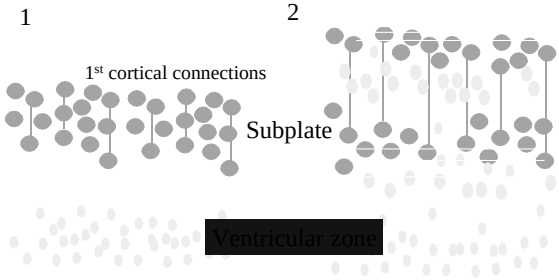
new adult glial cells??

nib

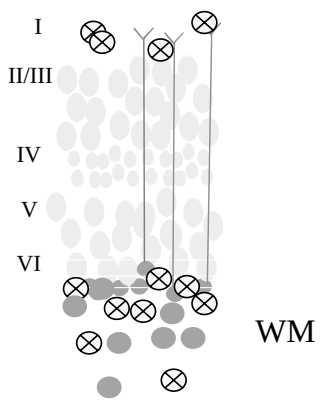
how does cortex develop?

1

2



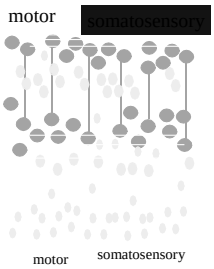
Mature cortex

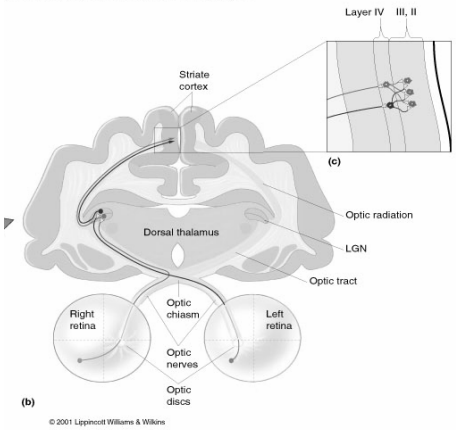


differentiation of brain regions

QUILT

- requires thalamus AND SUBPLATE



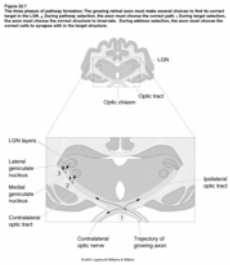


HOW DOES AN AXON GROW?

3 "DECISIONS" for Neurites (IN ORDER)

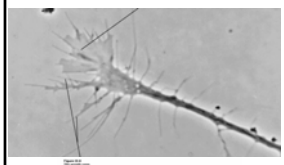
1. PATHWAY
2. Pick STRUCTURE (TARGET)
3. Pick specific NEURONS (ADDRESS)

different kinds of control mechanisms



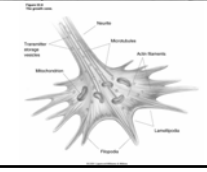
GROWTH CONES

follow molecular gradient patterns still being worked out



Lamellipodia – leading edge

Filopodia – “spikes”



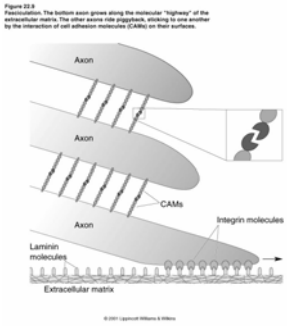
Actin filaments –proteins

Pioneer axons follow “segments” of extracellular molecular concentration gradients

other axons stick together

FASICULATION

- CAMs sticking together

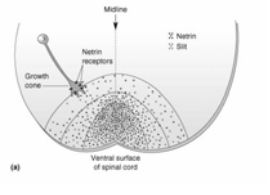


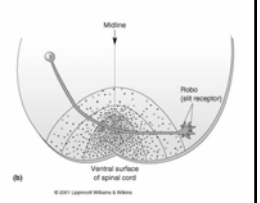
not sticking together

CHEMOATTRACTION CHEMOREPULSION

how to solve the midline crisis?

Netrin and netrin receptors
slit – but slit requires RECEPTORS ROBO
SO at midline CELLS PRODUCE “ROBO



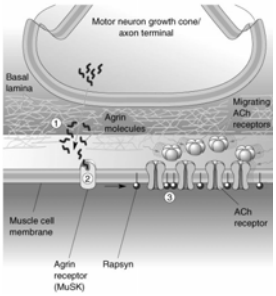


how do synapses form?

- motor neuron and a muscle fiber
- BOTH PRE AND POST PARTICIPATE

KEY PLAYERS:

1. agrin
2. basal lamina
3. Muscle-specific kinase (MuSK)
4. rapsyn
5. ACh receptors



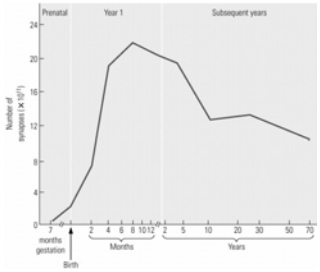
1.agrin is released from motor neuron (yes, PREsynaptic) into basal lamina

2. agrin binds to MuSK receptor on muscle cell (Postsynaptic)- MuSK activates rapsyn

3. rapsyn “gathers” ACh receptors (postsynaptic)

pruning – up to 5000 per second!!!!

