Lecture 39 – – (Chapter 56) - Carol Mason

Early Sensory Experience and the Fine Tuning of Synaptic Connections

I. Effects of social deprivation
- Birds
- Humans
- Monkeys

II. Visual system - from eye to thalamus to cortex
- Physiological features of ocular dominance columns in the visual cortex
- Experimentation: eye closure; critical periods
- Postnatal vs. prenatal inputs; neural activity
- Mechanism for "winner-take-all" (open eye) and synapse elimination (closed eye)

III. Topics/Controversies in recent research (*not in the text book*)
- Mechanisms other than sensory input for establishment of ocular dominance columns?
- Dendritic Spines are motile; continued plasticity into adulthood?
- Reactivation of plasticity in the adult by degradation of the extracellular matrix
- Changes in steroid hormone levels induce dendritic alterations and loss of synapses
- Barn owls and visuo/auditory localization: functional and structural plasticity

THEMES

*There is a connection between neural development and learning

*The immature brain is highly plastic, with developing circuits molded by patterns of electrical activity.

*There is a critical period during which developing system is particularly susceptible to environmental deprivation, during the development of social behavior.

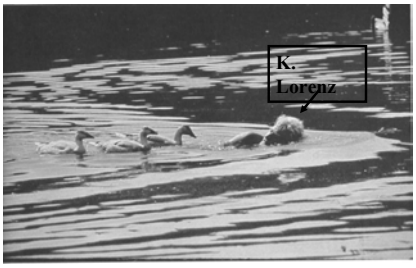
I. Effects of social deprivation

Lorenz and imprinting

Spitz and institutionalized children

Harlow and monkeys with surrogate, inanimate mother

There is a connection between neural development and learning



Konrad Lorenz' work on "imprinting":
Just after birth, birds become indelibly attached or "imprinted" to any prominent moving object in their environment, e.g., their "mother"

Observations of Rene Spitz - 1940's:

Young children were raised in two different institutions,
*Prison nursing home: with open cribs, a lively environment and *extensive interaction with the mother*, (even though she lived in the prison next door)

*Foundling home with nurses caring for several babies: where cribs were shielded, there was no intimate interaction with the mother or other caregiver, and *little opportunity for other social interaction*

By the first birthday, children in the foundling home had susceptibility to disease;
they were not walking or talking properly at 2-3 years old

1960's: Harry and Margaret Harlow studied monkeys reared in isolation for 6-12 months

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

In isolation, monkeys were healthy but behaviorally devastated (autistic-like features)

With a surrogate mother, most extreme symptoms not present; peer contact alleviated further symptoms.

Isolation of animals after 18 months did not have such consequences.

*A critical period is a limited developmental period when extrinsic influences can induce permanent changes in both structure and function of circuits.

The developing nervous system is particularly susceptible to environmental deprivation, resulting in aberrant development of social behavior.

The role of early experience in human development has become a political issue:

"Fifteen years ago, we thought that a baby's brain structure was virtually complete at birth. Now we understand that it is a work in progress, and that everything we do with a child has some kind of potential physical influence on that rapidly forming brain. A child's earliest experiences…determine how their brains are wired….These experieinces can determine whether children will grow up to be peaceful or violent citizens, focused or undisciplined workers, attentive or detached parents themselves.

Hilary Clinton, 4/97

-from an article by Malcom Gladwell, "Baby Steps", New Yorker, January 10, 2000

II. The Visual system - from eye to thalamus to cortex

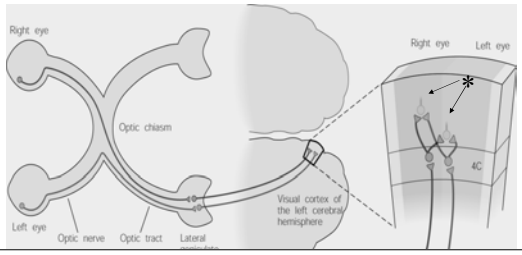
Physiological features of ocular dominance columns in the visual cortex (work of Hubel and Wiesel)

Experiment: eye closure; critical period for affecting visual behaviors

Postnatal vs. prenatal inputs; neural activity

Mechanisms - "winner-take-all",
elaboration of axon branches and synapses (open eye)
and synapse elimination (closed eye)

Afferent pathways from the two eyes remain segregated from eye to visual cortex



In the cortex above layer 4c, cells * respond to stimuli presented to either eye.

