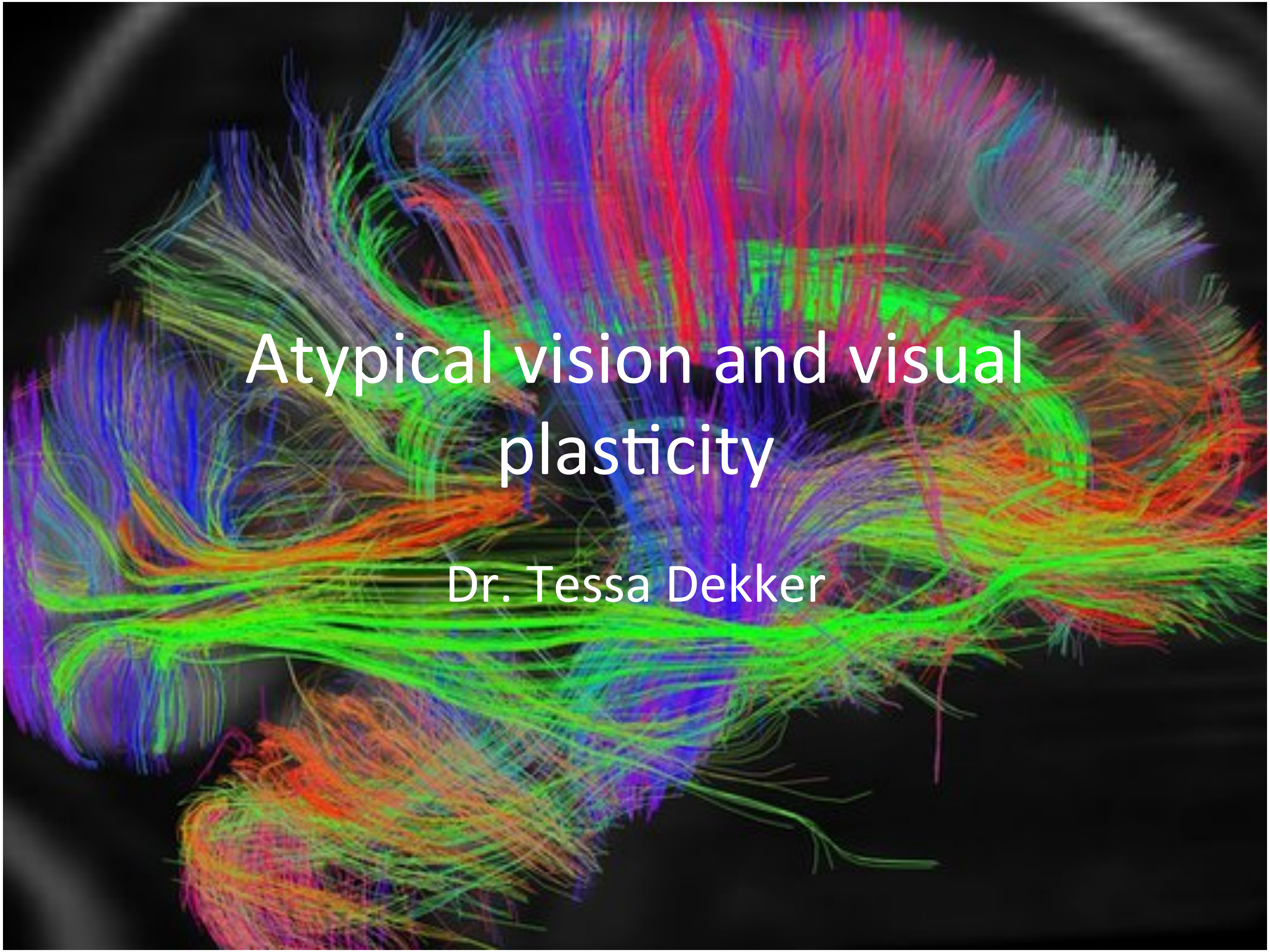


Atypical vision and visual plasticity

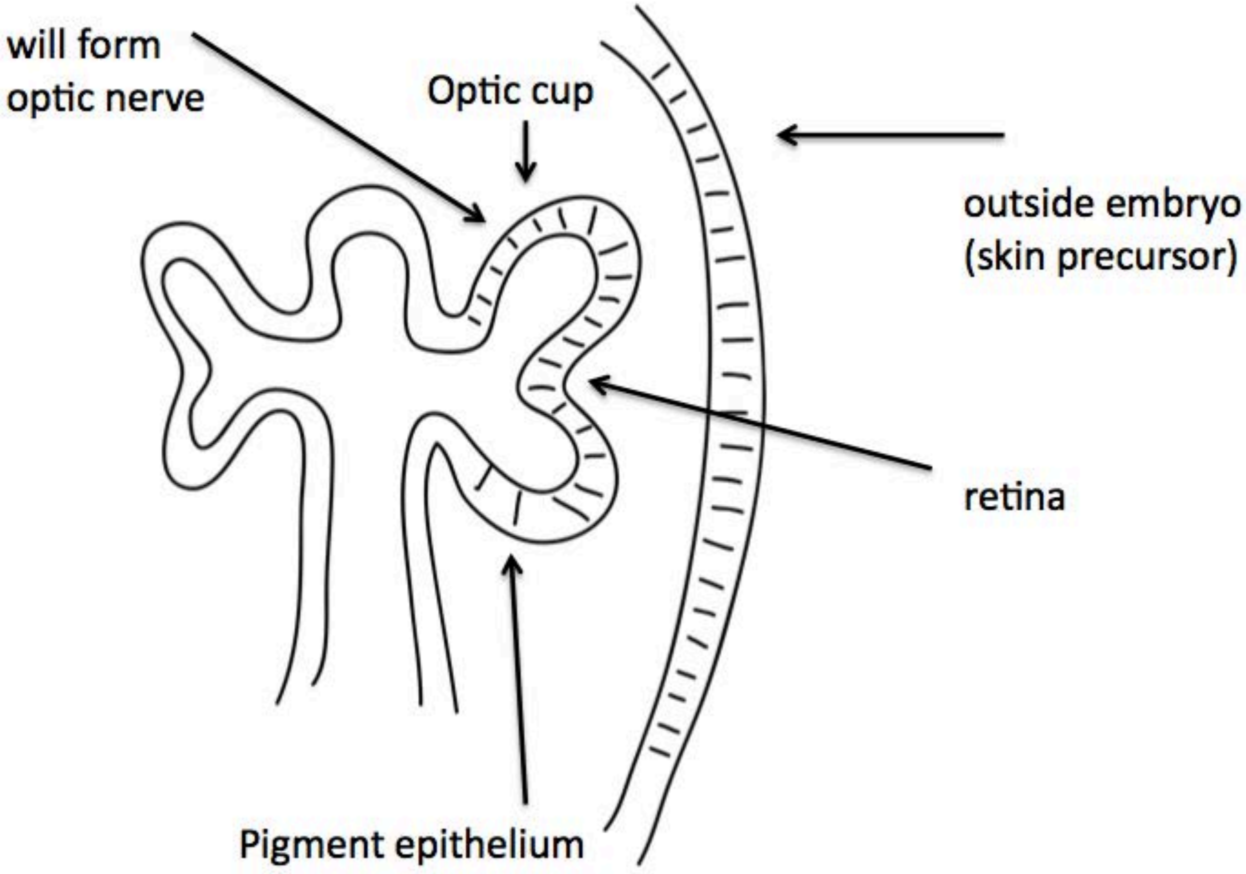
Dr. Tessa Dekker

outline

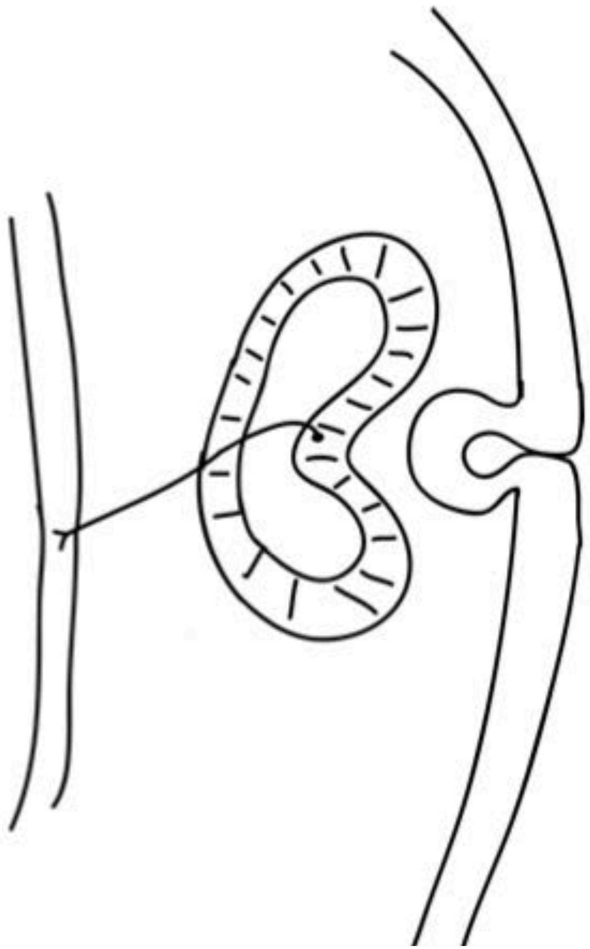
- Development of the retina
- Connecting the eye to the brain
  - Forming the optic chiasm and retinotopic map
  - Albinism and congenital blindness
- Development of binocularity
  - Binocularity in LGN; pre-natal experience
  - Binocularity visual cortex; post-natal experience
  - When things go wrong: amblyopia and binocular depth perception
  - Experience-dependent tuning of other aspects of vision
- Cross-modal plasticity and the role of other senses in shaping vision