HOW SYNAPSES DIE



BUT WHY? very EXPENSIVE strategy!!!
needed for experience-based activity

Competition sometimes determines which cells and connections grow and which die.

HOW DO CELLS DIE - apoptosis

Is this neural Darwinism?

Cell death begins in ventricular zone

WHY??? CELL DEATH GENES?
Genes can determine which grow and which die

Also may be competition for trophic factors (kinase receptors)
Nerve growth factors (NGF), BDNF

remember genes and environment interact

NOTE: death from necrosis and excitotoxins DIFFERENT (?)

WHY DO CELLS DIE
normal apoptosis?
1/2 MOTOR NEURONS
Most SUBPLATE

abnormal?
AD – neurons die , ACh
ALS – alpha motor neurons die
alpha – directly innervates muscles
gamma – keeps motor muscles "spindles" active

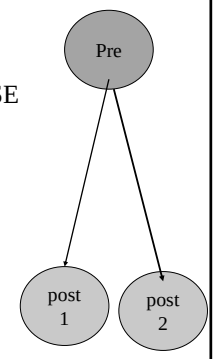
SOMEHOW INDUCE CELLS TO DIE?
SUBSTANCE P NEURONS

WAVES

- synchronous waves of electrical activity
- BEGINS BEFORE BIRTH
  - retinal waves help segregate visual input
  - neurons that fire together have a relationship

HEBB

- connectivity strengthened by USE
- basis for computer models
- but not all!
  - some circuits need to be ready to respond even when not often used



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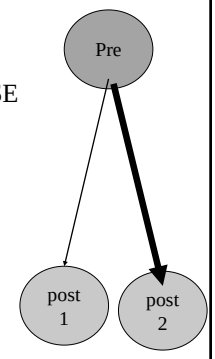

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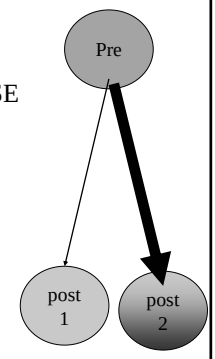
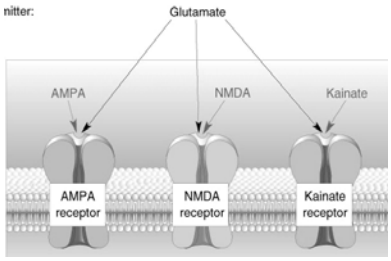


remember NMDA receptors

- AMPA
- NMDA
- CA and some NA

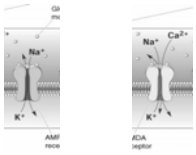
another kind of plasticity LTP

- strengthening of synaptic transmission
- glutamate synapses
- strong NMDA receptor activation



NMDA
voltage dependent
based on Mg++ block

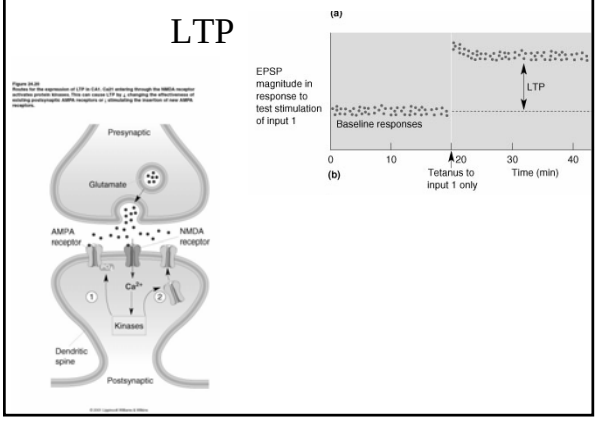
let Ca++ in (LTP)



NMDA without AMPA
(development)

"silent"

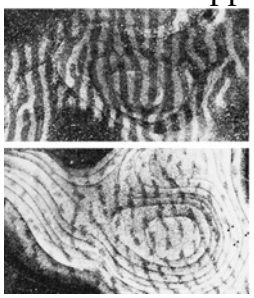
LTP



Critical periods striate cortex

- activity-dependent synaptic rearrangement
- strabismus must be corrected early
- HUMANS CPS END BY ABOUT AGE 10 (?)

WHEN INPUTS FROM ONE EYE ARE STRONGER look what can happen!

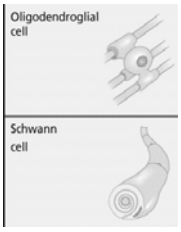


when are we finished??

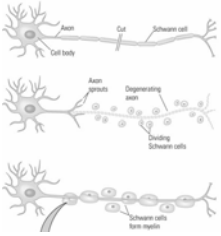
- plasticity until death – particularly in frontal and temporal lobes

why not always plasticity?

- PNS axons regenerate
- CNS axons do NOT



differences olgliodendrocytes and Schwann cells:



) **Structure**

) **Repair activity**
Schwann cells aid in regrowth

olgliodendrocytes produce
NOGO

(alpha, gamma motor neurons)

plasticity

It is not restricted to development!

It is happening RIGHT NOW!