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Fig. 56.01

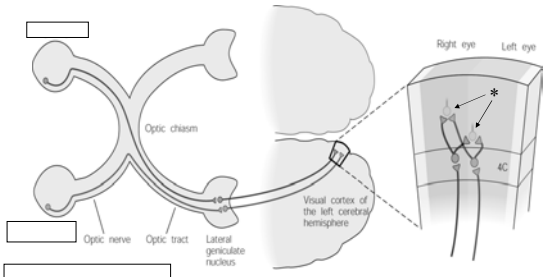
Early visual experience:

Children or chimps who receive only diffuse light input during early childhood subsequently have difficulty in pattern recognition.

David Hubel and Torsten Wiesel - won the Nobel prize for studies in the 70's and 80's on sensory deprivation.

They deprived animals of visual input (*by closing/suturing the eyelid of one or both eyes*) and analyzing the consequences on visual cortical development and visual behavior.

Afferent pathways from the two eyes remain segregated from eye to visual cortex



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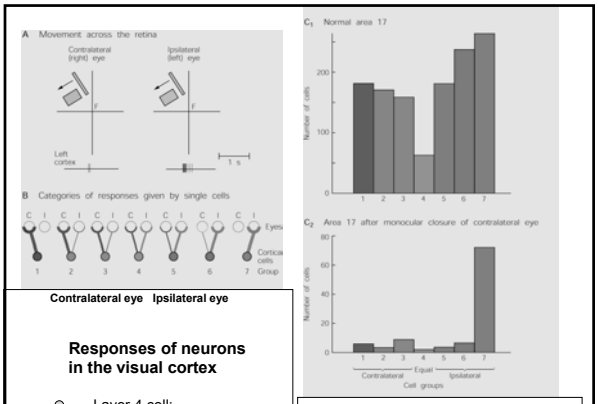

Responses of neurons in the visual cortex

○ = Layer 4 cell;

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Fig. 56.02

Are there structural changes after monocular eye closure?

Inject radioactive tracer into one eye…
and cut brain sections*

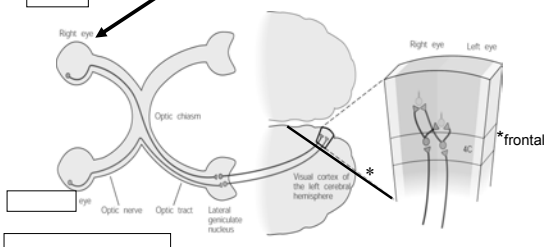

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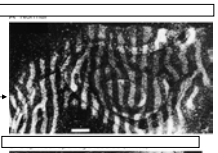
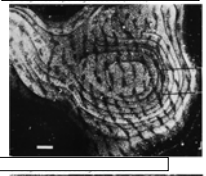
Fig. 56.01

After injecting radioactive tracer into eye,
cutting sections of visual cortex,
followed by autoradiography of sections.

NORMAL



DEPRIVED: INJECT OPEN EYE



DEPRIVED: INJECT CLOSED EYE

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Fig. 56.01

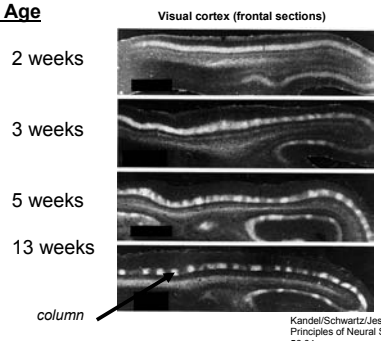
WHAT ARE THE TEMPORAL PARAMETERS of sensory deprivation?

- **THERE IS A CRITICAL PERIOD DURING THE FIRST 6 WEEKS OF LIFE**
- **ONE WEEK OF DEPRIVATION IS ENOUGH TO CAUSE IRREVERSIBLE CHANGES**
- **LONGER PERIODS OF DEPRIVATION *LATER* IN LIFE DO NOT HAVE THE SAME EFFECT**

Normal Development of Ocular Dominance Columns

Tracer injected into one eye, transneuronally transported across retinal axon synapse in thalamus (LGN), to cells projecting to visual cortex