Development of the retina

The eye is part of the brain

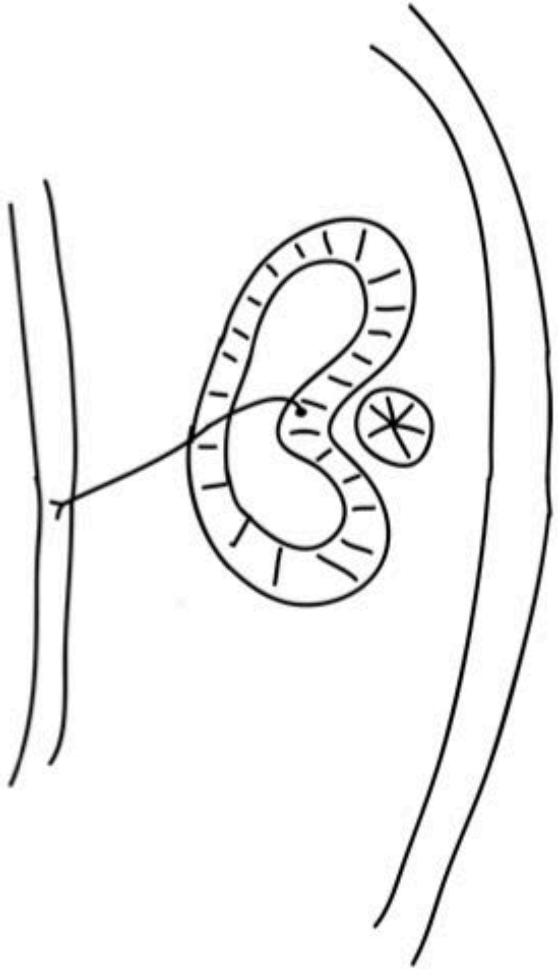


The eye is part of the brain



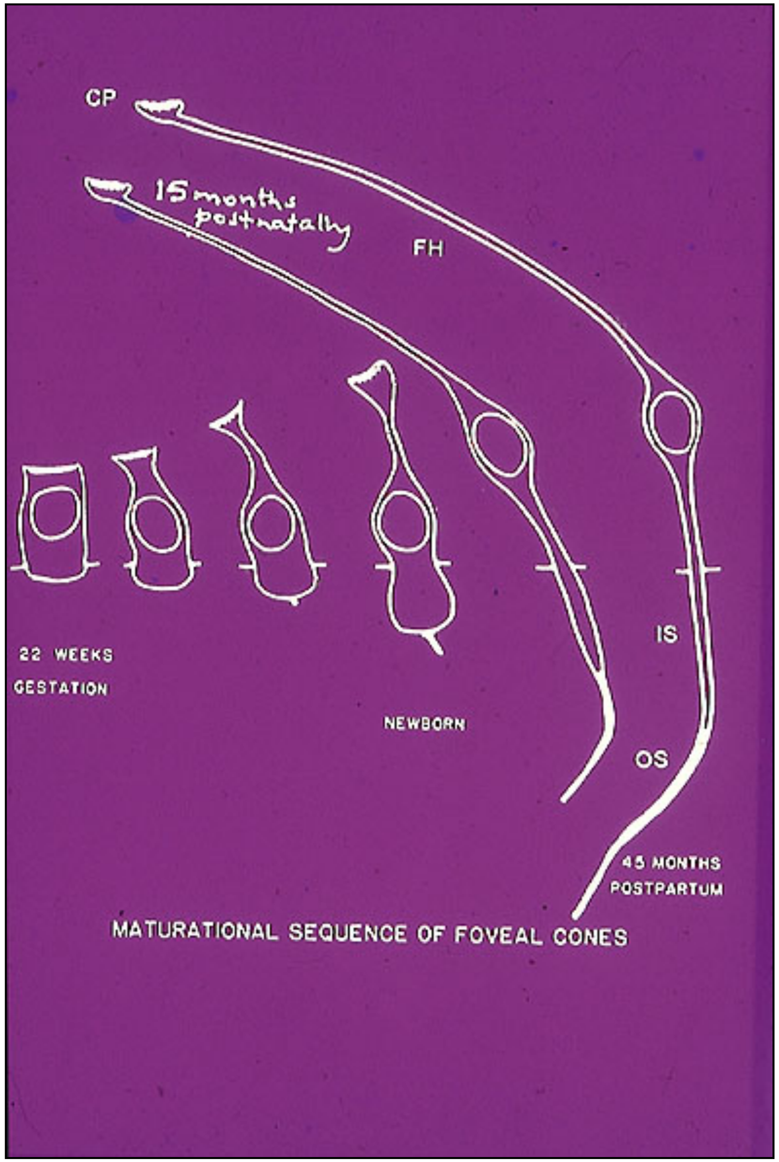
- stalk dies off
- optic nerve grows through debris
- skin folds into itself to form lens

The eye is part of the brain



- Cells between lens and "skin" die.
- This programmed cell death is called apoptosis
- Lens has formed

Development of photoreceptors



- OS = outer segment; contains photosensitive pigment
- short OS = inefficient at detecting light
- fat inner segment (IS) = cones aren't tightly packed = poor spatial sampling of the image
- Development of long fibre = cones displaced to allow dense packing in foveal pit

Development of photoreceptors

Cones become much denser in the fovea postnatally

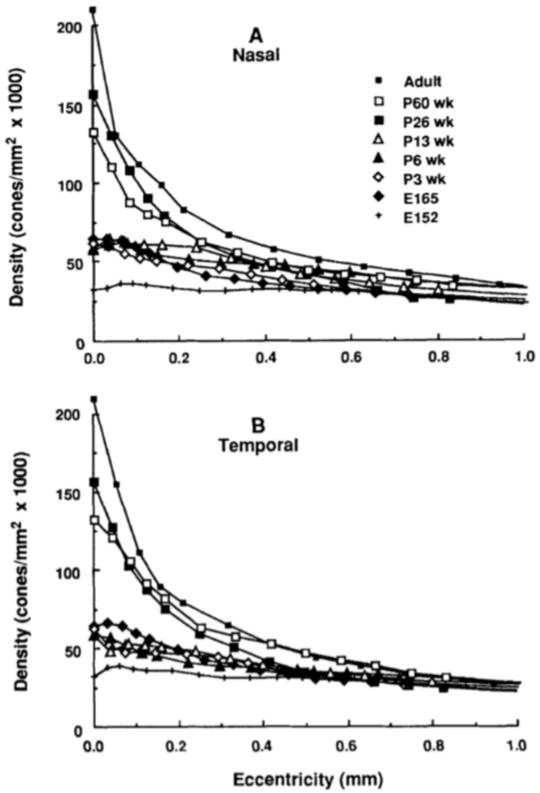


Fig. 5. Graphs of cone density as a function of eccentricity along the nasal (**A**) and temporal (**B**) horizontal meridians for 7 animals of different ages and the adult average of 3 animals. Only the central 1 mm is shown. Each curve is the average of three meridians (the horizontal, 45° above horizontal, and 45° below horizontal).

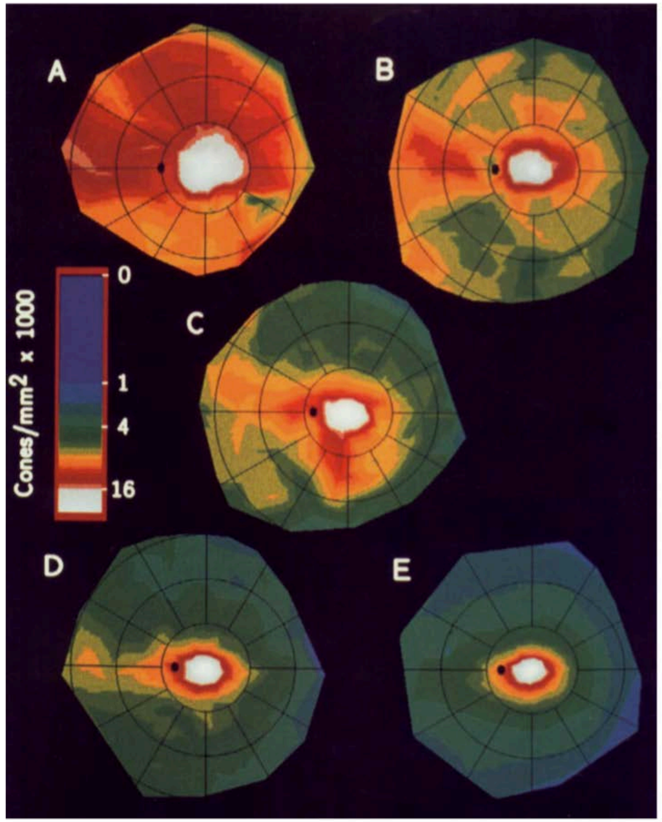


Fig. 6. Maps of cone density in the entire retinas of five animals: (**A**) E152 (**B**) P3 weeks, (**C**) P13 weeks, (**D**) P60 weeks, (**E**) average of 3 adults. The maps of peripheral retina are keyed to the color scale, which represents cone densities ranging from 0 to 16,000 cones/mm² at a contour interval of 1,000 cones/mm². The rings and rays of the overlay pattern are spaced at intervals of 30 spherical degrees and the black spot represents the optic disk. Areas above 16,000 cones/mm² are represented by white. All retinas are displayed as if they are the same size but in fact differ in area by more than a factor of 2 (Table 1).

Development of photoreceptors

Rods (not present in fovea)decrease in concentration with age

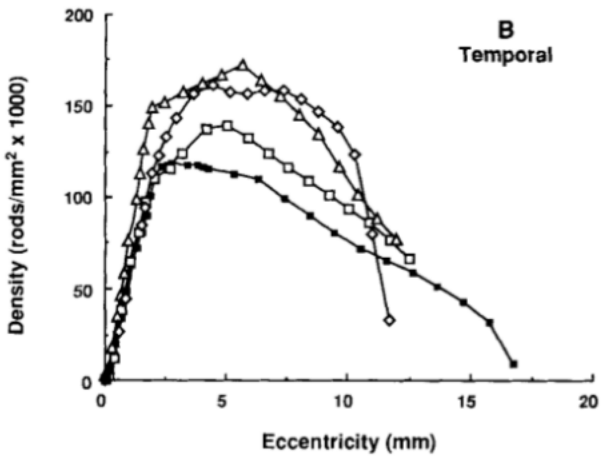


Fig. 10. Graphs of rod density as a function of eccentricity along the (**A**) nasal and (**B**) temporal horizontal meridians of 3 monkeys of different ages and the average of 2 adults. Each curve is the average of the horizontal and the two meridians at plus and minus 45°. The stippled area on the abscissa represents the optic disk.

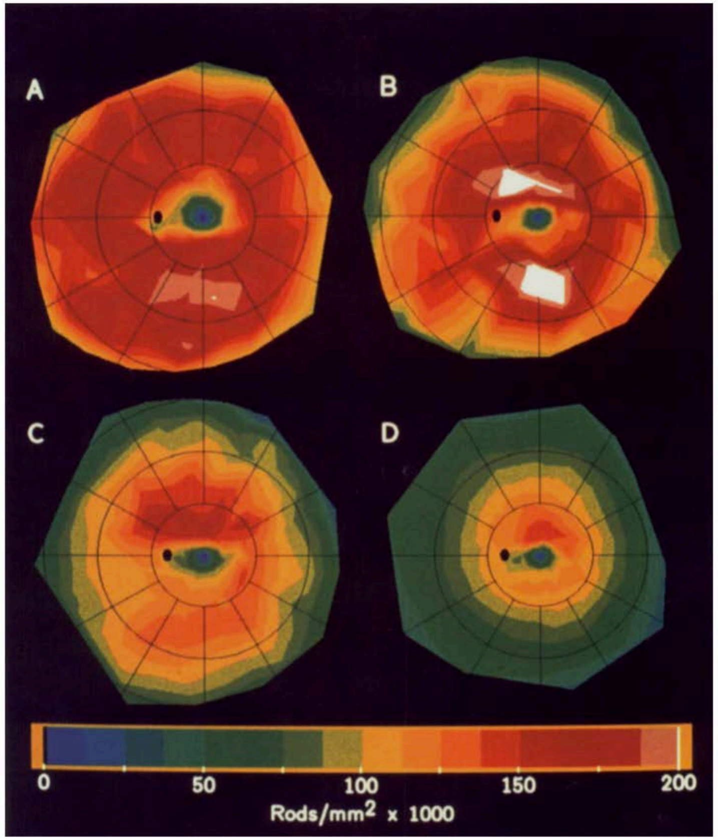
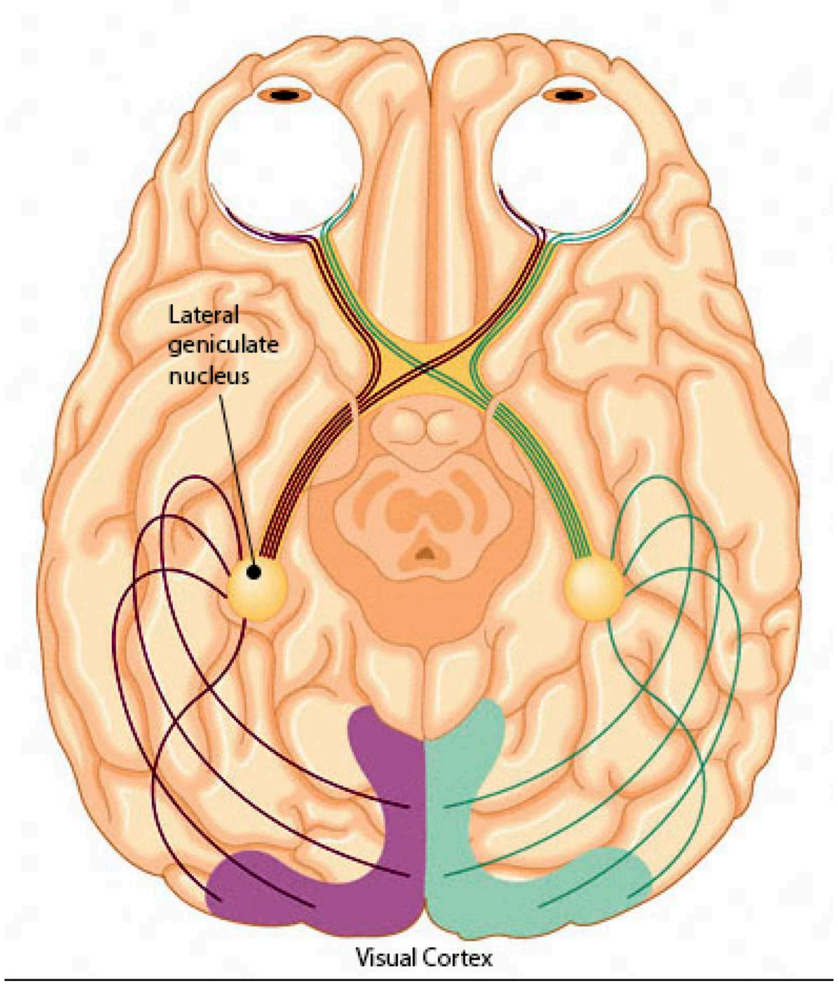


Fig. 9. Maps of rod density in young and adult retinas: (**A**) P3 weeks, (**B**) P13 weeks, (**C**) P60 weeks, (**D**) average of 2 adults. The color scale represents rod densities between 0 and 200,000 rods/mm² with a contour interval of 12,500 rods/mm². Areas of the maps that exceed a density of 2000,000 rods/mm² are colored white. The rings and rays of the map overlay are spaced at intervals of 30°. All retinas are displayed as if they are the same size but in fact differ in area (Table 1).

Connecting the retina to the brain

Optic nerve projection



experience-dependence?

- In newts, eyes were rotated upside down and healed
- Post healing, newts aimed down and left, to food presented upward and right
- coloring changes as if hiding against a bright bottom of pond (sky rather than floor)
- So: if the eyes are rotated 180 degrees axons regenerate to original destination rather rotated position
- strong evidence for predetermined axonal guidance

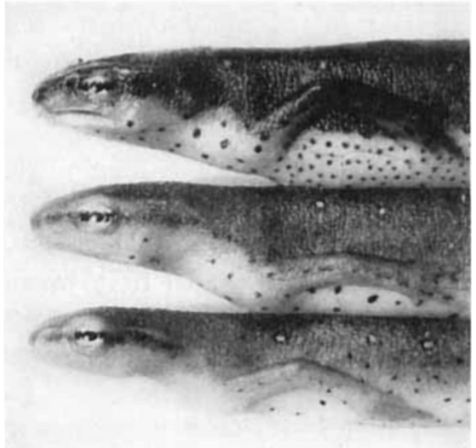


Fig. 1 A control case (top) with eye in normal position is shown with two experimental cases with eyes rotated 180 degrees, 4½ months after operation. The golden ventral surface of the eyeball, after rotation, shows through the translucent upper lids making them appear lighter. Contrast between the characteristic brownish black dorsal surface of the control case and the light olive green of the cases with rotated eyes is only poorly indicated in the black and white photograph.

Sperry, 1943

Chemical factors

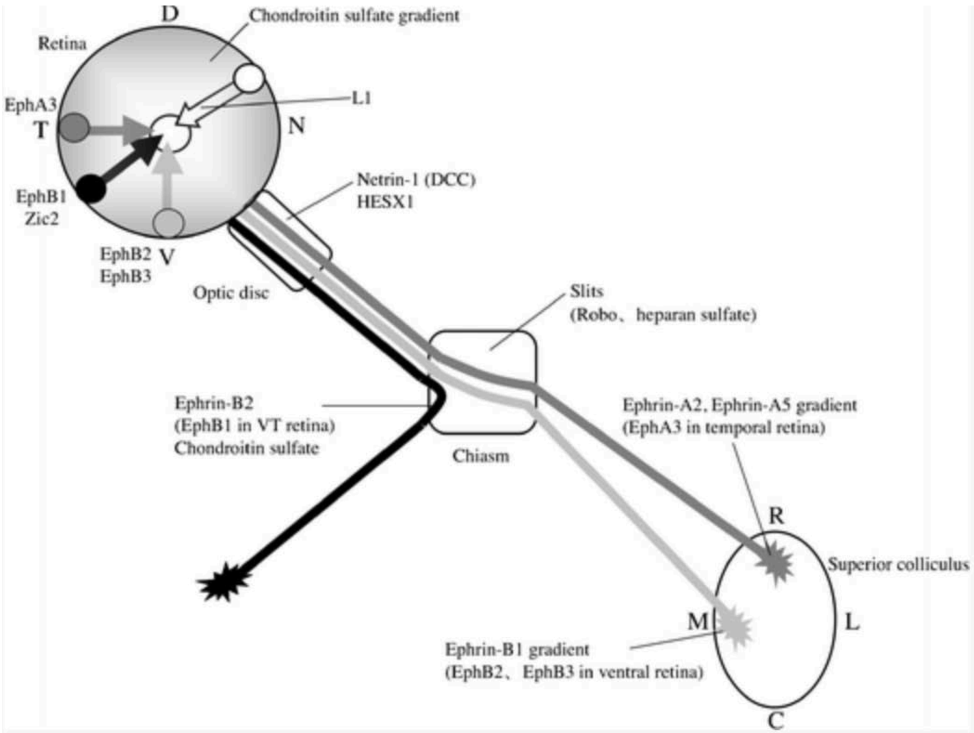


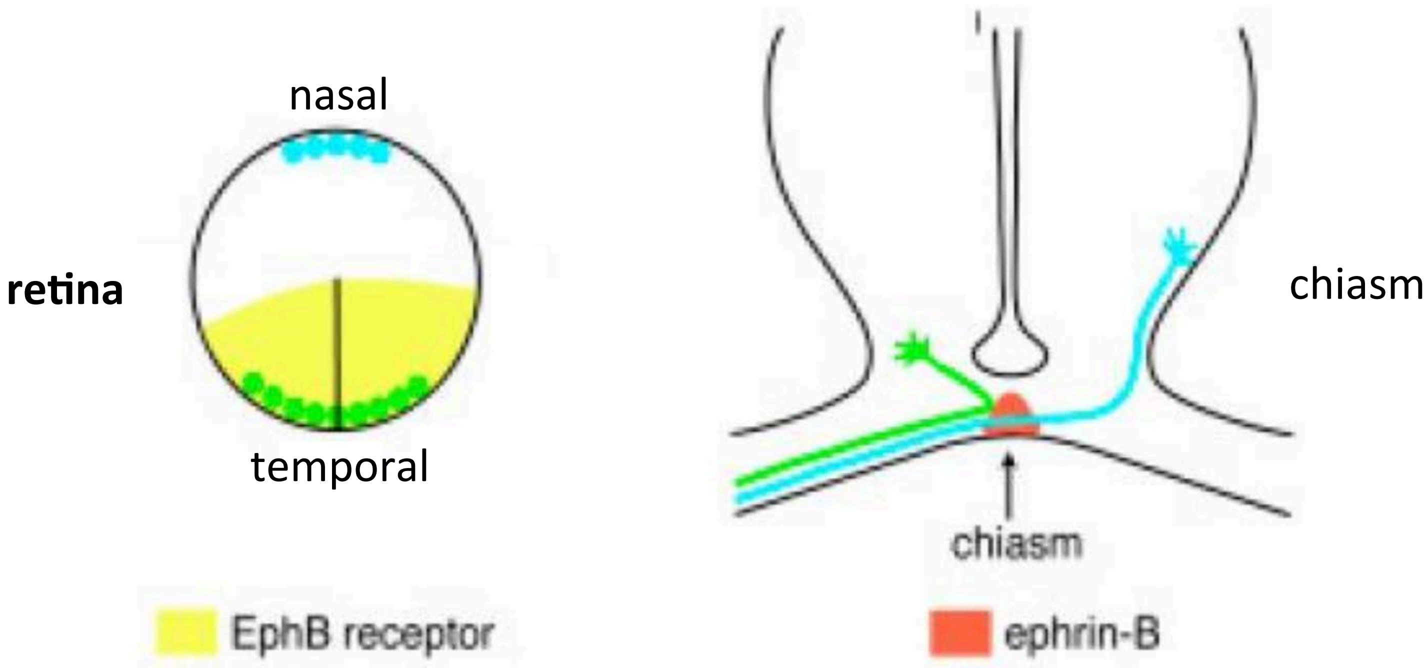
Fig. 1

Guidance molecules involved in mouse optic axon guidance. *Parentheses* indicate surface molecules on optic axons interacting with the guidance molecules. *C* indicates caudal; *D*, dorsal; *L*, lateral; *M*, medial; *N*, nasal; *R*, rostral; *T*, temporal; and *V*, ventral. (reproduced with permission from the Kanehara-shuppan editorial office)

Chemical factors

Decussation of optic nerve

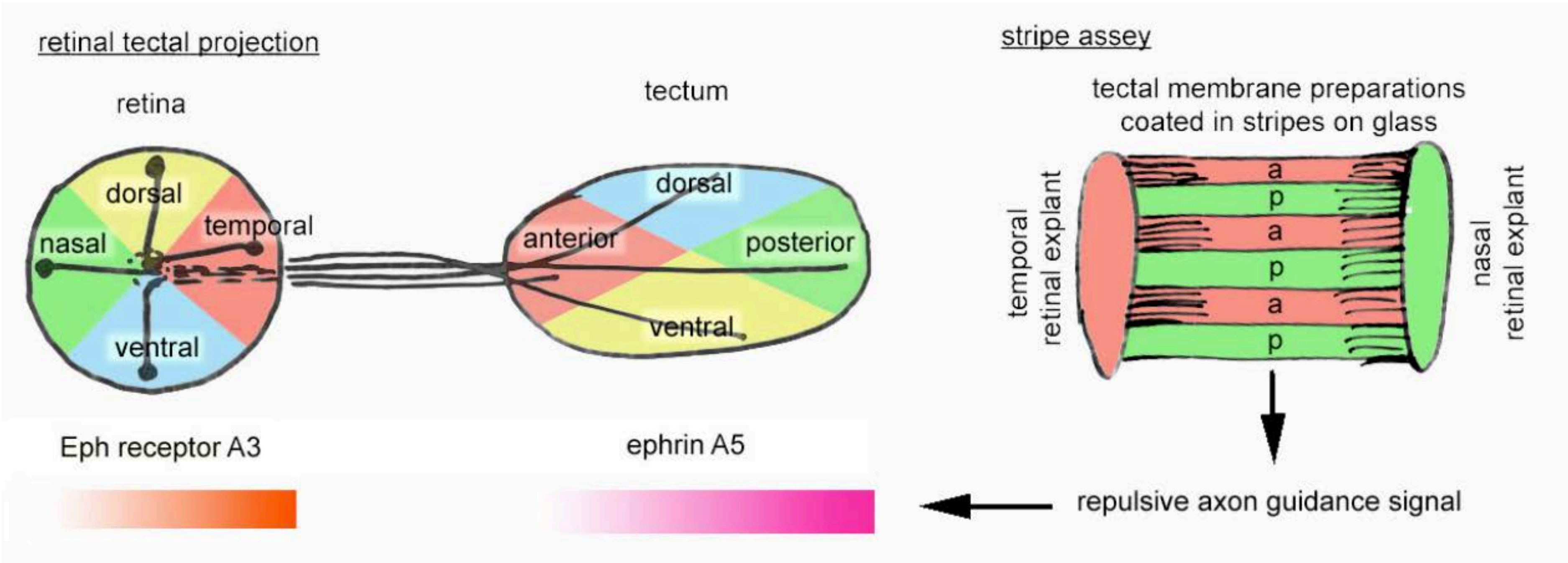
- EphrinB/Zic2 receptor expressed in high concentrations on the temporal side of the retina
- Ephrin B guidance molecule expressed at chiasm
- Repulses optic nerve from temporal side of the retina away from the chiasm so it does not cross to other side



Chemical factors

Topographic maps

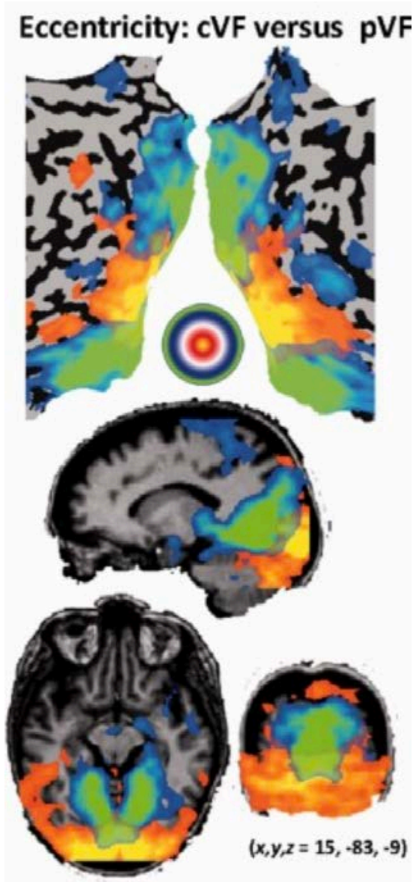
- Ephrin A5 is repulsive to axons with EphA3 receptors.
- EphA3 follow N/T gradient in retina, Ephrin A5 a P/A gradient in tectum
- Temporal axons (high EphA3) repulsed by EphrinA, stop anterior
- Nasal axons (low EphA3) no such restriction so grow to posterior



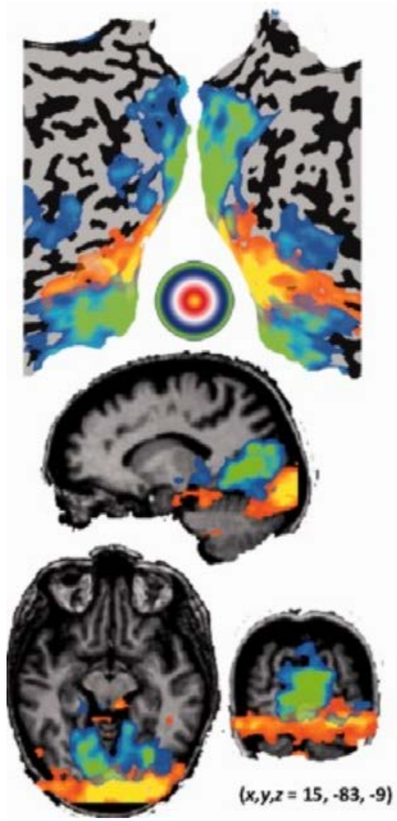
Chemical factors
Congenitally blind

- Subjects kept eyes closed in the scanner (resting state fMRI)
- Time courses in V1 normally representing center vs periphery of gaze were correlated with other time courses
- Similar correlation structure suggests eccentricity map maintained in congenitally blind
- This even persisted in higher-order areas (FFA and PPA)

Sighted person



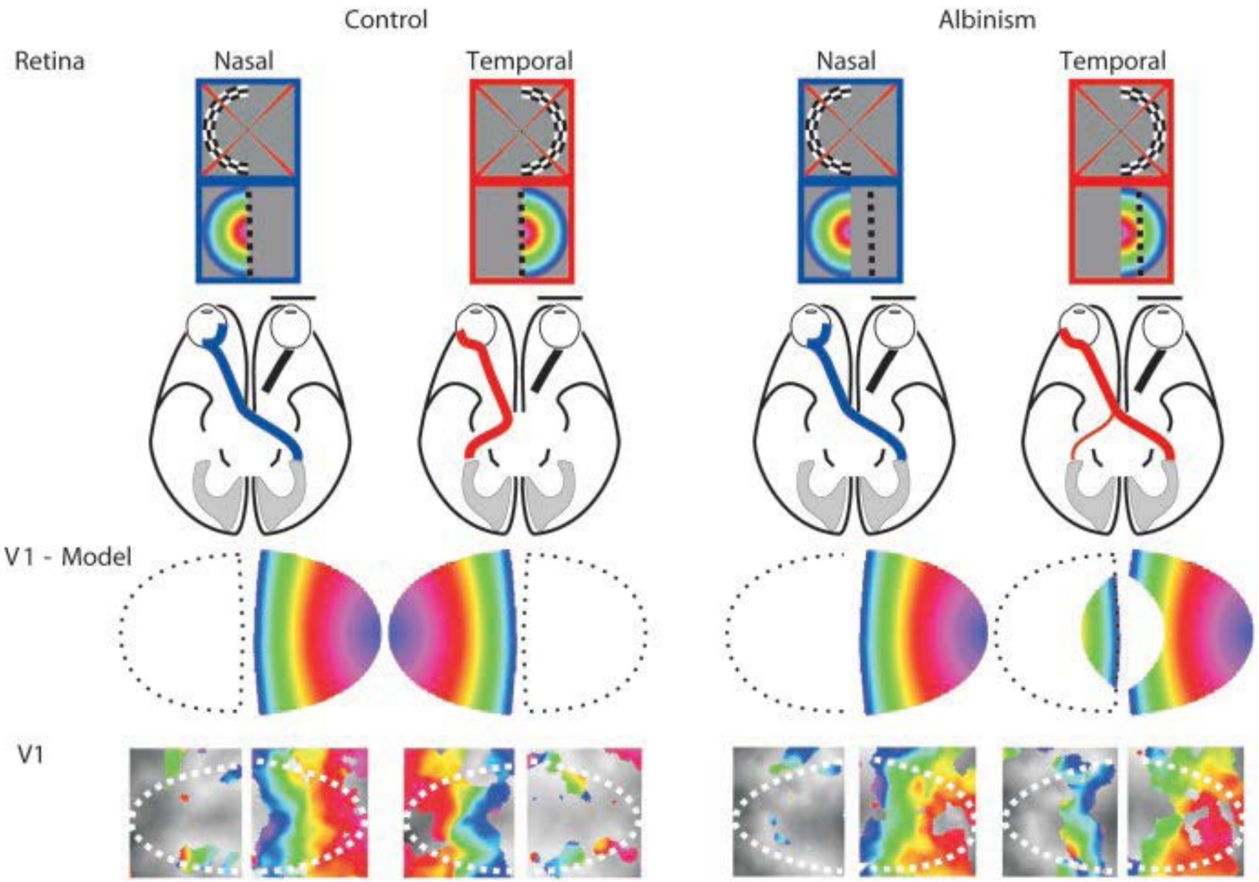
blind person from birth



Striem-Amit et al., 2015

Chemical factors

albinism



Normal crossing of nasal fibres

Abnormal crossing of temporal fibres

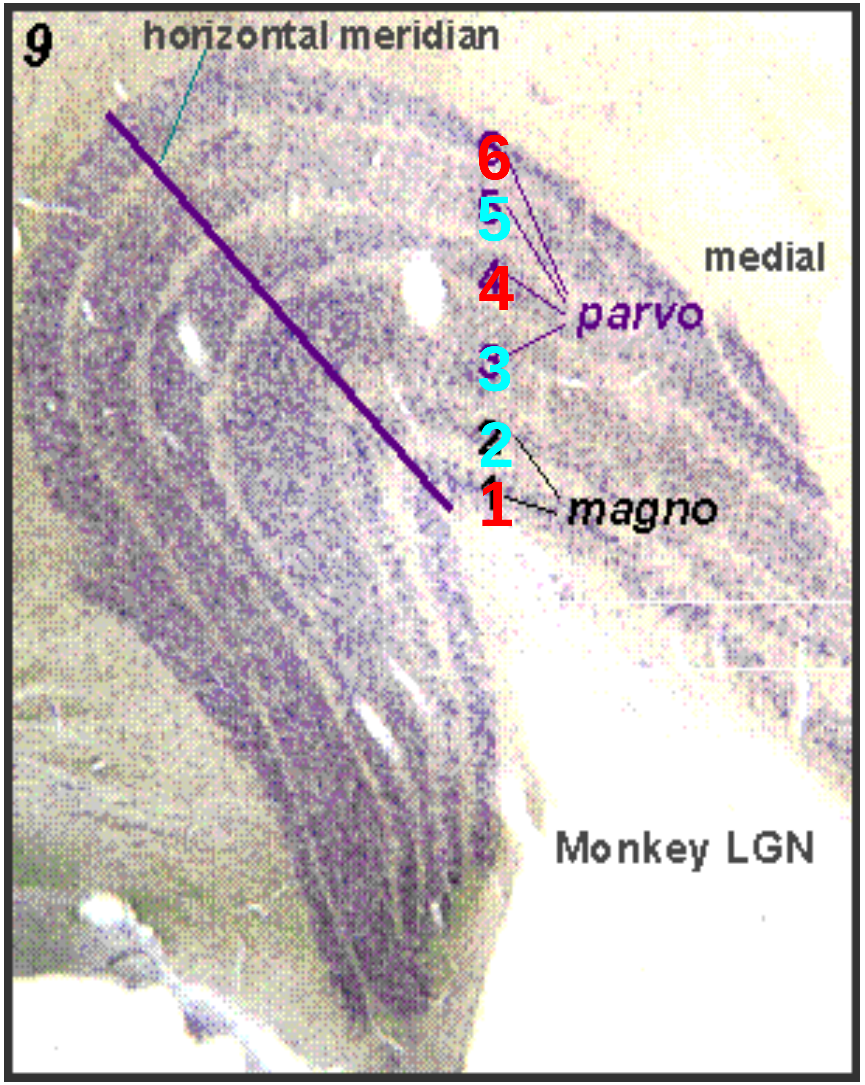
Abnormal right visual field representation overlayed on the normal Left visual field representation

summary

- Retina projects to the visual cortex in a highly organised manner
- Both optic nerve decussation and retinotopic maps are sculpted by chemical factors
- Receptors to repulsive and attractive chemicals are expressed in gradients across the retina
- This structure is robust to experience
  - Newts optic nerves grow back in normal map-structure despite detrimental effects on perception
  - Map structure dependent on these chemical gradients persist in congenitally blind and in albinism
- Note that refinement of the retinotopic map also requires an intact retina during development (spontaneous activation waves)
- It is possible for primary sensory cortex to take on functions that classically belong to other senses

Binocular representations in LGN

Binocular organization in the visual pathway: primate LGN segregates inputs from two eyes



layers 1,4,6:

contralateral eye

layers 2,3,5

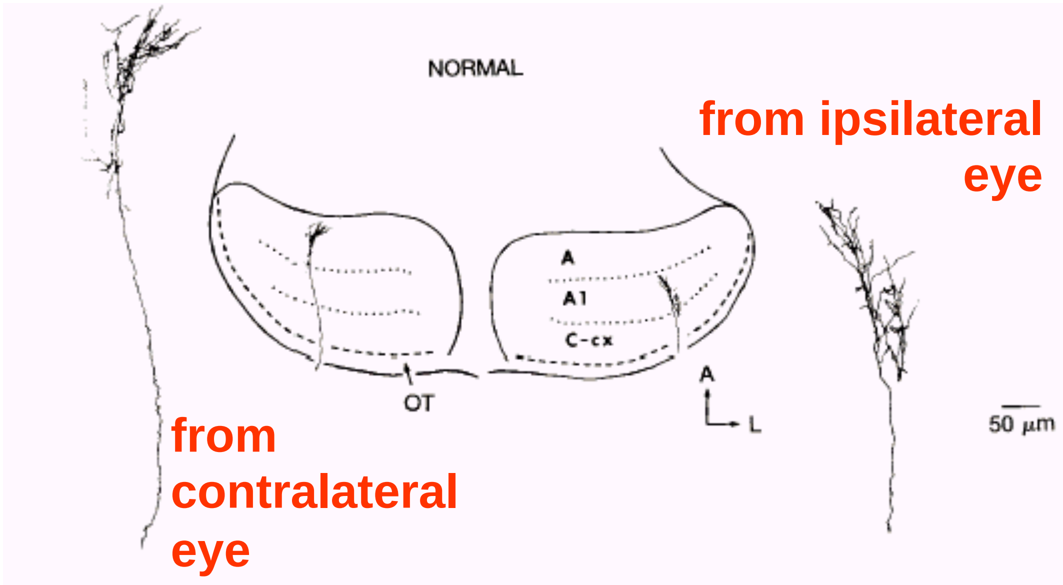
ipsilateral eye

Shatz: effects of spontaneous retinal activity
(experiments with kittens & ferrets)

- LGN layers not initially distinct – they segregate during foetal development
- TTX (tetrodotoxin – blocks action potentials) infused into retinal ganglion cells can block this segmentation

(see Shatz, 1996)

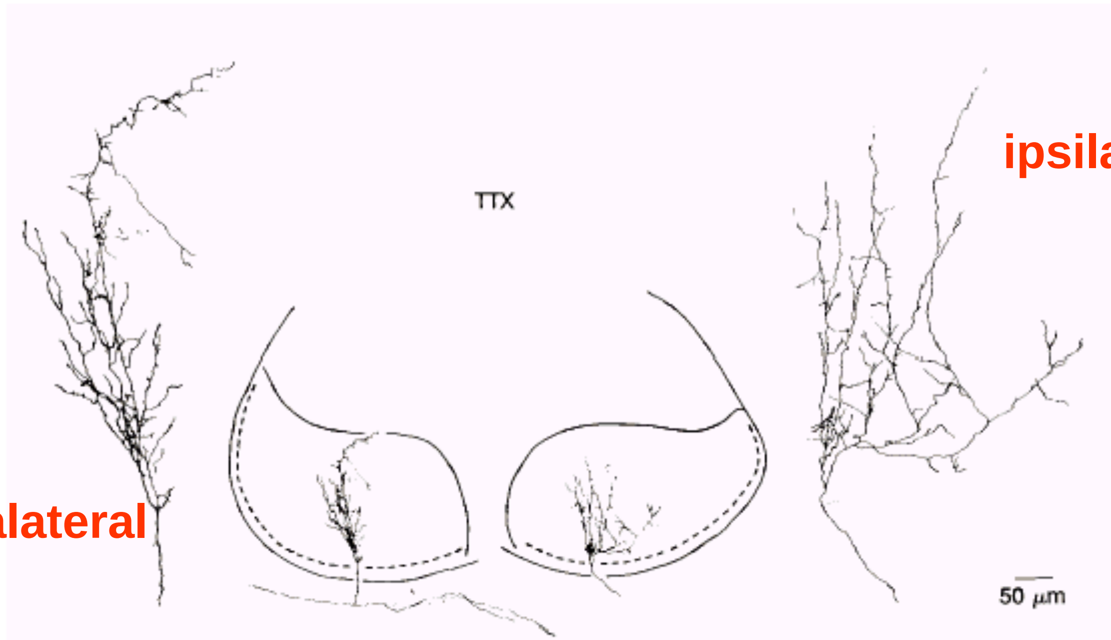
(cat- 3 LGN layers)



from ipsilateral eye

from contralateral eye

Typically reared animal



from ipsilateral eye

from contralateral eye

TTX injection prenatal

Fig. 2. Examples of the terminal arborizations of retinogeniculate axons at E58 in normal animals (*Upper*) and in animals that received minipump infusion of TTX between E42 and E58 (*Lower*). In both cases, axons were labeled by using the *in vitro* HRP-filling technique. In the normal case, axons from the contralateral (*Left*) and ipsilateral (*Right*) eyes are shown, and their restricted arborization within the appropriate LGN layer (either layer A or layer A1) is indicated (*Center*). With TTX treatment, axons branch extensively and indiscriminately within the LGN without regard for (implied) laminar borders. [Reproduced with permission from ref. 30 (copyright 1988 Macmillan Magazines Limited).]

Shatz: effects of spontaneous retinal activity

(experiments with kittens & ferrets)

- LGN layers not initially distinct – they segregate during foetal development
- TTX (tetrodotoxin – blocks action potentials) infused into retinal ganglion cells can block this segmentation

- Not simply arrest of growth – axons more exuberant in LGN with TTX
- Retinal activity appears to be necessary for LGN segmentation

(see Shatz, 1996)

(ferret)

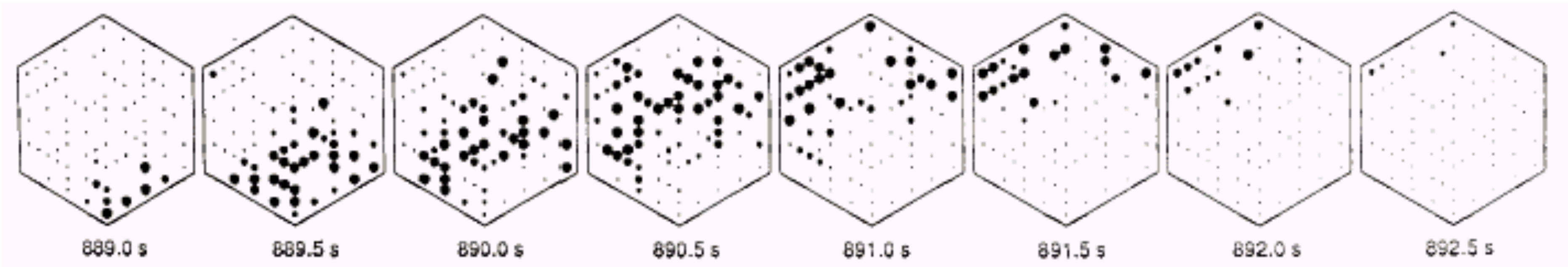
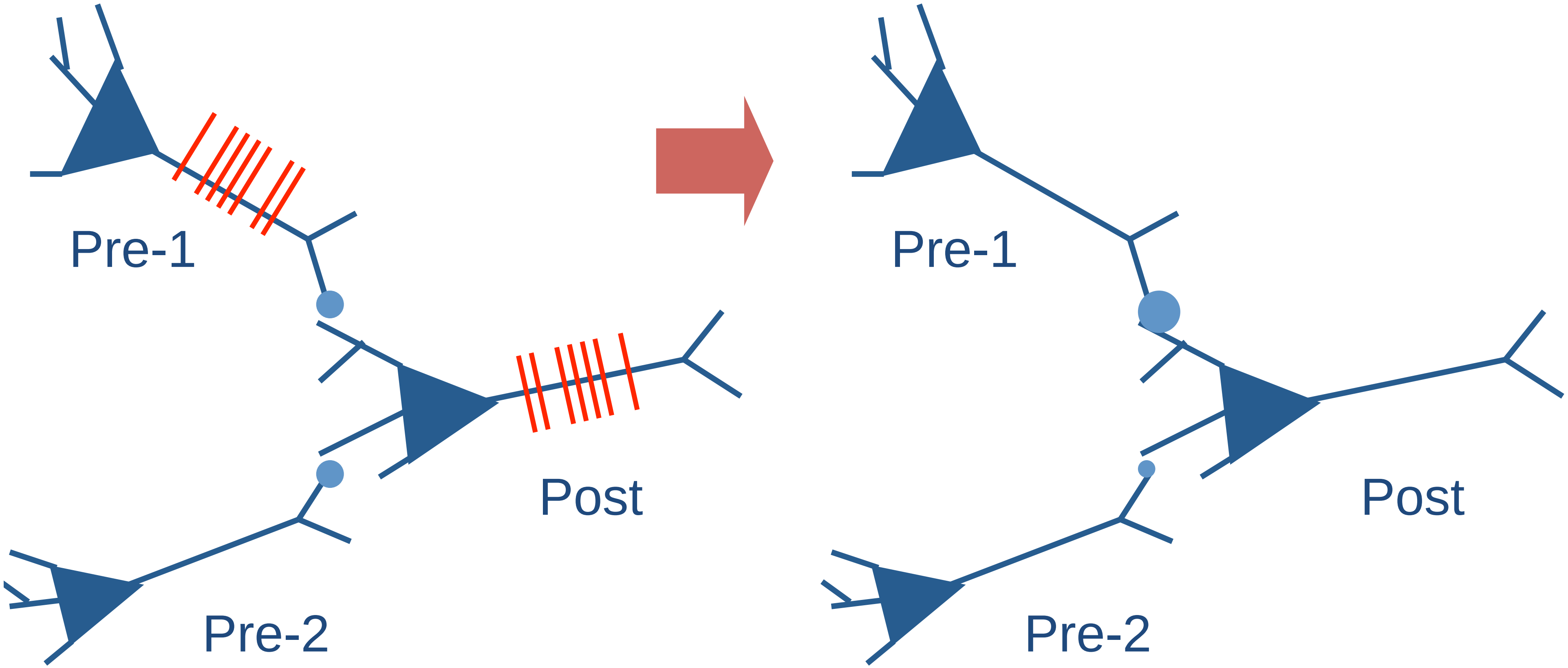


FIG. 3. The pattern of spike activity over the multielectrode recording array is plotted for eight successive intervals during one burst of ganglion cell firings covering the time interval from 889 s to 893 s during the recording session. Each frame shows the averaged firing rate during an 0.5-s interval. Each of 82 neurons is represented with a small dot at its approximate spatial location on the electrode array. The dot area for each cell is proportional to its average firing rate during the relevant 0.5-s interval: the larger the diameter, the higher the average firing rate. During this recording, ganglion cells located in the lower right hand corner of the array commenced firing together at the beginning of a burst (889.0 s), and then activity progressed in a wave-like fashion across the array so that at the end of the burst period (892.5 s), ganglion cells at the upper left hand edge of the array were active. Recordings are from a postnatal day 5 (P5) ferret retina. [Reproduced with permission from ref. 40 (copyright 1991 American Association for the Advancement of Science).]

Hebb synapse

-strengthened by synchronous pre- and post- synaptic activity

-‘neurons that fire together, wire together’



Shatz: effects of spontaneous retinal activity

What activity?

- record from neonatal ferret retinas (immature, eyes closed at birth, LGN layers segregate postnatally)
- Rhythmic bursts of action potentials
- Waves of activity sweep across the retina
- Successive waves in random direction, and not correlated between eyes
- Waves only present during postnatal days 1-21, when photoreceptors very immature; disappear before eye opening

(see Shatz, 1996)

Shatz: effects of spontaneous retinal activity

Are the retinal waves critical?
Is activity ‘permissive’ – ie required in a non specific way – or ‘instructive’ – directing connections?

Manipulating cAMP increases wave frequency

This manipulation in one eye increases size of corresponding LGN layers

Injection in both eyes leaves layers unaltered

Conclusion: an instructive, and competitive effect

(see Stellwagen & Shatz, 2002)

Shatz: effects of spontaneous retinal activity

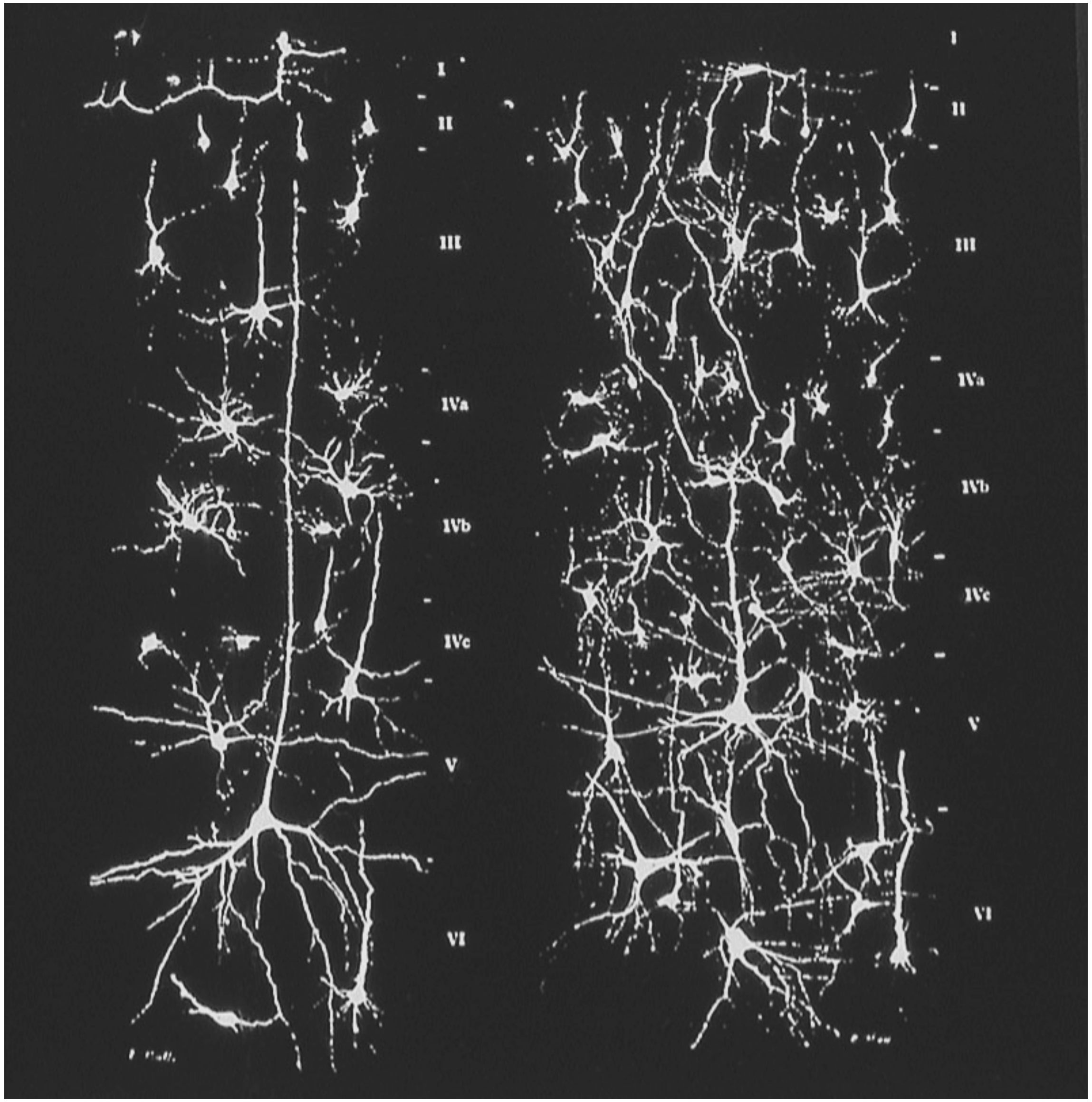
- Proposal: correlated activity from nearby ganglion cells in the same eye establishes activity dependent synapses ('Hebb synapses')
- Because the two eyes are uncorrelated, synapses from the two eyes do not become established on the same LGN neurons – leading to layering

- Note: Spontaneous activity across retina also crucial for refining retinotopic map
  - When RGC firing is blocked, maps in V1 are blurrier (e.g., Cang et al., 2005)

(see Shatz, 1996)

Binocular representations in cortex

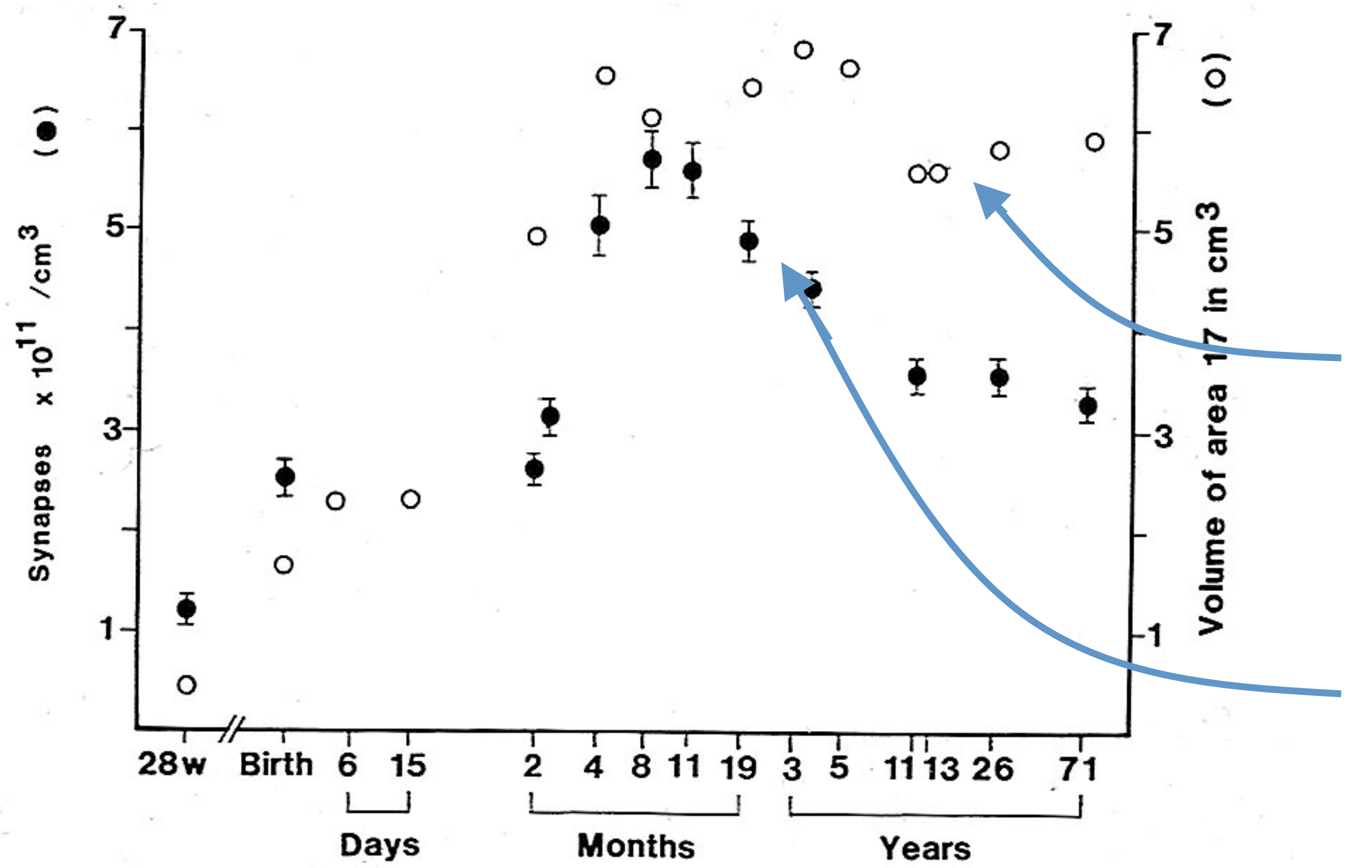
newborn **3 month old**



Golgi-stained samples of visual cortex at different ages (Conel, 1939)

Major changes in cortex after birth – larger role for experience-dependent plasticity

Synapse numbers increase, then decrease
(Huttenlocher)



Total synapses =

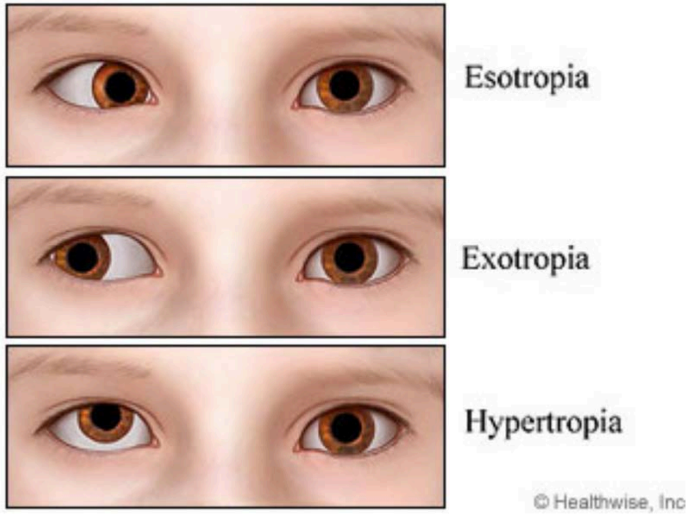
volume

x

synapses/cm^3

Fig. 4. Mean synaptic density values for all layers of area 17 are indicated by the closed circles (left-hand scale). Each point represents the mean of several thousand counts. Vertical bars represent the standard error of the mean of 6 separate synapse counts in the same brain in strips of cortex 3 μm in width. The open circles are the values for volume of the right area 17 (right-hand scale). Age is plotted on a logarithmic scale. (From ref. 35).

Developmental failures of binocularity postnatally



cataract

developmental failures of binocularity postnatally

Strabismus and other eye diseases that results in unbalanced input of eye can cause **Amblyopia: loss of acuity without visible pathology, not correctable by spectacles**

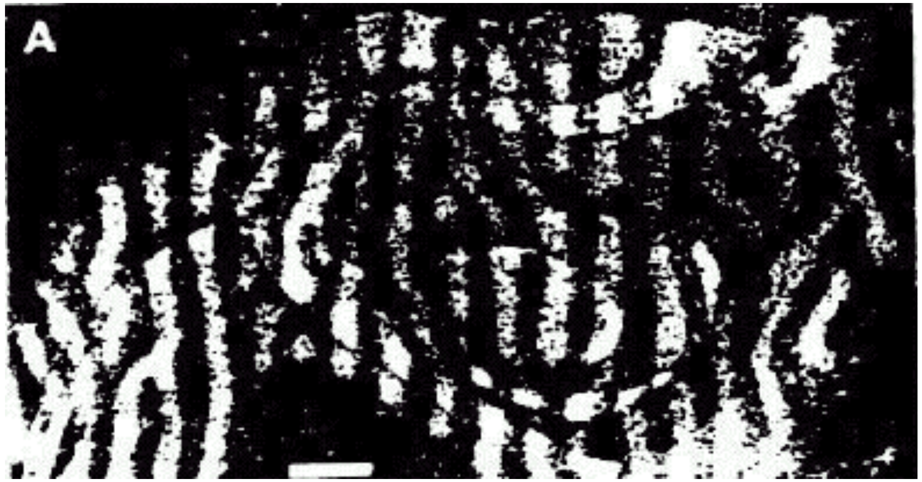
Strabismic amblyopia = loss acuity in deviating eye
Anisometropic amblyopia = loss acuity in out-of-focus eye
Deprivation amblyopia (e.g. monocular cataract)

Often also paired with loss of binocularity/ stereopsis

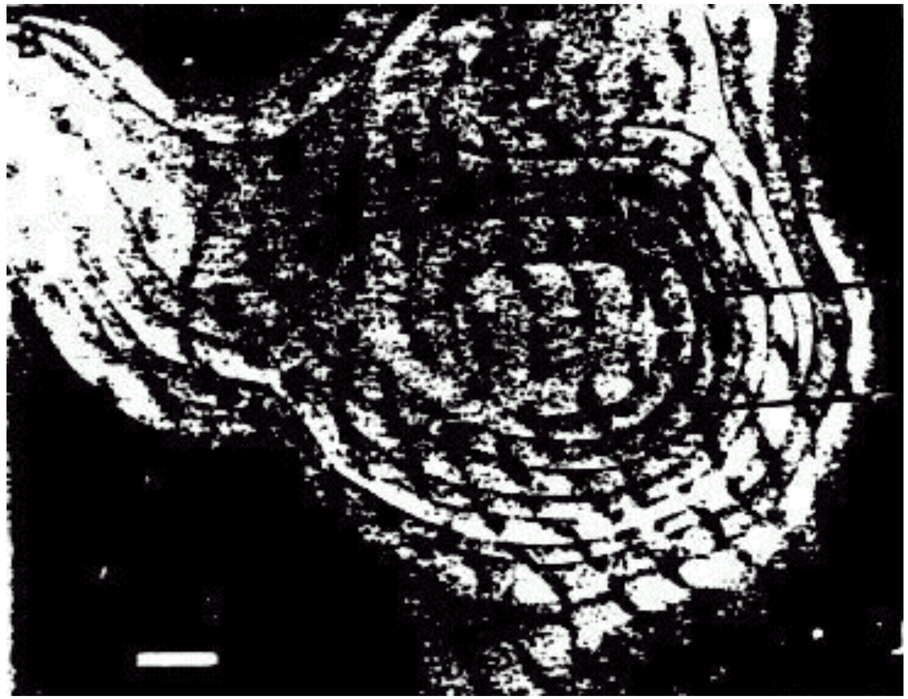
Animal model of deprivation amblyopia

Ocular dominance columns in…

Normally reared monkey

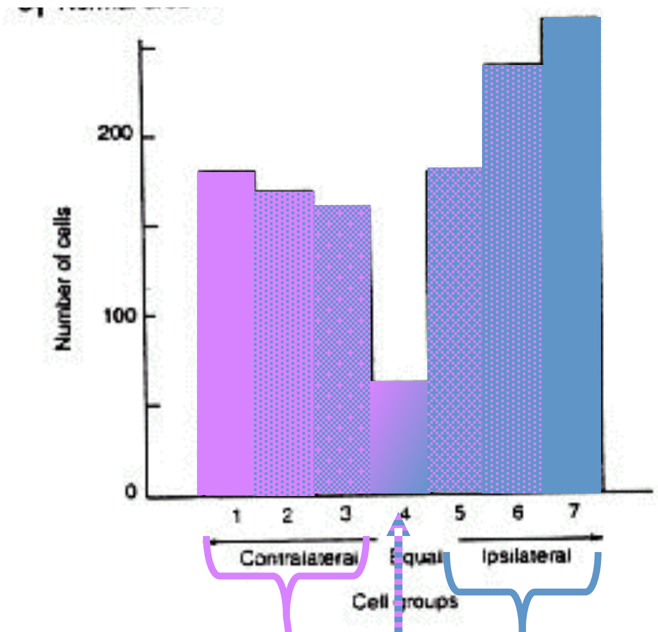


Monocularly deprived monkey



at single-neuron level -
based on ocular dominance distribution (Wiesel & Hubel)

area 17 in cat reared with ***unrestricted*** vision



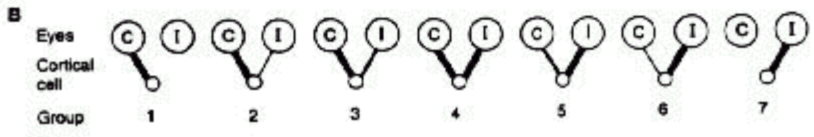
cortical neurons…

dominated by contralateral input

balanced input from both eyes

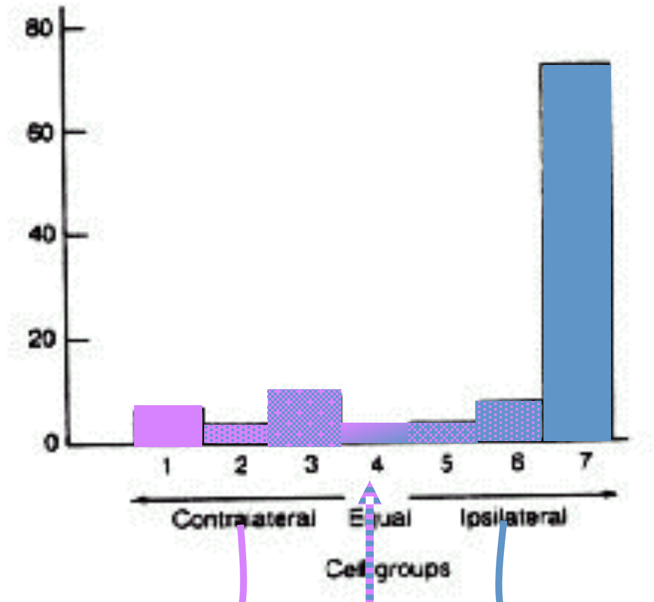
dominated by ipsilateral input

Ocular dominance groups



at single-neuron level -
based on ocular dominance distribution (Wiesel & Hubel)

area 17 in cat reared with ***one eye occluded*** during the critical period



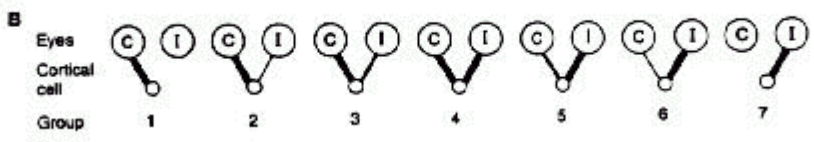
cortical neurons…

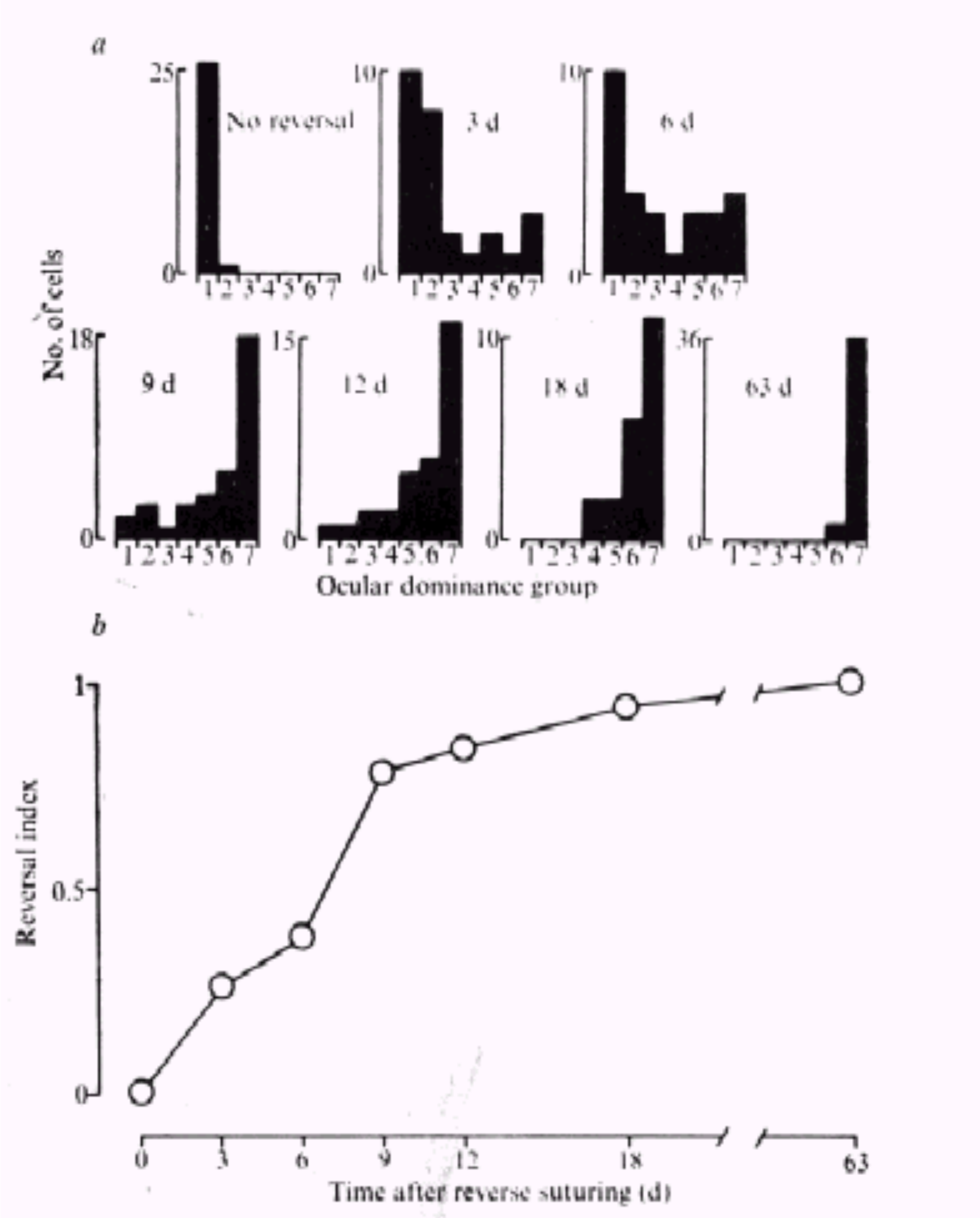
dominated by contralateral input

balanced input from both eyes

dominated by ipsilateral input

Ocular dominance groups





The ‘reverse suture’ procedure –

Ocular dominance can be reversed in a few days during the critical period

Kittens - ipsilateral eye occluded until 5 wks – then opposite eye occluded for various intervals before recording (Movshon & Blakemore, 1974)

OD histogram in a monkey with early binocular deprivation

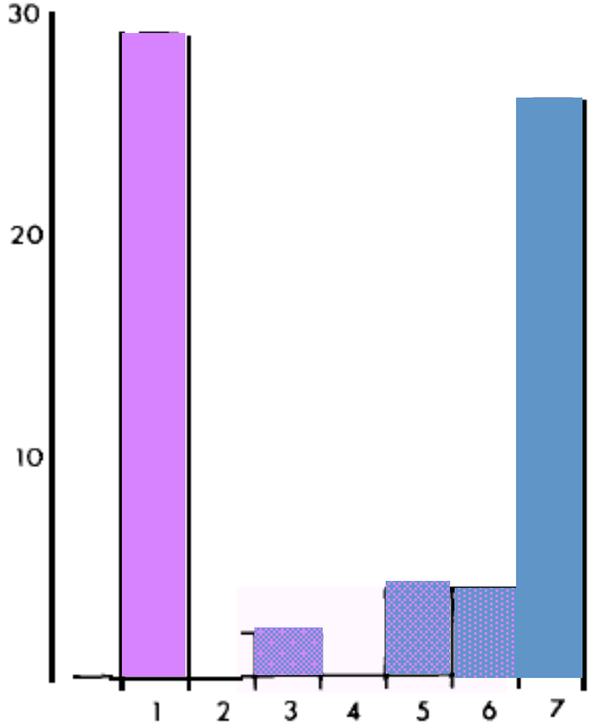


Fig. 10. Ocular dominance histogram of a monkey with binocular lid suture from birth to 30 days of age. Note the low number of binocular cell.[44]

No competition – but no correlated binocular input

Artificial strabismus

(lateral muscle cut to misalign one eye)

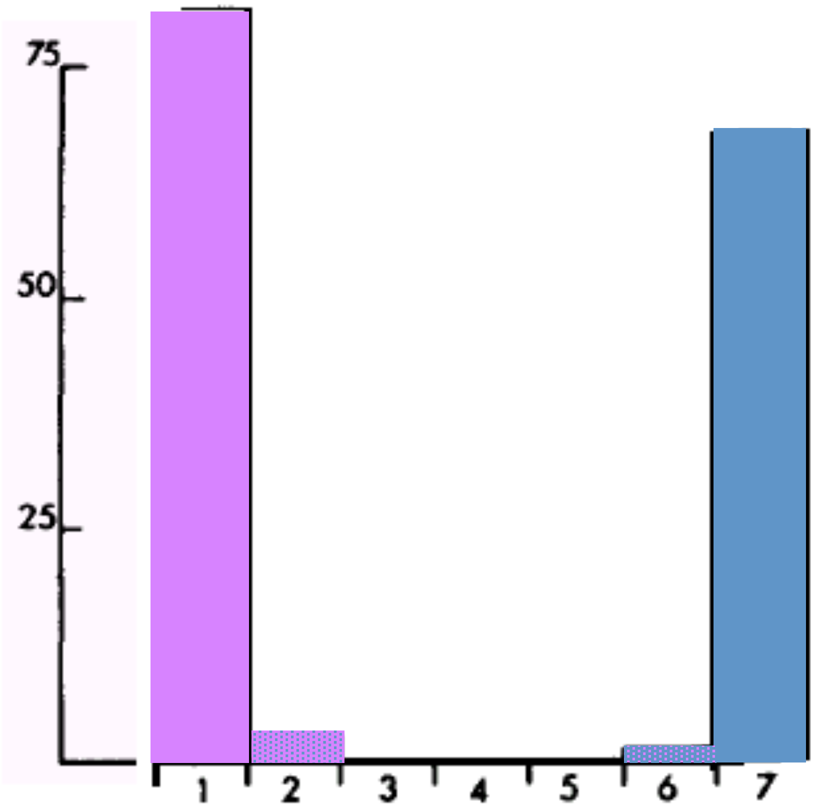


Fig. 11. Ocular dominance histograms of cells recorded in the striate cortex of two strabismic rhesus monkeys.[48]

Left: Histogram shows the eye preference of cells recorded in a 3 year old monkey in which the lateral rectus of the right eye was sectioned at 3 weeks of age. There is a nearly complete absence of

No competition – but no correlated binocular input

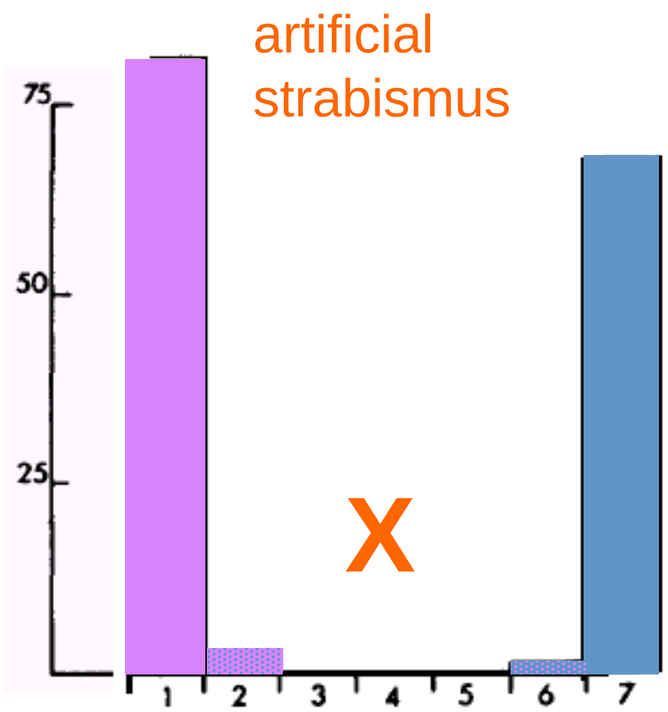
What does this mean for strabismic amblyopia??

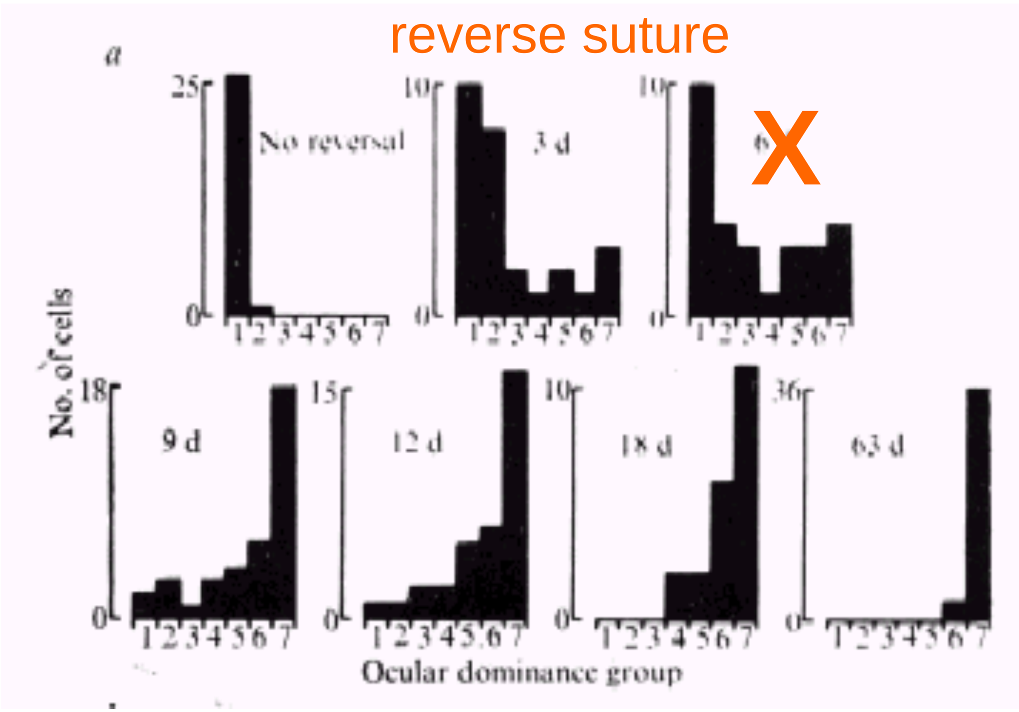
Occlusion therapy (patching) – counters amblyopia

Surgical correction of strabismus

-need to be done in critical period for good results

-Can binocularity be achieved, or just balanced acuity?





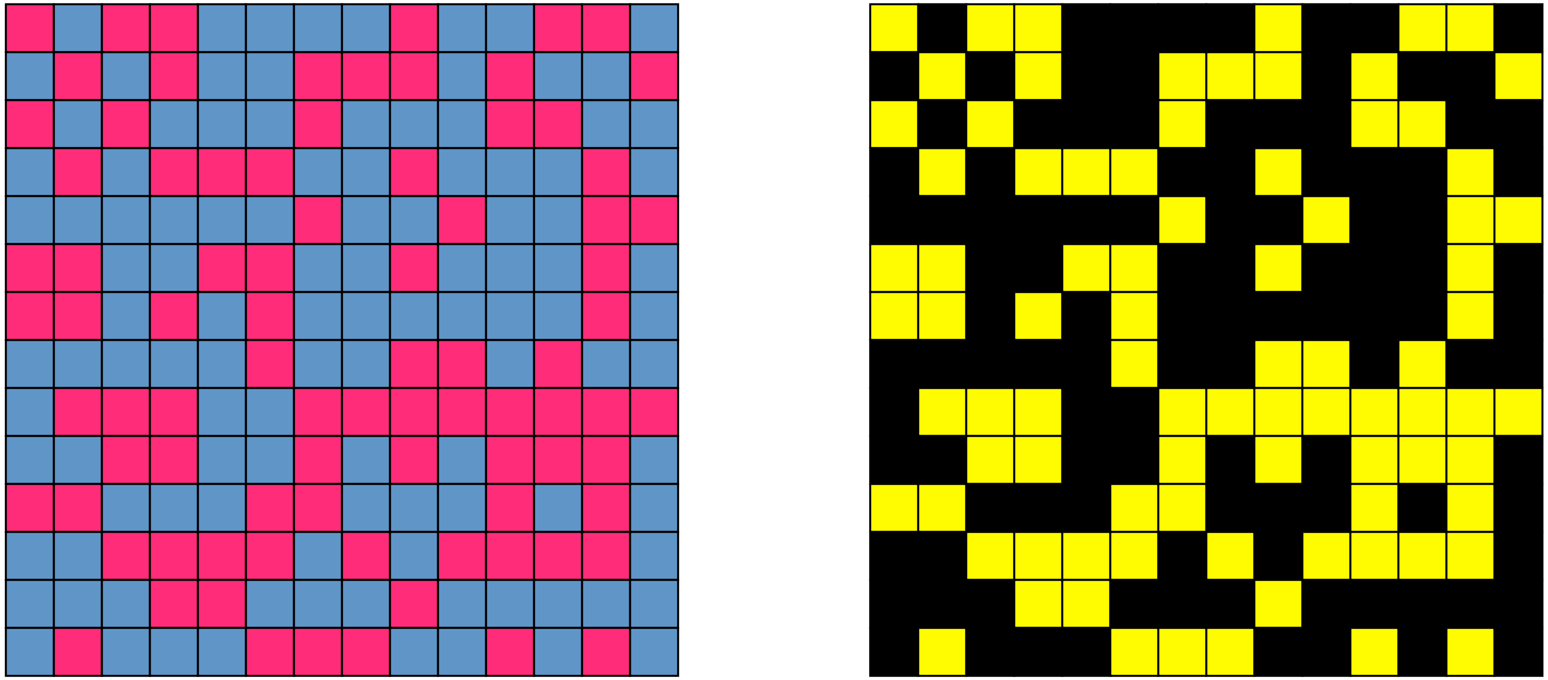
Binocular disparity / stereopsis

- