The Visual System

Plasticity

Casagrande

March 15, 2004

Phone: 343-4538

Email: vivien.casagrande@mcmail.vanderbilt.edu

Office: T2302 MCN

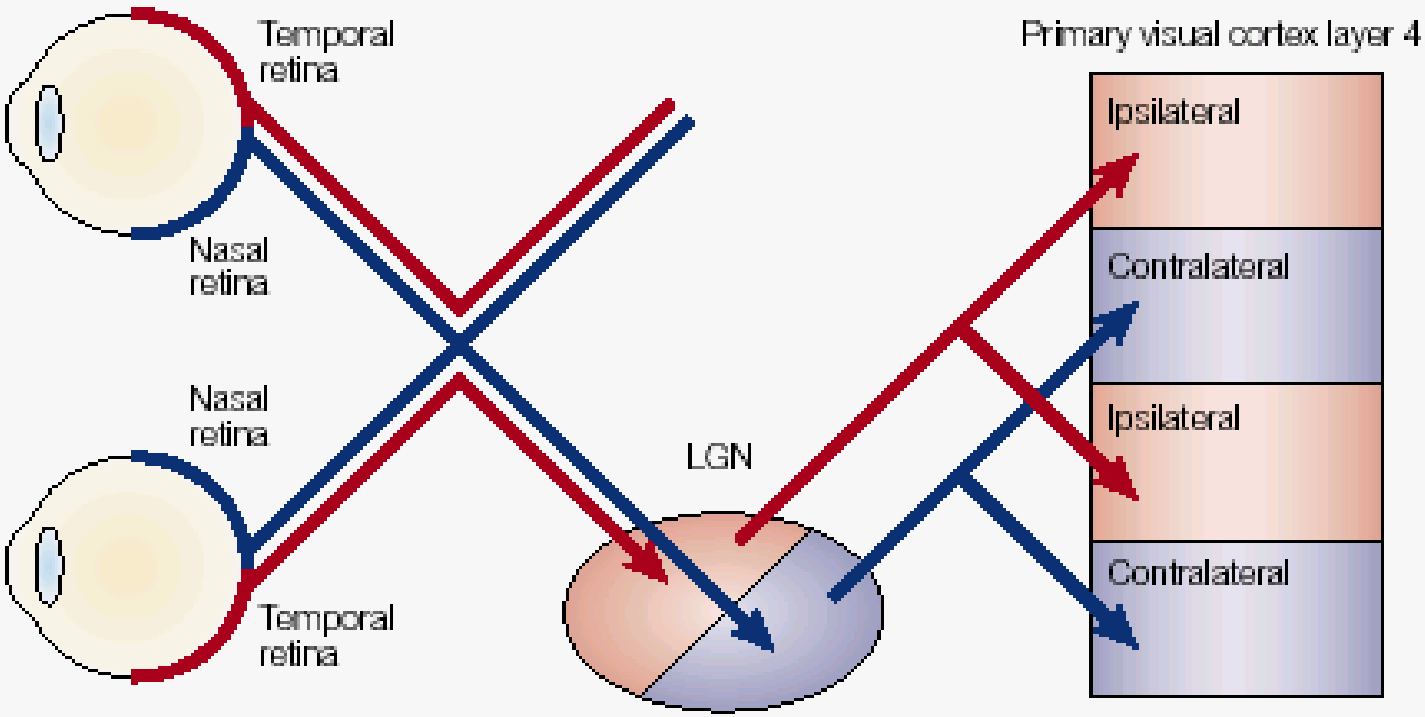


Figure 1 | **Segregation of eye-specific information at the early stages of visual processing.** In mammals with binocular vision, the nasal portion of one retina encodes the same part of the visual world as the temporal portion of the other retina. The axons of retinal ganglion cells from the nasal portion of each retina cross the optic chiasm and project to the same lateral geniculate nucleus (LGN) as the axons from the temporal portion of the other eye. These projections form discrete, eye-specific LGN layers. The projection from the LGN to layer 4 of the primary visual cortex maintains this eye-specific segregation by terminating in eye-specific patches that are the anatomical basis for ocular dominance columns. Ocular dominance columns can therefore be considered to correspond to an eye (left or right) or a retinal location (nasal or temporal).

Question from the readings

- Is neural activity important to the segregation of left and right eye axons within the LGN or visual cortex?

Is Neural Activity important to segregation of light and right eye axons in LGN or visual cortex?

- Blockade of all activity with tetrodotoxin (TTX), a sodium channel blocker, in vivo blocks segregation.

- Eye removal before geniculo-cortical axons segregate blocks segregation of axons from the left and right eye.

CAN VISUAL EXPERIENCE INFLUENCE THE DEVELOPMENT OF LGN AXONS IN CORTEX?

Children that are born with any condition the compromises vision in one eye are at risk for permanently losing vision (e.g developing ambyopia) in the compromised eye if the condition is not corrected within the first 2 to 3 years of life.

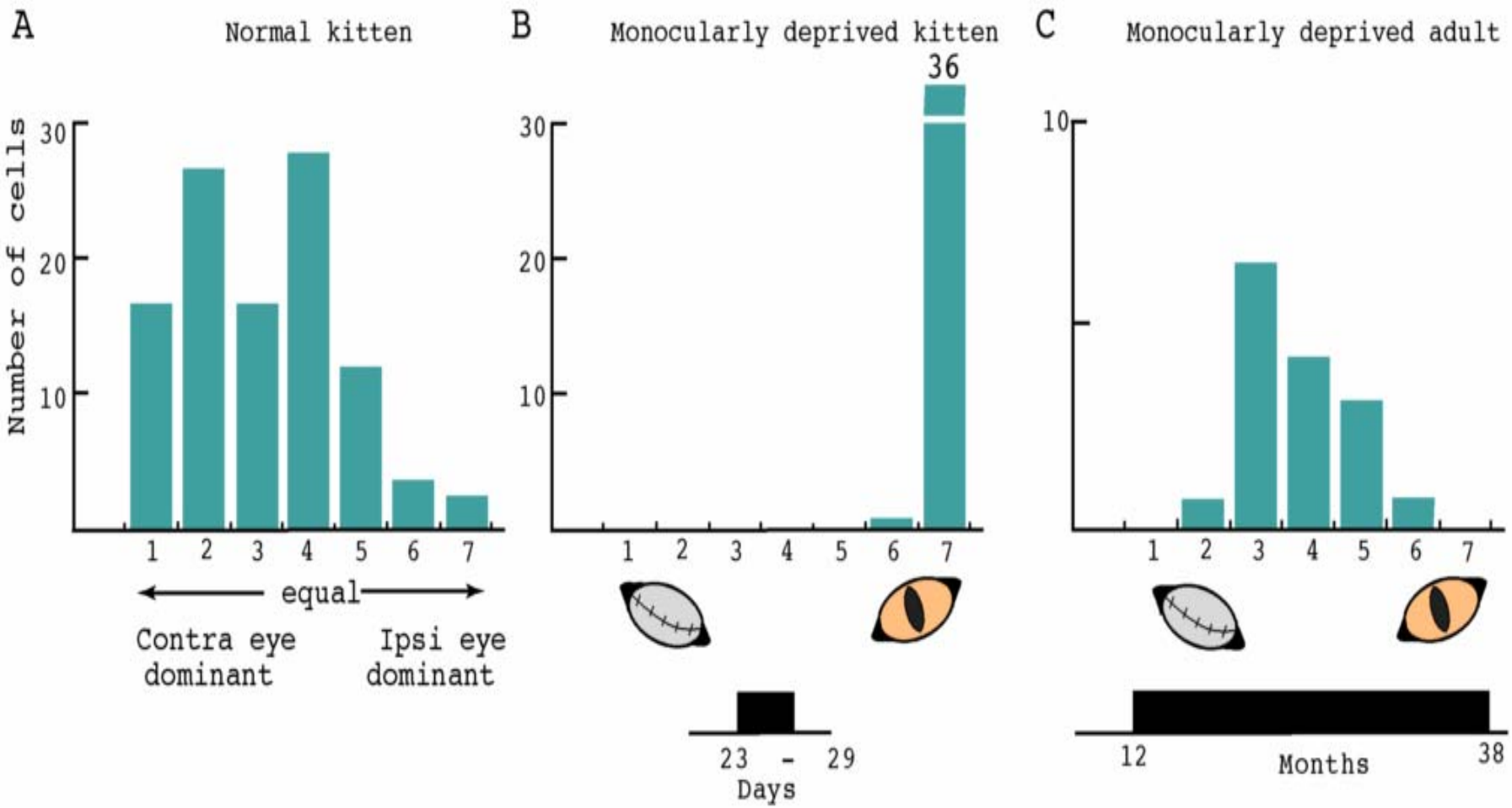
Monocular Deprivation

Studies by Hubel and Wiesel showed that raising a cat or a monkey with one eye deprived of useful patterned vision by *suturing one eye-lid closed* could cause almost all of the cells in visual cortex to respond to the non-deprived (open) eye.

- The anatomy showed that deprived layer cells were smaller in the geniculate nucleus than non-deprived cells and that axons of these deprived cells occupied less territory in cortex.

- Behaviorally monocularly deprived animals have poor visual resolution of non-optical origin (**amblyopia**) when using the deprived eye

There is a critical period during which monocular deprivation can affect the wiring of the developing visual system.



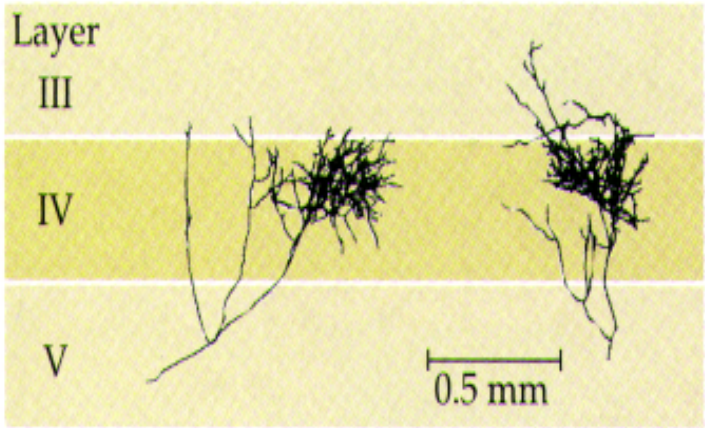
- In cats the critical period for experience to affect left and right eye connections (ocular dominance columns) in visual cortex is the first 3 months, in humans it is the first 2-3 years.

- This period may correspond to the period that axons are still developing and refining their connections.

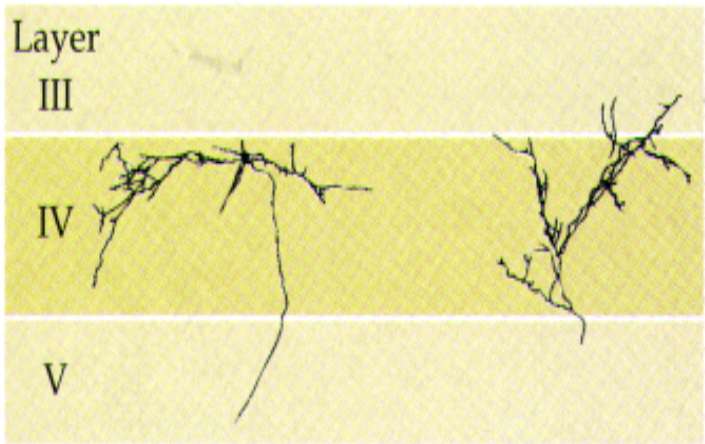
- During the critical period very short periods of deprivation of a few hours can shift the response of cortical cells toward the open eye.

(A) SHORT-TERM MONOCULAR DEPRIVATION

Open eye

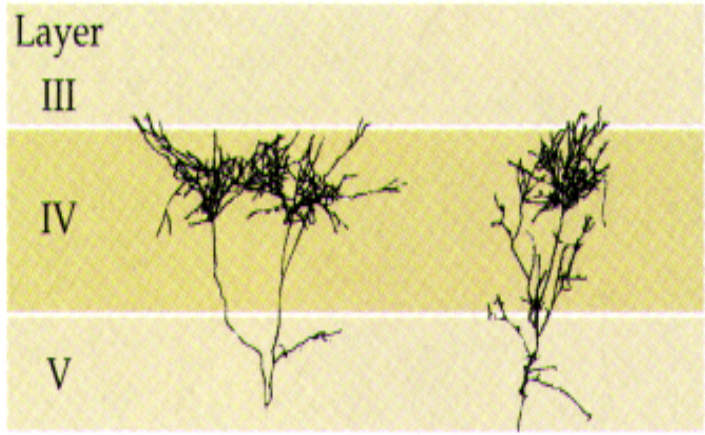


Deprived eye

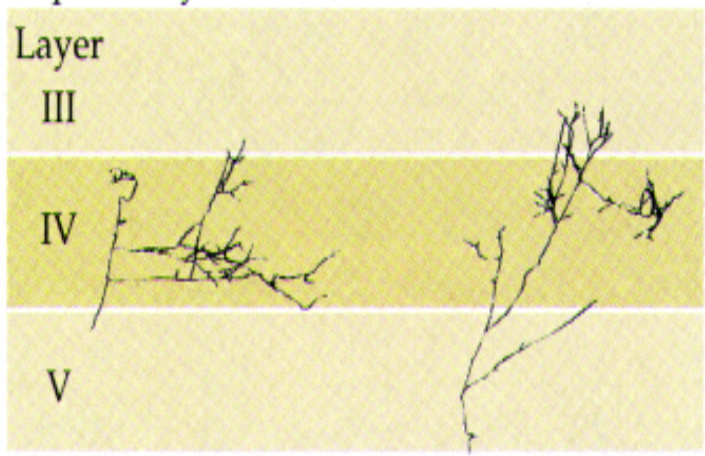


(B) LONG-TERM MONOCULAR DEPRIVATION

Open eye



Deprived eye



Does monocular deprivation cause atrophy of connections due to disuse?

Hubel and Wiesel sutured both eyes of kittens and raised these animals with lids sutured for a few months and found that most cortical cells could be driven by both eyes as in normal animals so the results of monocular deprivation could not be explained by disuse alone.

They proposed that axons from each eye compete (BINOCULAR COMPETIION) with each other for cortical space

How can neural activity affect competition between the two eyes for territory in the LGN or visual cortex?

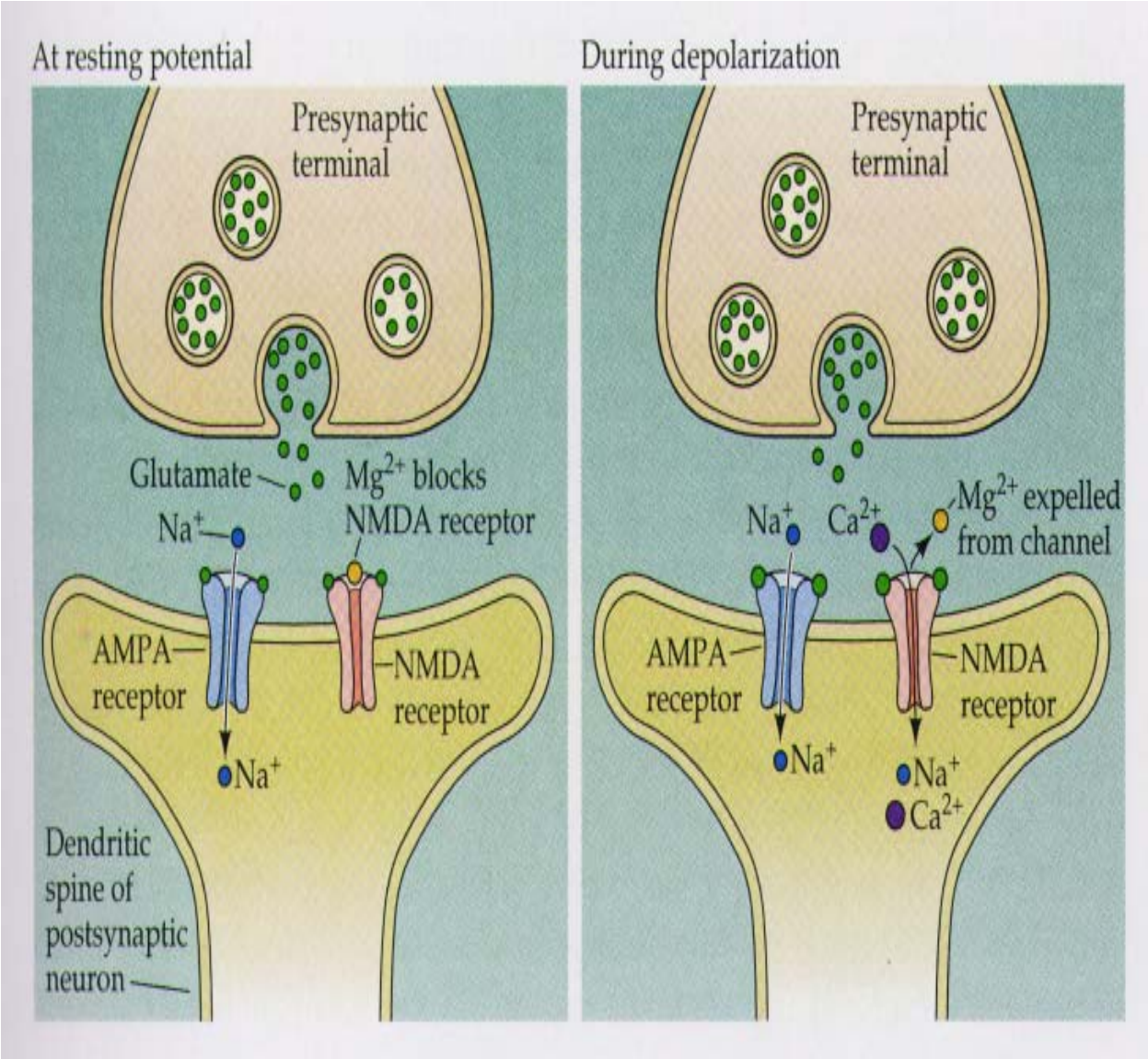
Neural Activity is important to stabilizing synapses

Cells that are active receive more nutrient materials (neurotrophic molecules from potential postsynaptic targets)

Cells that are near neighbors in the retina tend to be active active at the same time synapse close together in their targets where cells are also more likely to be simultaneously active. Cells that **fire together tend to wire together.**

Neural activity in the left eye is not correlated with neural neural activity in the right eye. Therefore, cells in each eye tend to develop synapses with separate populations of of central cells.

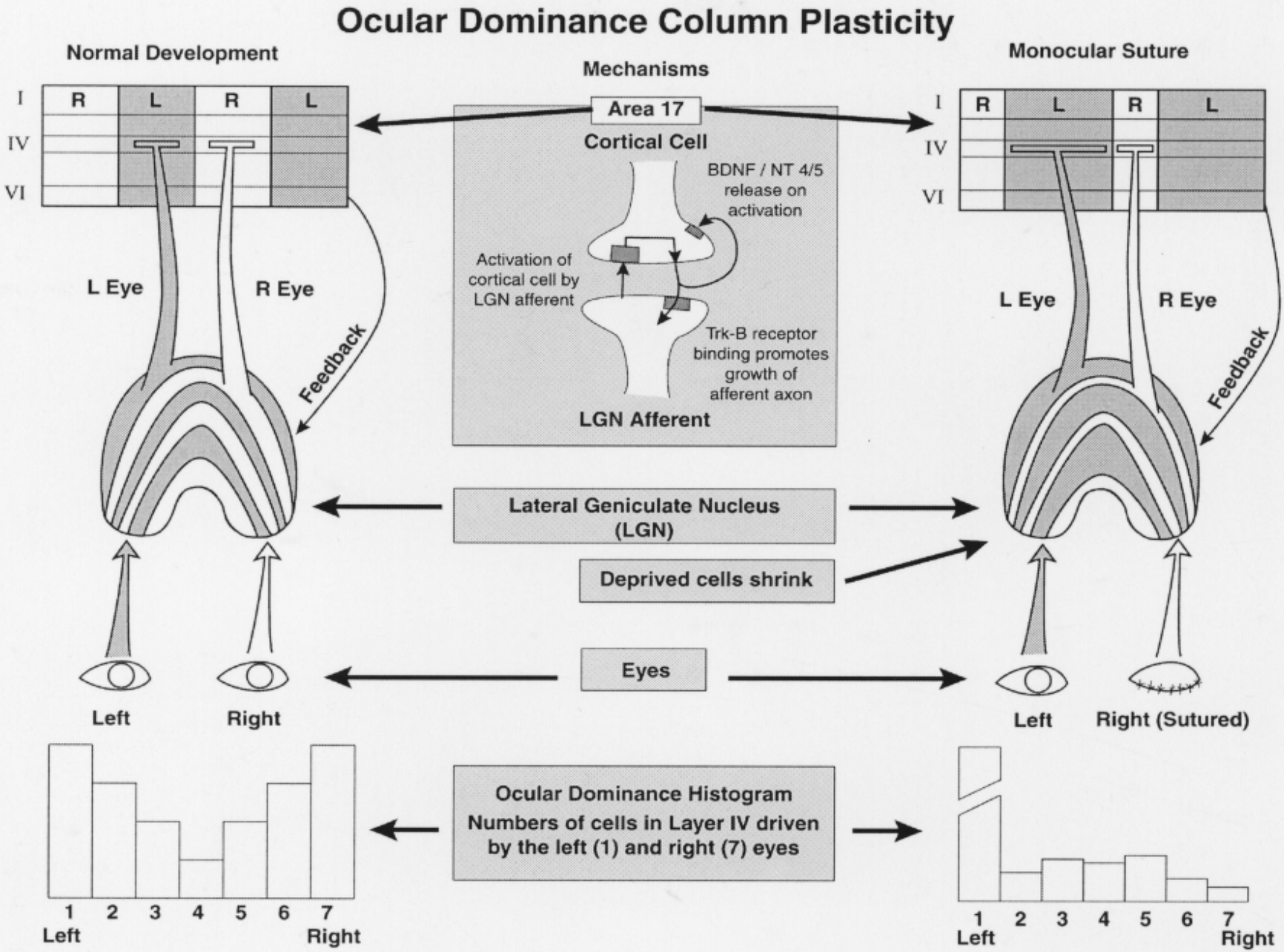
How can activity strengthen synapses?



The **N-methyl-D-aspartate** (NMDA) glutamate receptor channel can open only during depolarization of the postsynaptic cell. Calcium entering the postsynaptic cell can trigger events that eventually lead to strengthening a synapse or allowing a synapse to develop.

Cooperation and competition among neurons in visual cortex fine tune connections

Active cells release transmitters and other molecules. These molecules activate the postsynaptic cell which, in turn, can release a **growth factor** that helps the presynaptic cell to develop larger axons or establish more synapses. These growth factors may exist in limited supplies. Cells may **compete** for these factors as a normal part of development with the winner establishing a synapse.


Ocular Dominance Column Plasticity
Normal Development
Mechanisms
Monocular Suture
I
IV
VI
R
L
R
L
Area 17
Cortical Cell
BDNF / NT 4/5 release on activation
Activation of cortical cell by LGN afferent
Trk-B receptor binding promotes growth of afferent axon
LGN Afferent
L Eye
R Eye
Feedback
Lateral Geniculate Nucleus (LGN)
Deprived cells shrink
Eyes
Left
Right
Right (Sutured)
Ocular Dominance Histogram
Numbers of cells in Layer IV driven by the left (1) and right (7) eyes
1 2 3 4 5 6 7
Left
Right

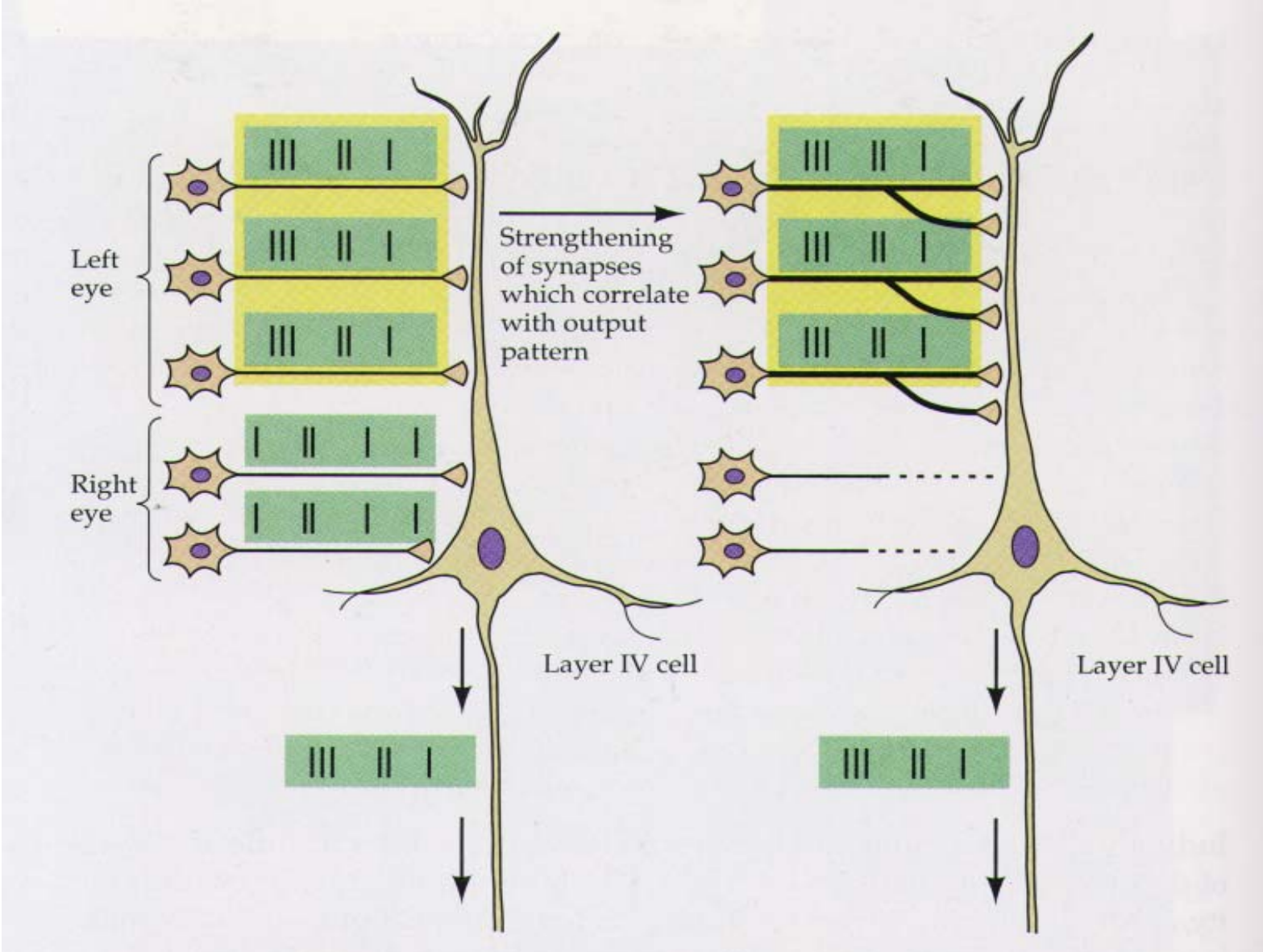
HOW CAN ACTIVITY CHANGE THE GROWTH OF AXONS?

One model suggests that synchronous activity between axons may trigger the postsynaptic cell to depolarize enough to stimulate NMDA glutamate channels to open.

The influx of calcium may trigger the postsynaptic cell to release a growth factor (e.g., BDNF) that is taken up by presynaptic axons when the presynaptic cell (axon) is also active.

This could, in turn, stimulate the presynaptic cell to grow a larger terminal or make more synapses.

Inactive terminals would fail to grow and be withdrawn. If two terminals driving the same cell were active at different times the "bigger" one would win.

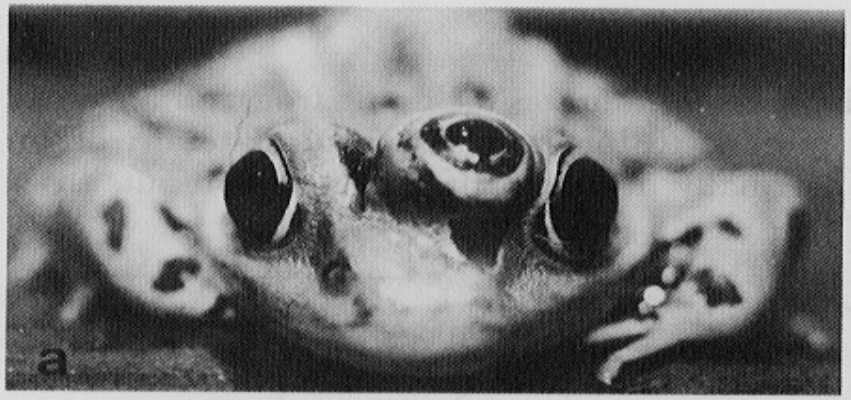

Left eye
Right eye
Strengthening of synapses which correlate with output pattern
Layer IV cell
Layer IV cell

Do neural activity and availability of growth factors really matter? What is the evidence?

Axons do not segregate into ocular dominance bands in cortex if neural activity is blocked (TTX) during development or if the neural trophic factors neurotrophin 4/5 (NT4/5) or brain-derived growth factor (BDNF) are provided directly to the cortex.

Blocking activity or providing growth factors directly prevents ocular dominance columns from forming.

There are no ocular dominance columns in normal frog tectum but ocular dominance columns can be created by adding an eye and forcing the axons to compete for space in the tectum.



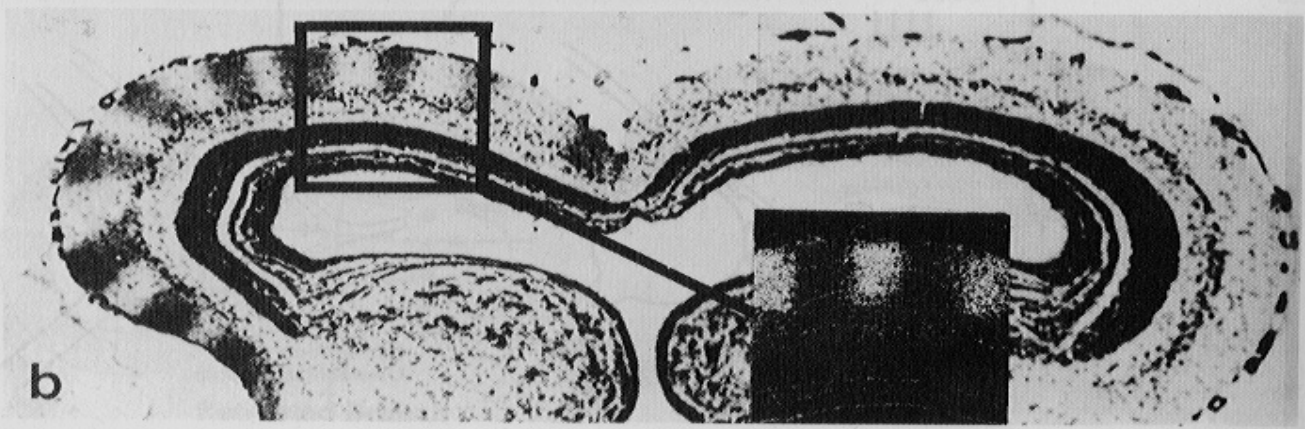
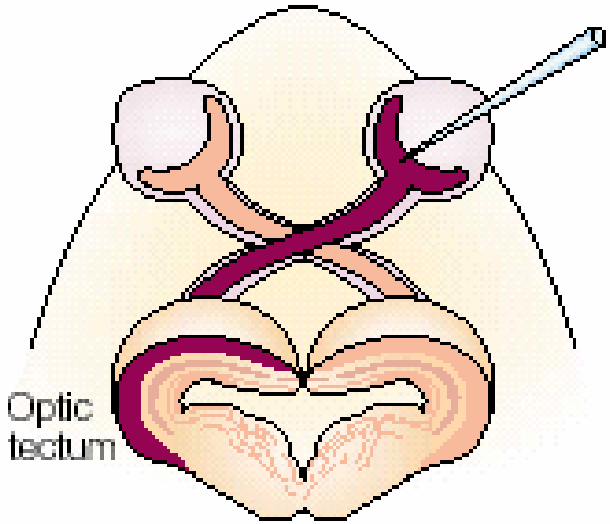
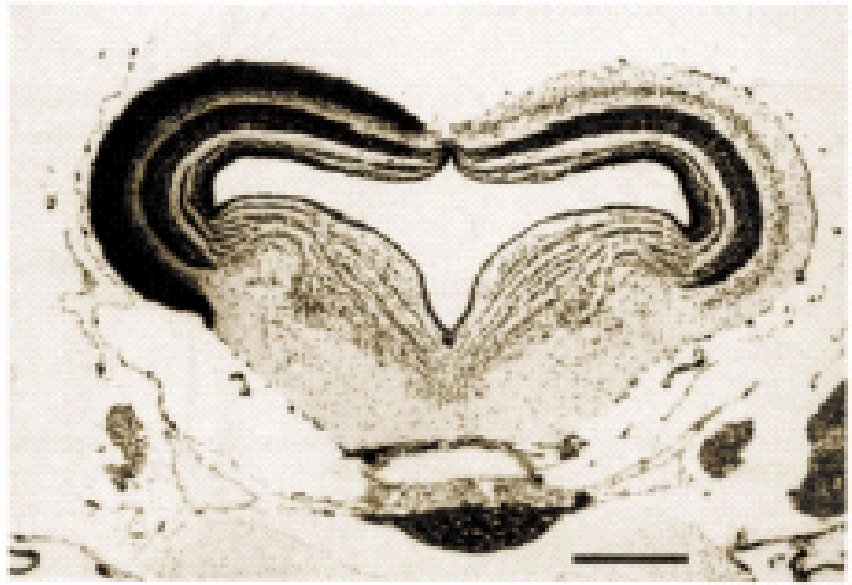
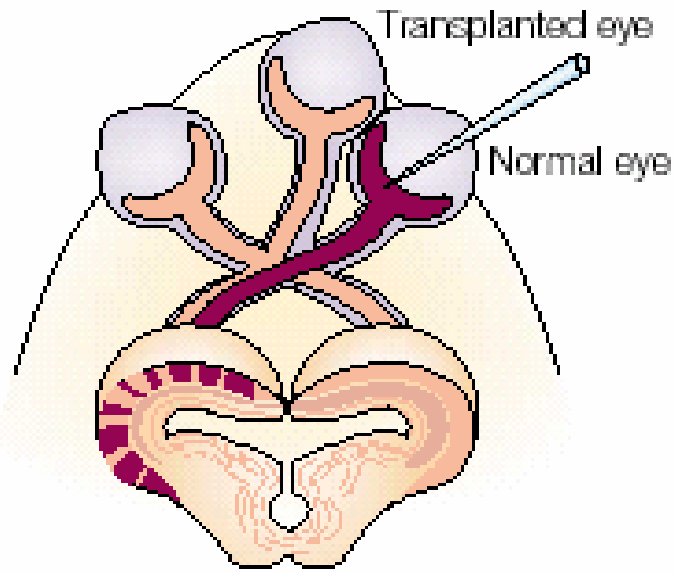
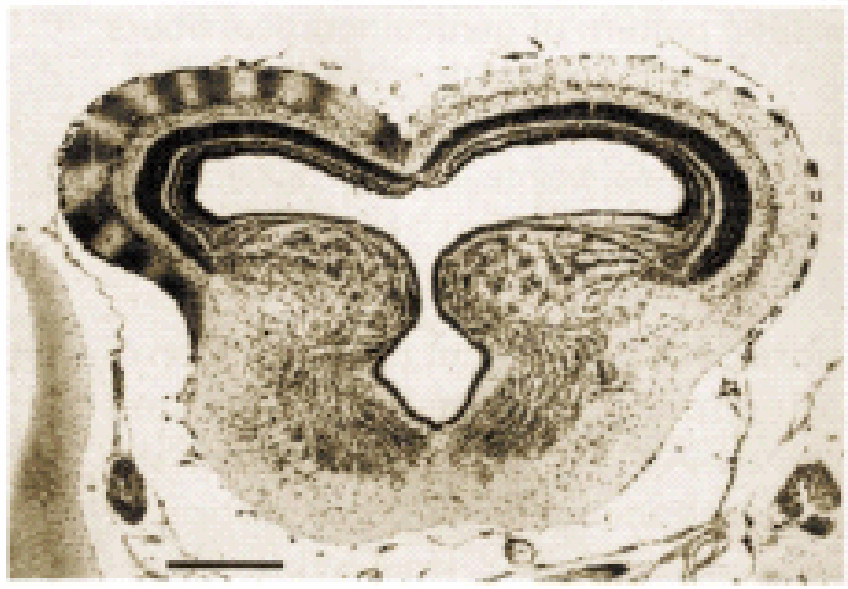


Figure 16-6. The three-eyed frog. *a:* Three-eyed frogs have been studied by Martha Constantine-Paton and her colleagues. *b:* An autoradiograph of the tectum shows the formation of stripes of inputs from the normal and the implanted eye. The inset shows an enlargement under dark-field illumination (Constantine-Paton and Law, 1978).



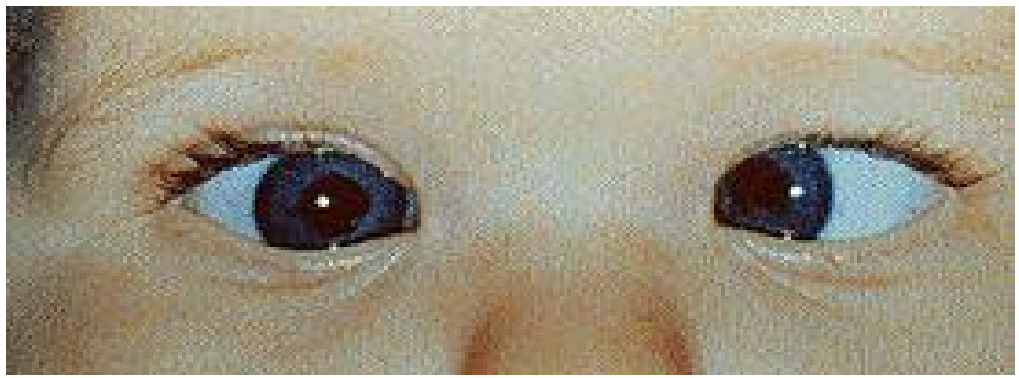




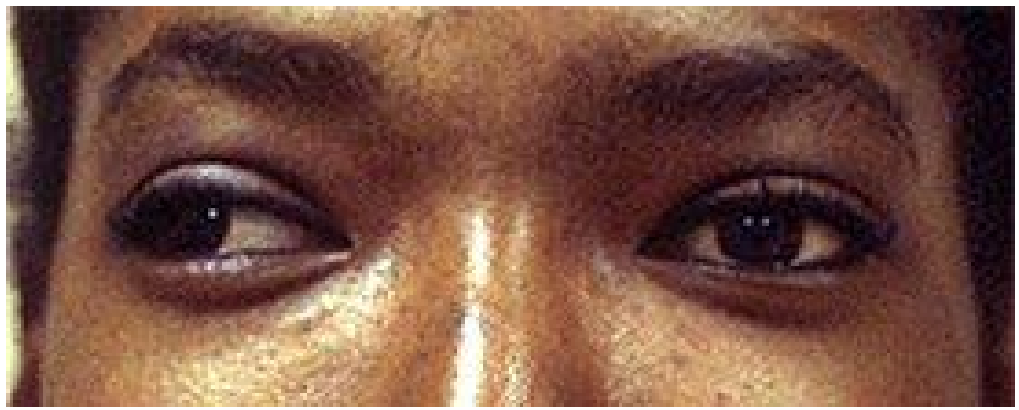


Blockage of NMDA receptors with APV blocks segregation

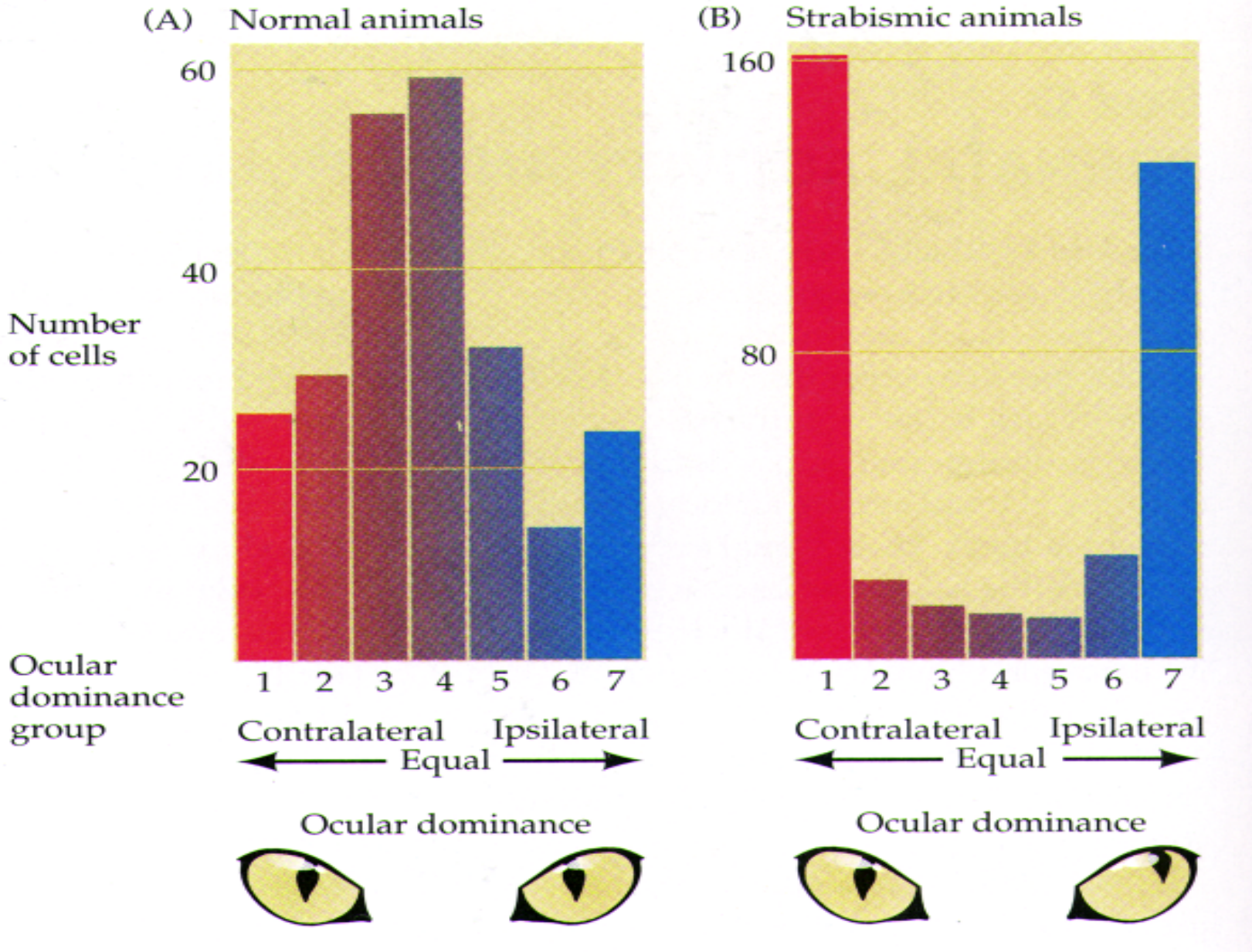
Other forms of abnormal visual experience such as strabismus (cross-eyed or wall-eyed, extreme nearsightedness, alternate patching of each eye, or abnormal visuomotor experience can cause changes in the developing visual cortex.



Esotropia (cross-eyed)

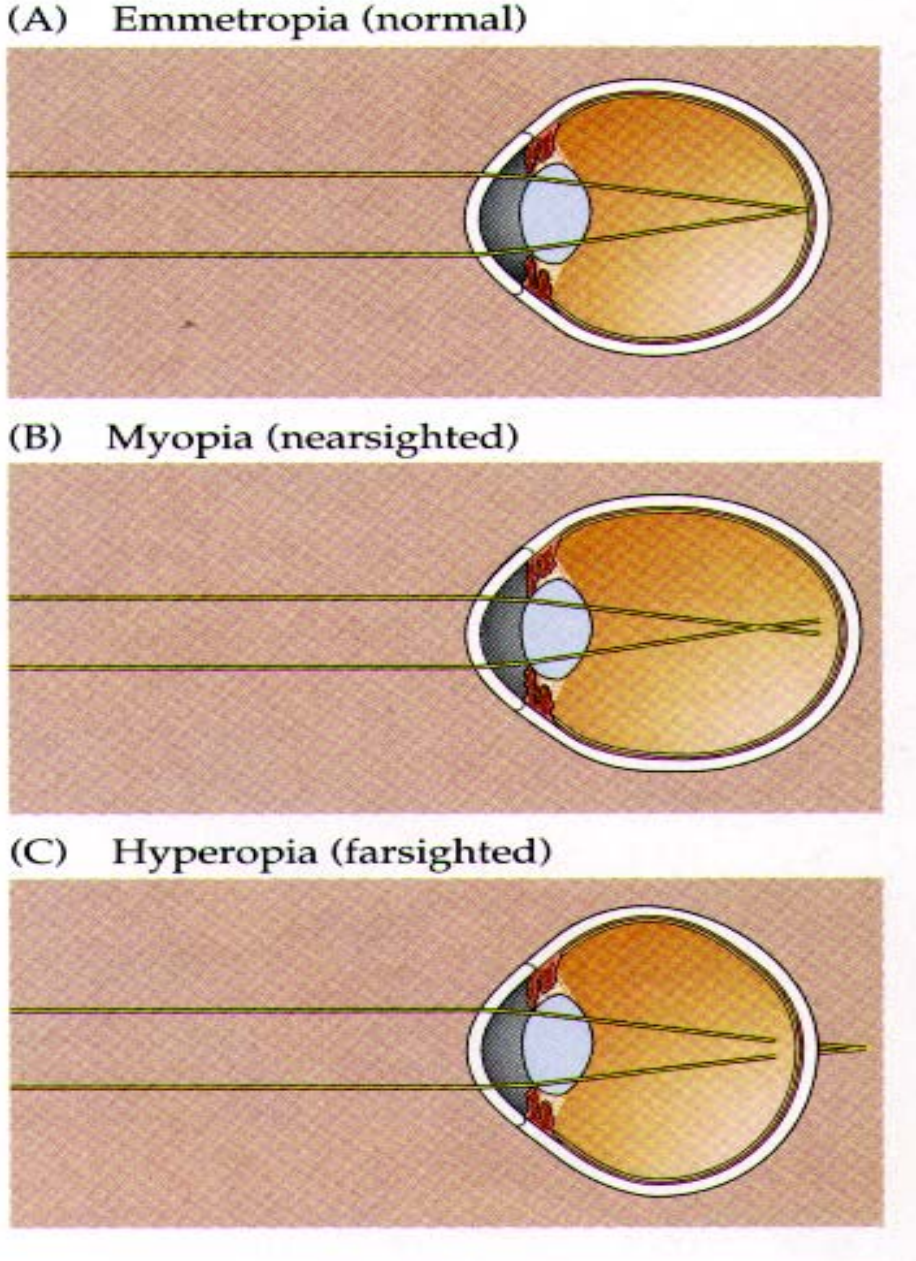


Exotropia (wall-eyed)


(A) Normal animals
(B) Strabismic animals
60
40
20
160
80
Number of cells
Ocular dominance group
1 2 3 4 5 6 7
Contralateral
Ipsilateral
Equal
Ocular dominance

Initial Ocular segregation of LGN axons in cortex does not require visual experience in primates

- Ocular dominance columns form *before birth* in macaque monkeys and can form (although not completely) in cats that are dark reared or binocularly sutured from birth.
- This finding suggests that abnormal visual experience can modify ocular dominance columns but may not be necessary for them to form originally. Neural activity, however, is likely to be important because if all activity is blocked before ocular dominance form, columns do not develop.



Why are we nearsighted or farsighted?

The Problem-
Many people become Nearsighted

- 25% of American adults are myopic
- Percentage is rising
- Glasses/contacts are expensive
- High myopia is a risk factor for glaucoma and retinal detachment

Is myopia caused by the environment?

or

Is there a genetic basis?

The Environment-

Does Nearwork Cause Myopia?

- Correlation of myopia with education level
- High percentage of myopes among college students
- Even higher among percentage among medical students, optometry students, law students, etc.

- … but might have inherited scholarly ability?

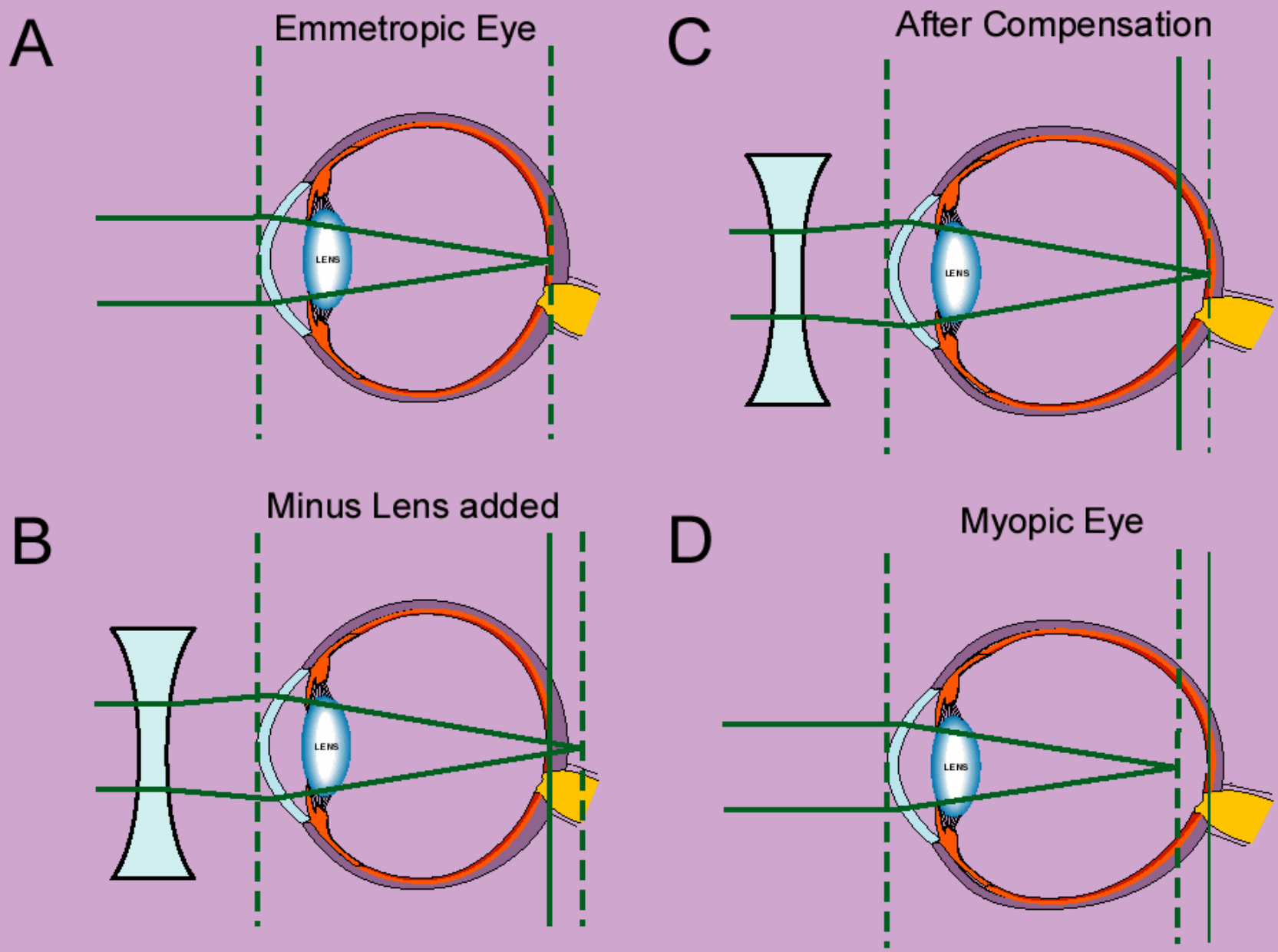
Do Genetics Cause Myopia?

- If neither parent myopic - 10% chance
- If one parent myopic - 20-25% chance
- If both parents myopic - 40-50% chance

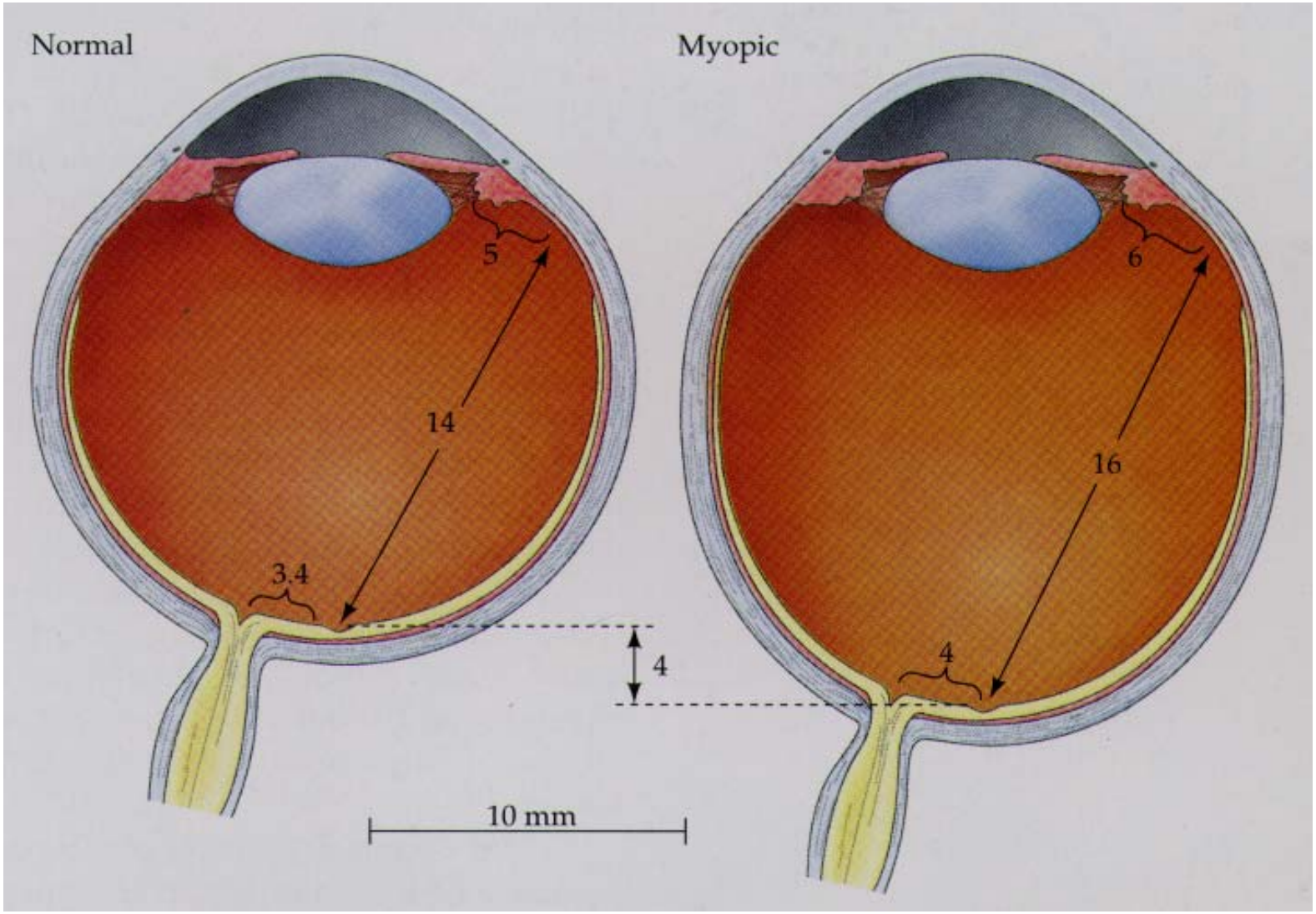
- … but myopic parents might provide an environment that produces myopia

Evidence suggests that visual experience can also modify the structure of the eye

Animal Experiments


A
Emmetropic Eye
LENS
C
After Compensation
LENS
B
Minus Lens added
LENS
D
Myopic Eye
LENS

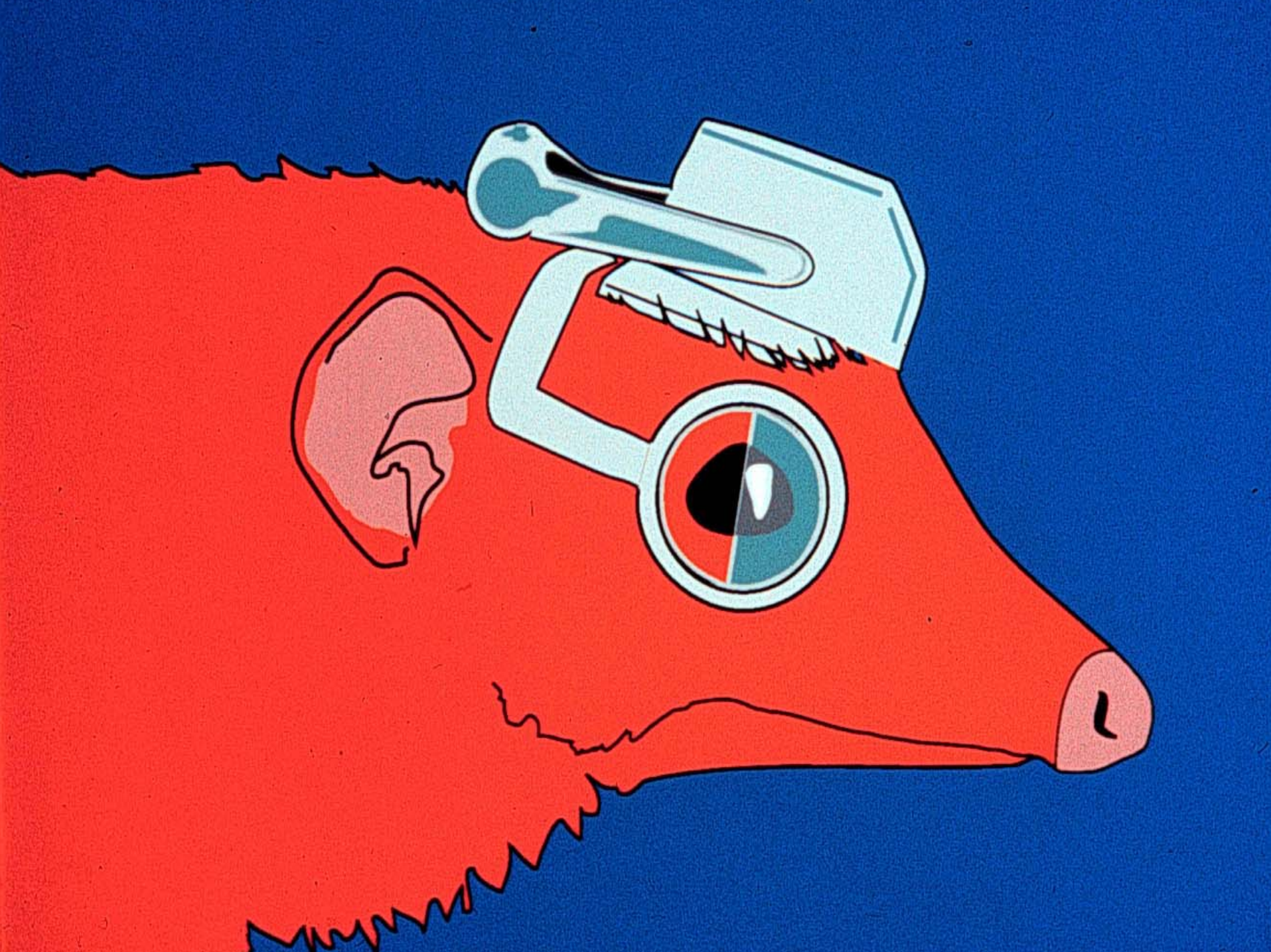
Myopic eyes have a deeper vitreal chamber

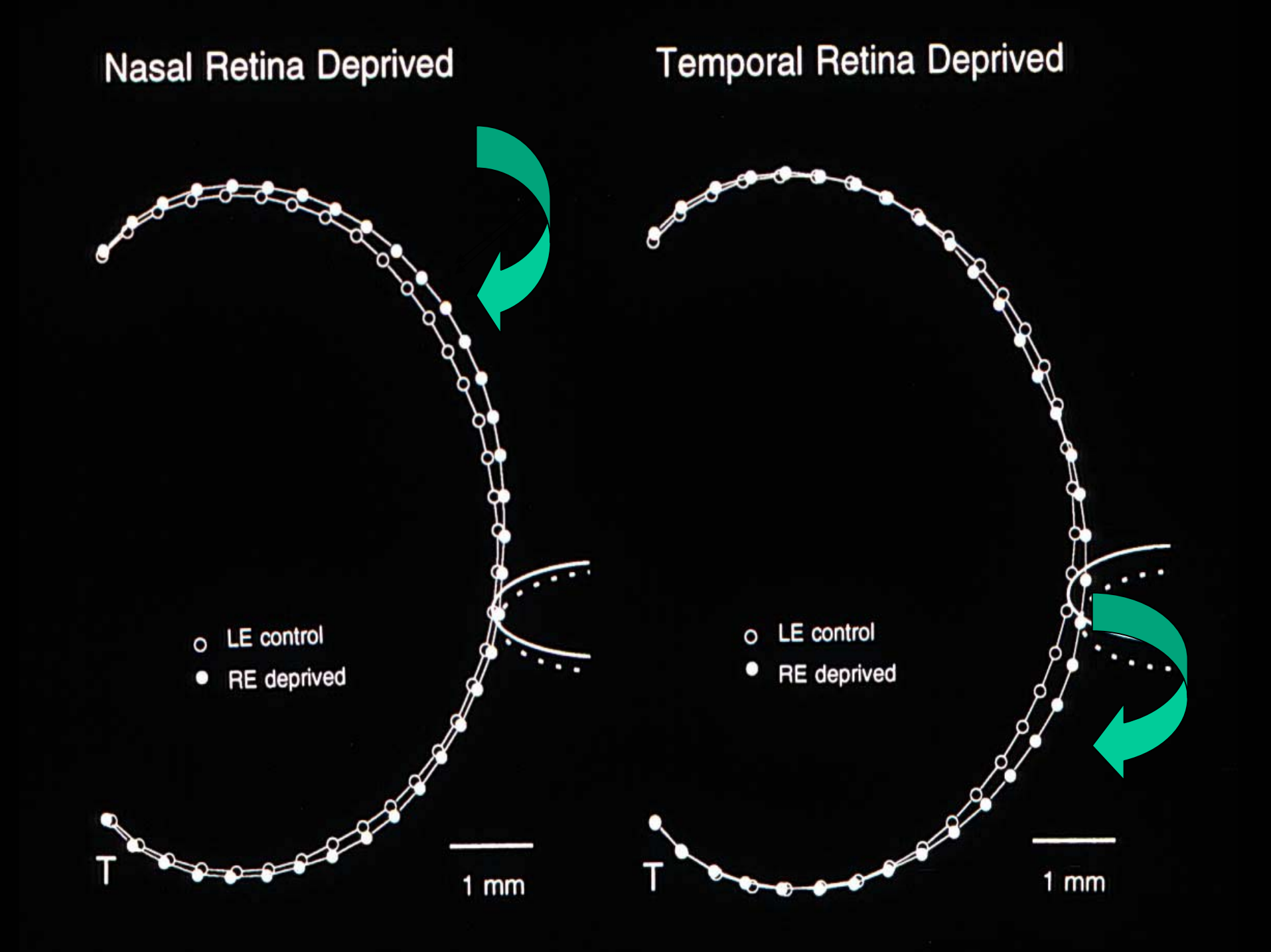


Studies in which the optic nerve is cut or activity blocked with TTX (blocks sodium channels and therefore action potentials) show that feedback from the brain is not required to produce lid-suture myopia. myopia.

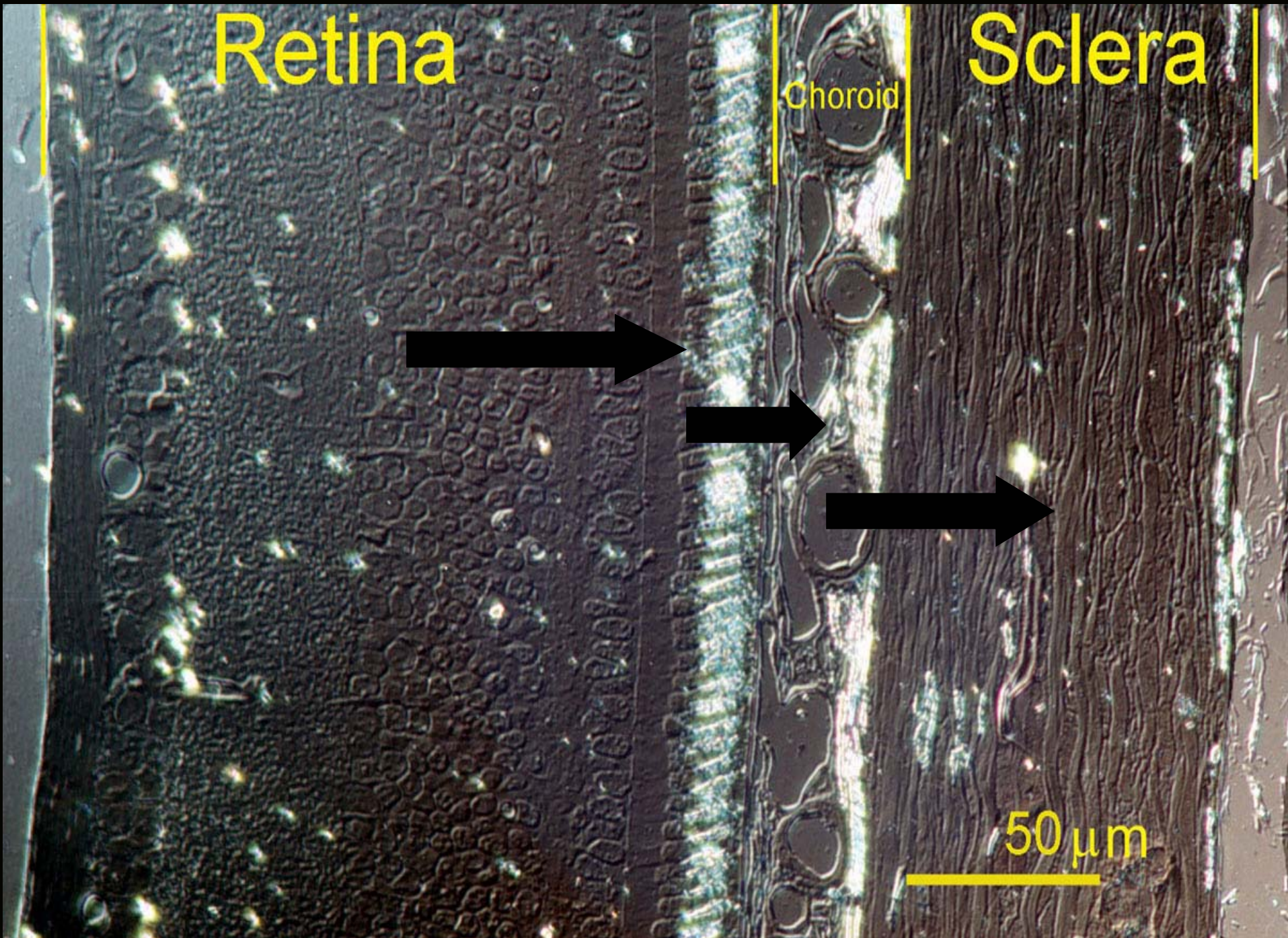
Dark rearing, however, produces tree shrews with variable refractions suggesting that light signals are important.

Depriving one half of the eye of an animal with a a diffuse goggle can cause half of the eye to grow longer.




Nasal Retina Deprived
LE control
RE deprived
T
1 mm
Temporal Retina Deprived
LE control
RE deprived
T
1 mm

Current research asks how a focused or defocused image on the retina can influence eye growth.


Retina
Choroid
Sclera
50 µm

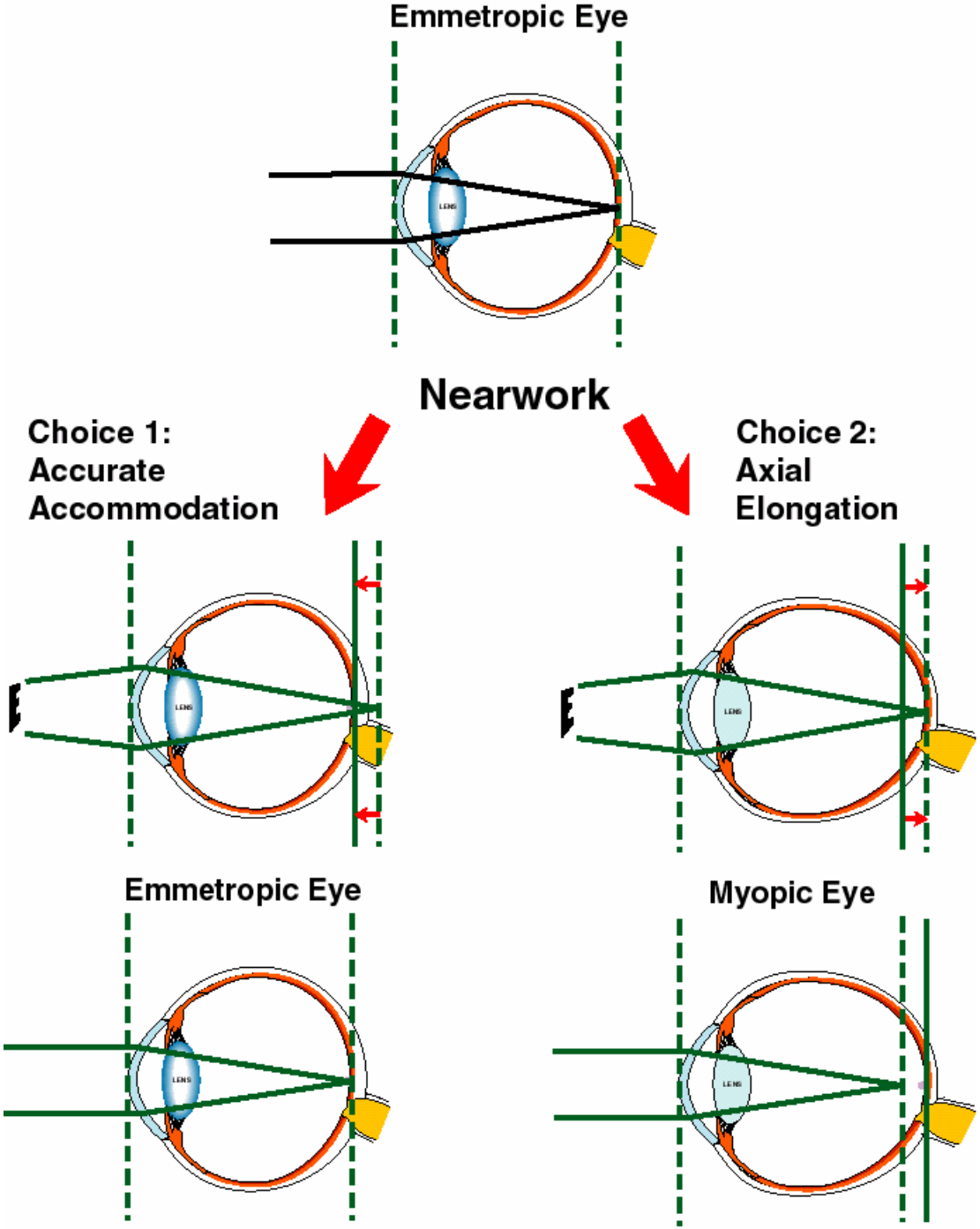
What signals might be involved?

- A variety of molecules including growth factors and transmitters have been examined to determine how the signals in the retina regulate eye growth but results are conflicting.

- In tree shrews the evidence suggests that there is only one signal required since developing eyes normally start out hyperopic (i.e too short for the correct focus of the visual image) and move toward emmetropia and finally become myopic. Once they are myopic and the eye is beyond the emmetropic adult size the myopia is not reversible.

Can the same thing be happening in children?

- Children who are developing myopia have been found to under accommodate to near targets
- Creates a situation like wearing a concave lens.


Emmetropic Eye
Nearwork
Choice 1:
Accurate
Accommodation
Choice 2:
Axial
Elongation
Emmetropic Eye
Myopic Eye

Key Points

- Neural activity influences segregation of right and left eye axons in the LGN and cortex.
- Axons compete for limited supplies of “growth factors”.
- The timing and amount of neural activity is important in the competition for growth factors.
- Eye growth is a product of genetics and environment.
- There is a critical period during which visual experience can influence neural connections and eye growth.