Postnatal Age



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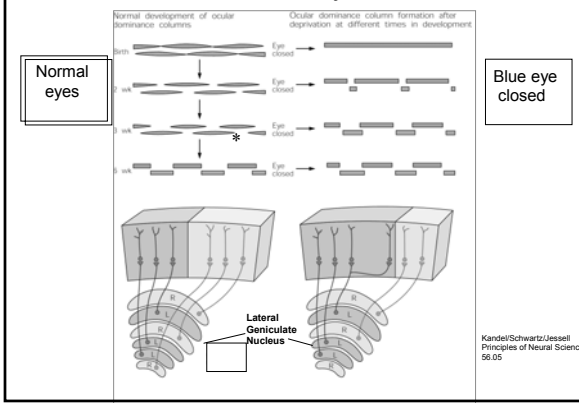
The effects of eye closure on formation of ocular dominance columns in layer 4c



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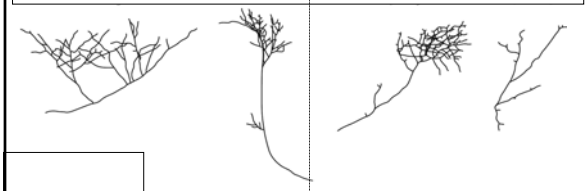
Branching Patterns of Geniculocortical axons

Normal Eye | After closure of one eye

Young | **Mature** | **Open eye** | **Deprived eye**



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After **binocular deprivation**, many cells remain responsive to both eyes.

-Monocular experiment: activity from afferent pathways is critical

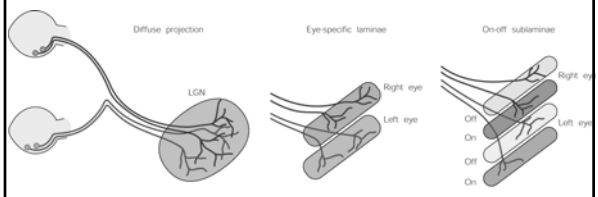
-binocular experiment : the ***balance*** of activity between inputs is also important.

Does neural activity play a role prenatally?

Postnatal critical period vs. prenatal "neural" activity ;

The lateral geniculate nucleus (first relay or target of retinal axons) and retinal "waves"

Segregation of eye-specific inputs from retinal to first relay in the Lateral Geniculate Nucleus occurs <u>before birth</u> in utero



This process is perturbed if neural activity is blocked in the eye or optic chiasm;

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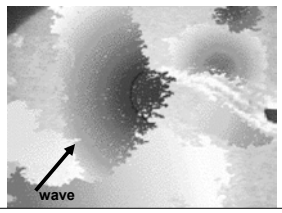
NATURE OF NEURAL ACTIVITY IN UTERO???

In the embryo, neighboring ganglion cells fire together in synchronous bursts or "waves"

This spontaneous but synchronous firing of retinal afferent fibers excites a group of target neurons in the LGN, and strengthens those synapses.



Fluorescent imaging of local calcium levels; each color represents a different "wave" event

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Fig. 56.10

HOW DOES NEURAL ACTIVITY INFLUENCE FORMATION OF THE CIRCUITRY?

"NEURONS THAT FIRE TOGETHER WIRE TOGETHER"

Mechanism for "winner-take-all" (open eye) and synapse elimination (closed eye):

-Cooperative, synchronous firing and competition (Hebb; LTP)

-Postsynaptic NMDA receptors open

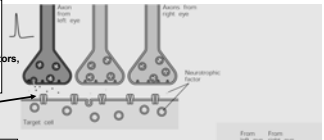
-Neurotrophins from postsynaptic cell released and taken up by active presynaptic terminals (ones that are strongly firing, cooperatively

-Neurotrophins act on presynaptic axons, axon arbors branch and expand

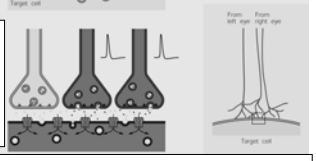
HOW COMPETITION BETWEEN NEURONS MIGHT MEDIATE THE FINE-TUNING OF SYNAPTIC CONNECTIONS IN THE DEVELOPING VISUAL CORTEX

Axon from left eye fires alone, this depolarization is insufficient to activate NMDA receptors and then release of neurotrophic factors, and the axon is not sustained.

NMDA RECEPTORS



Axons from right eye fire synchronously; large depolarization leads to NMDA receptor activation, neurotrophin release, and enhanced uptake by active terminals with active endocytosis.



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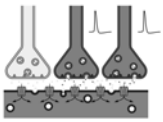
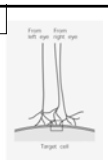
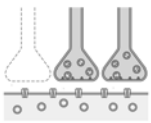
Axons from right eye fire synchronously; large depolarization leads to NMDA receptor activation, neurotrophin release, enhanced uptake by active terminals with active endocytosis.

