

### 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.

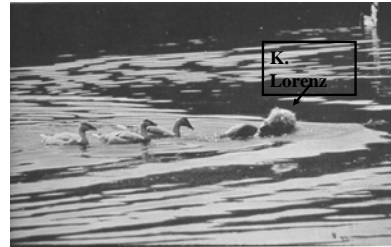
#### I. Effects of social deprivation

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 experiences 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

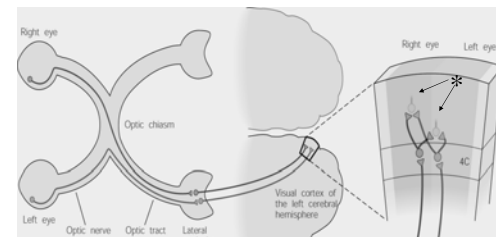
Physiological features of ocular dominance columns in the visual cortex (work of Hubel and Wiesel)

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.

Kandel/Schwartz/Jessell  
Principles of Neural Science  
Fig. 56.01

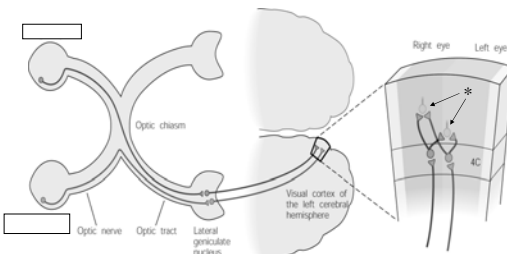
Early visual experience:

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.

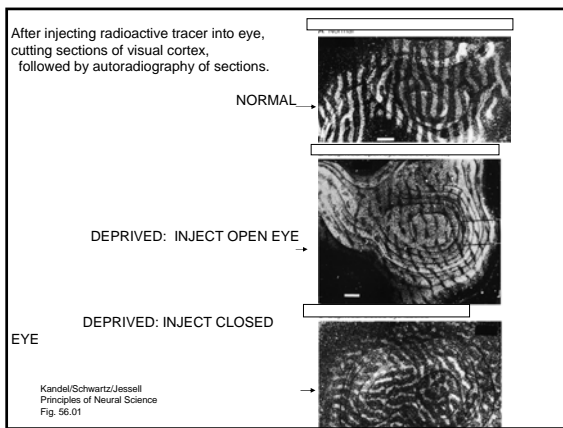
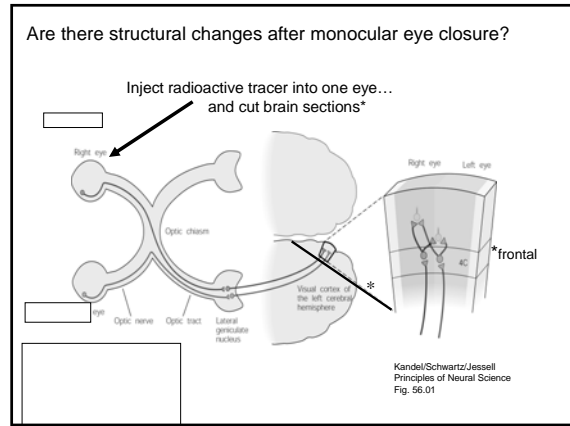
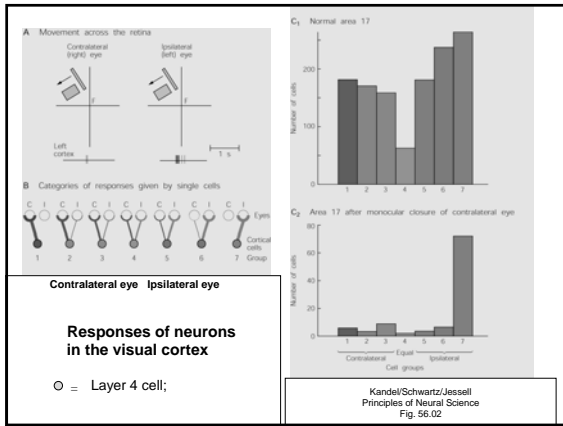
They deprived animals of visual input (*by closing/suturing the eyelid of one or both eyes*) and analyzing the consequences on visual cortical development and visual behavior.

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



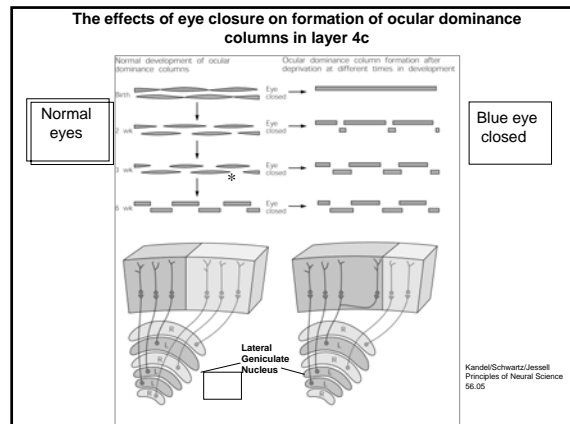
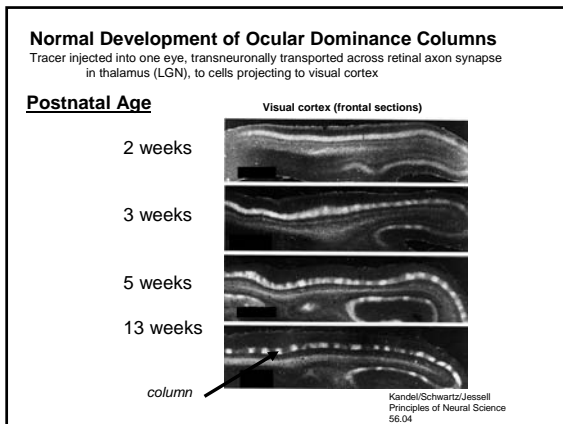
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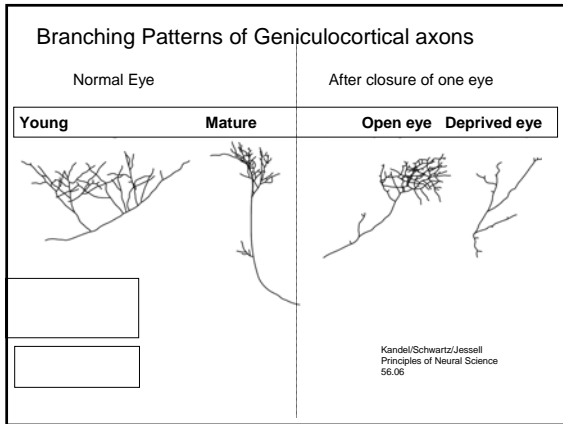
Kandel/Schwartz/Jessell  
Principles of Neural Science  
Fig. 56.01



**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





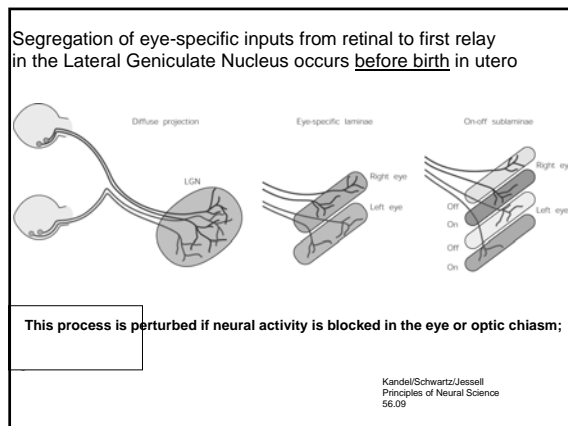
After **binocular deprivation**, many cells remain responsive to both eyes.

- 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"



### 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

Principles of Neural Science  
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.**

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

Kandel/Schwartz/Jessell  
Principles of Neural Science  
56.12

**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.**

Kandel/Schwartz/Jessell  
Principles of Neural Science  
56.12

**A Normal**

**B NGF or NT3 administration**

**C NT4,5 or BDNF administration**

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

Kandel/Schwartz/Jessell  
Principles of Neural Science  
56.11

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

Kandel/Schwartz/Jessell  
Principles of Neural Science  
56.07

**Normal development**

Low power	High power
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**NMDA Receptor blockade**     **NMDA Receptor activation**

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

Kandel/Schwartz/Jessell  
Principles of Neural Science  
56.08

**This mechanism, which resembles LTP,**

**explains how an initial relatively small bias towards one eye**

**can be progressively reinforced**

**until there is complete dominance.**

Kandel/Schwartz/Jessell  
Principles of Neural Science  
56.12

Lecture 39 – (Chapter 56) – Carol Mason

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- 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

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

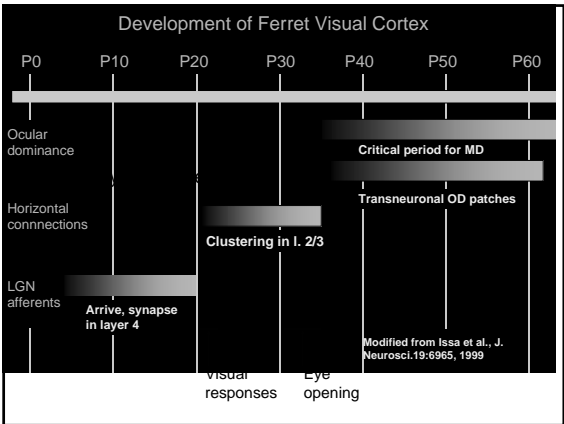
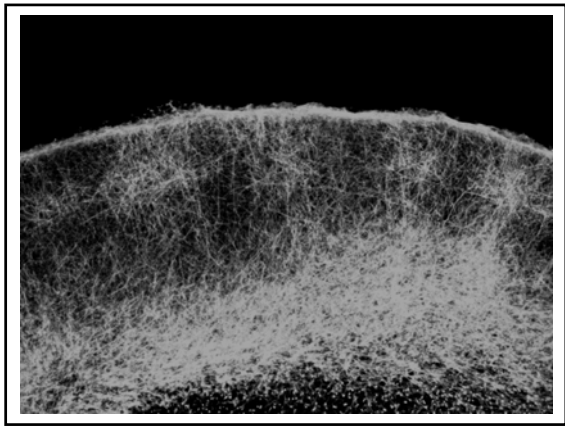
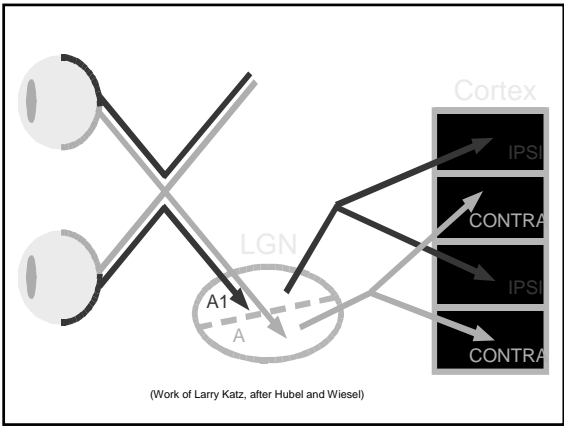
**B. Dendritic Spines (sites of excitatory synaptic input on large neurons)**

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?**

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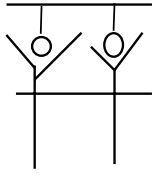


Ocular Dominance Development

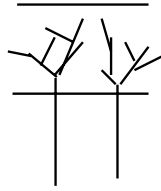
two phases:

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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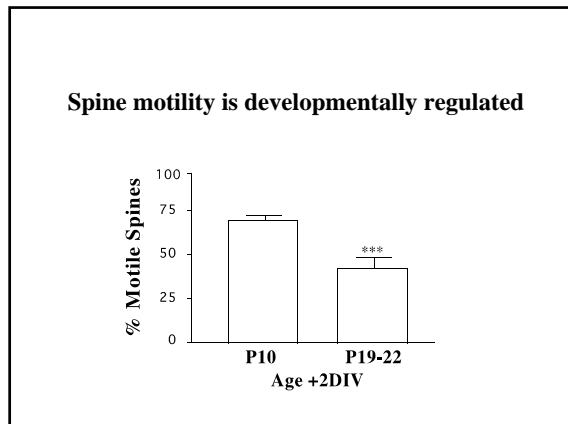
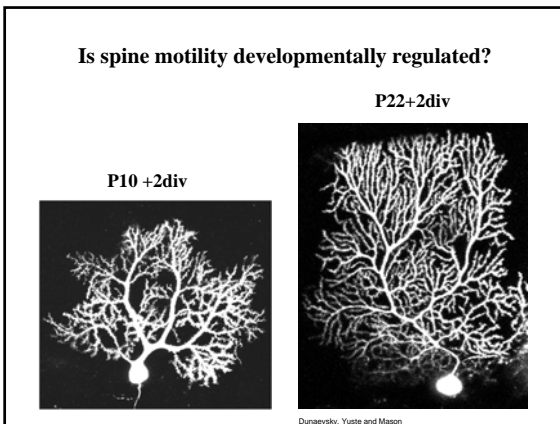
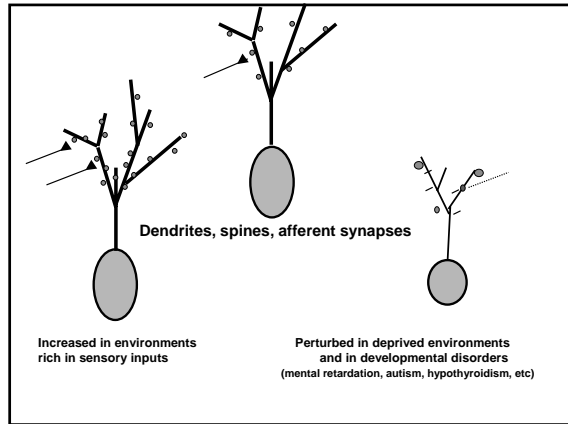
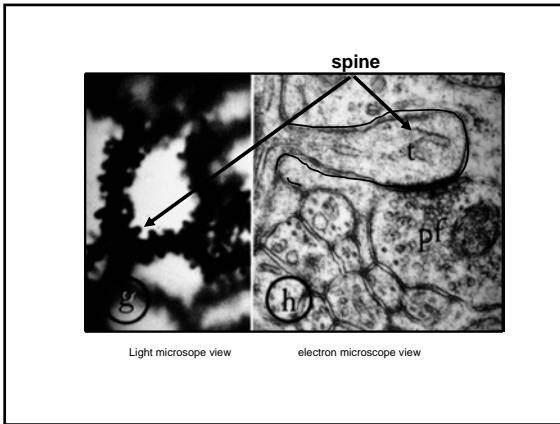
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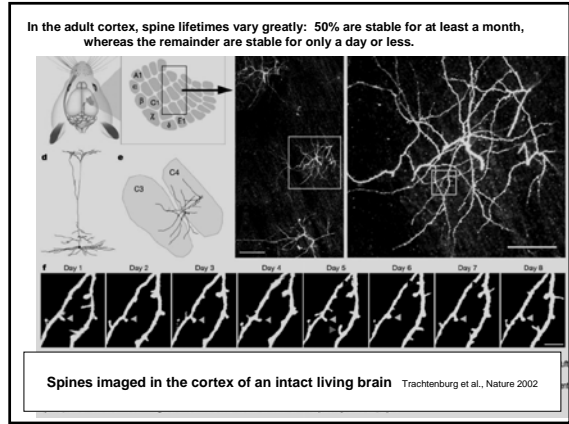
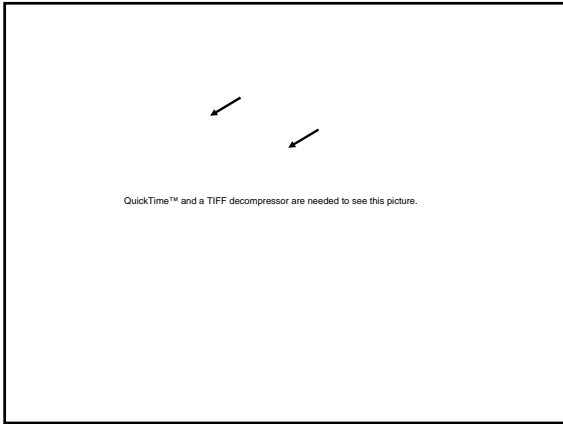
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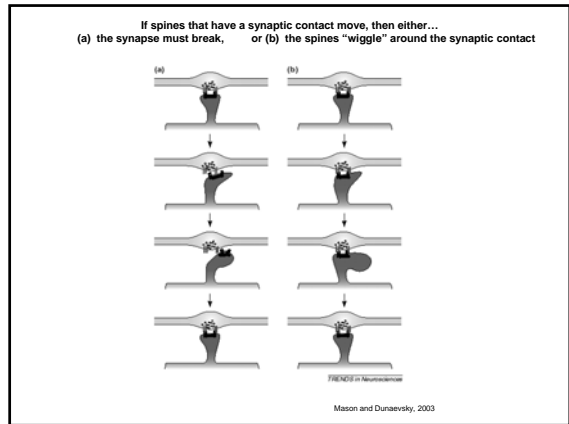
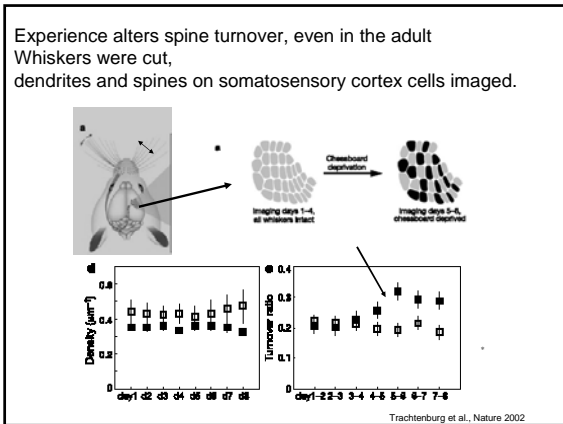
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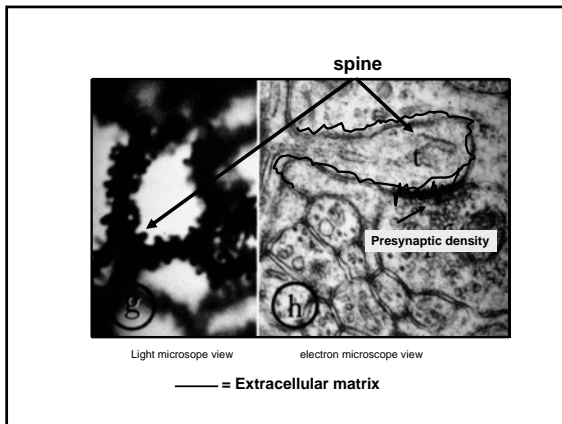
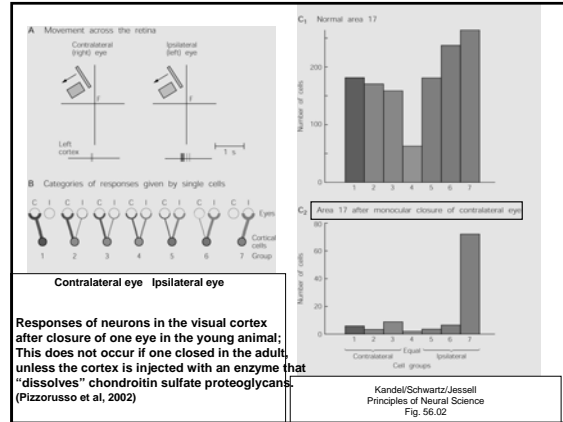
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Experience and changes in connections later in life?

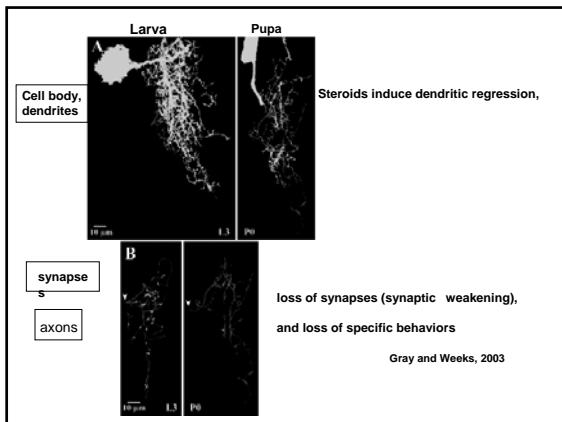


**Reactivation of plasticity in the adult  
by degradation of the extracellular matrix**



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