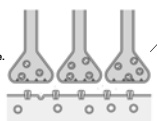




The inactive axon from the left eye did not take up neurotrophins, retracts.



Axons from the right eye, took up neurotrophic factor and branch, and occupy the vacated site from left eye.



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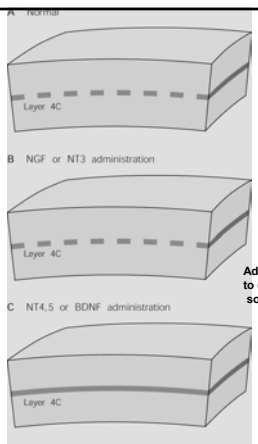

Administration of neurotrophins NT4, 5 or BDNF to developing cortex eliminates the need to compete, so no ocular dominance columns form.

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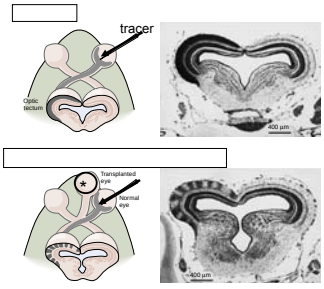
Ocular dominance columns can be induced experimentally in a frog by the transplantation of a third eye*



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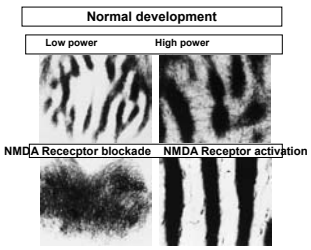

The activity of NMDA-type glutamate receptors controls the segregation of afferent input in the frog optic tectum.

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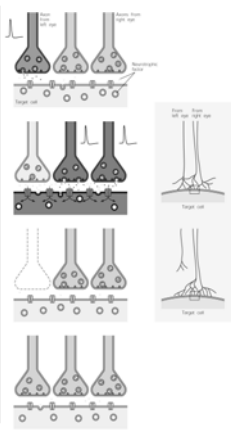
This mechanism, which resembles LTP,

explains how an initial relatively small bias towards one eye

can be progressively reinforced

until there is complete dominance.



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are highly dynamic, changing shape and synaptic contacts
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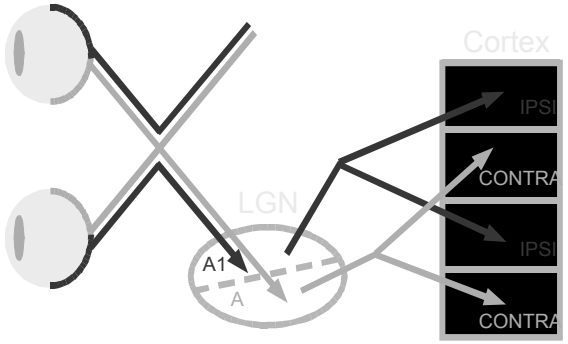
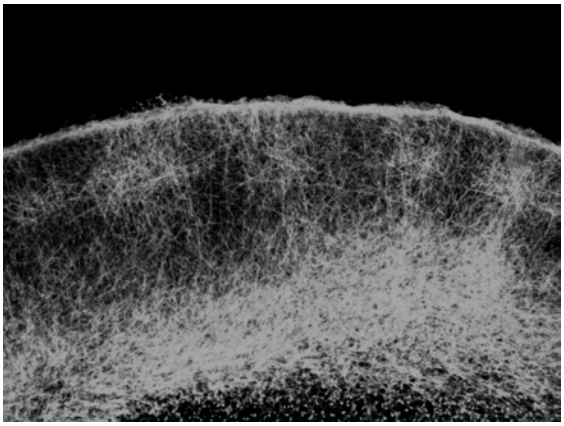
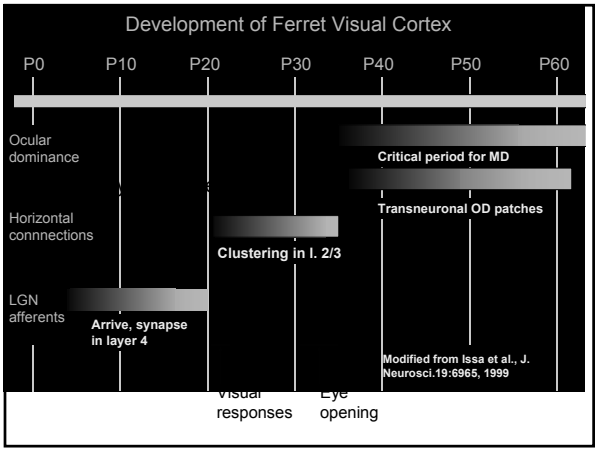


(Work of Larry Katz, after Hubel and Wiesel)



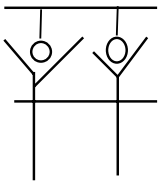


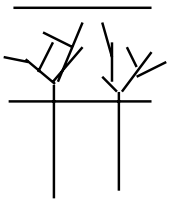
Ocular Dominance Development

two phases:

Establishment → Plasticity

Ocular dominance columns form before eye opening





By molecular "matching"?

Visual activity important for later branch addition, retraction?

Katz, Crowley, et al. Science 2000, 290:1321

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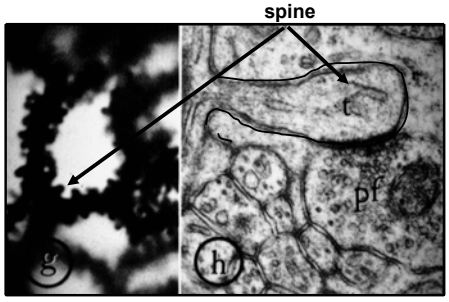
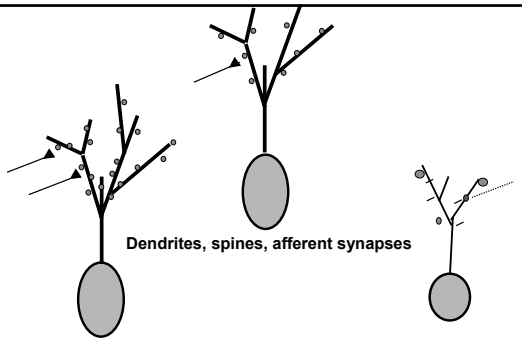


Light microsope view electron microscope view

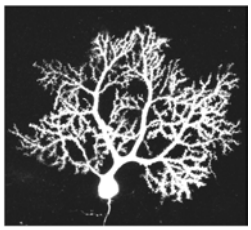


Increased in environments rich in sensory inputs

Perturbed in deprived environments and in developmental disorders (mental retardation, autism, hypothyroidism, etc)

Is spine motility developmentally regulated?

P10 +2div



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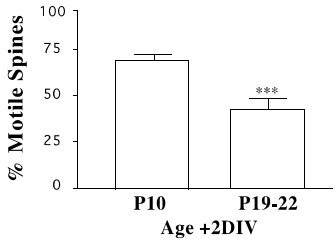
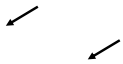
Dunaevsky, Yuste and Mason

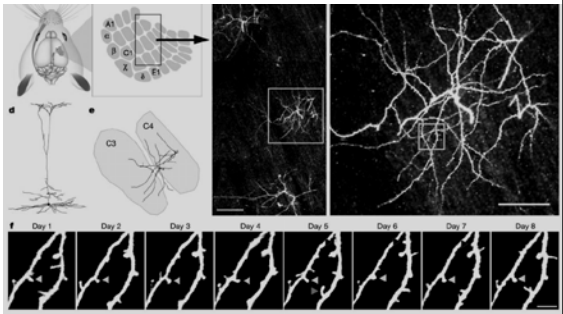
Spine motility is developmentally regulated





QuickTime™ and a TIFF decompressor are needed to see this picture.

In the adult cortex, spine lifetimes vary greatly: 50% are stable for at least a month, whereas the remainder are stable for only a day or less.



Spines imaged in the cortex of an intact living brain Trachtenburg et al., Nature 2002

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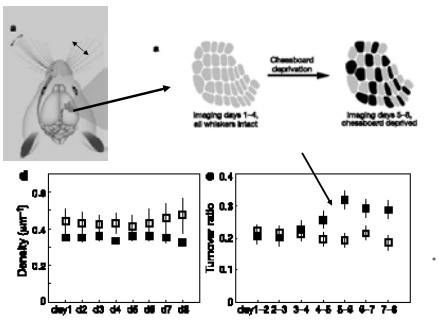
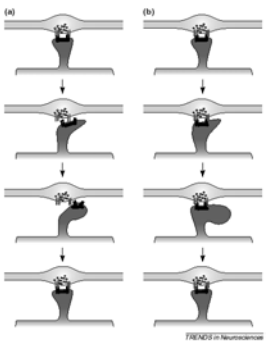
Experience and changes in connections later in life?

Experience alters spine turnover, even in the adult
Whiskers were cut,
dendrites and spines on somatosensory cortex cells imaged.



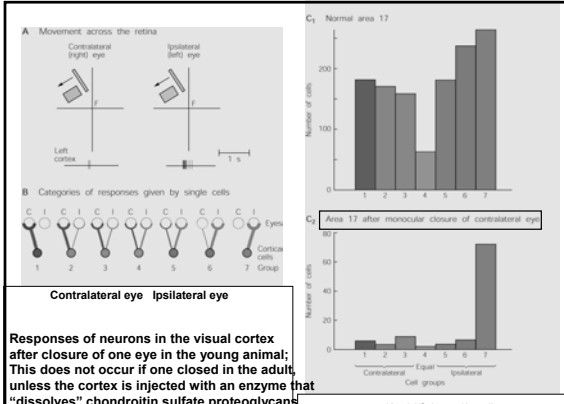
Trachtenburg et al., Nature 2002

If spines that have a synaptic contact move, then either…
(a) the synapse must break, or (b) the spines "wiggle" around the synaptic contact



Mason and Dunaevsky, 2003

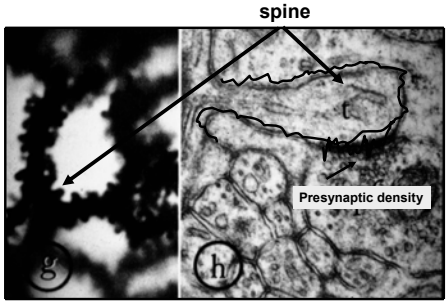
Reactivation of plasticity in the adult by degradation of the extracellular matrix



Responses of neurons in the visual cortex after closure of one eye in the young animal; This does not occur if one closed in the adult, unless the cortex is injected with an enzyme that "dissolves" chondroitin sulfate proteoglycans. (Pizzorusso et al, 2002)

Kandel/Schwartz/Jessell
Principles of Neural Science
Fig. 56.02

spine



Light microsope view electron microscope view

——— = Extracellular matrix

III. Topics/Controversies in recent research (*not in the text book*)

A. Are cortical ocular dominance columns set up prenatally in absence of neural activity? Molecular matching?

B. Dendritic Spines (sites of excitatory synaptic input on large neurons)

are highly dynamic, changing shape and synaptic contacts

-Increased dynamism in enriched environments;
perturbed in deprived contexts.

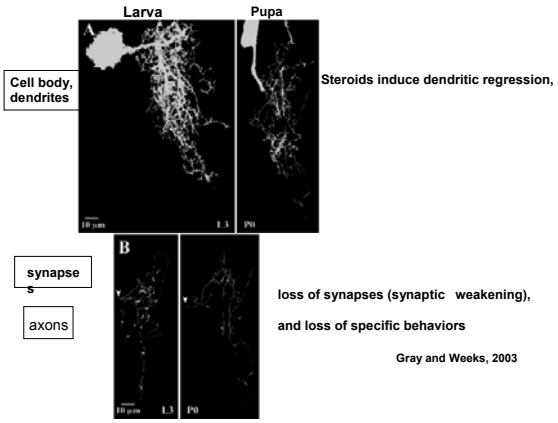
-Does morphological plasticity continue? At reduced levels?

C. Experience and changes in connections later in life?

-Reactivation of plasticity in the adult: by sensory experience, by degradation of the extracellular matrix

-Changes in steroid hormone levels induce dendritic alterations, and loss of synapses

-Barn owls and visuo/auditory localization: functional and structural plasticity



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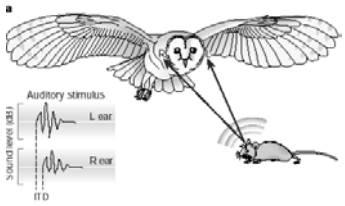
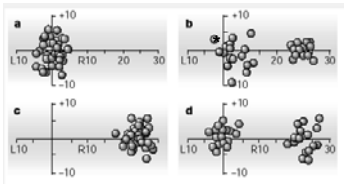


Work of Eric Knudsen, Nature 417: 322 (2002)

Before prisms

Day 42



Day 1

Prisms removed

Plasticity of auditory orienting behavior of a juvenile owl resulting from prism experience.

Visuomotor adjustment occurs more rapidly than auditory-visual realignment.

Plasticity of the anatomical projection from the ICC to ICX in adults after juveniles were raised with prisms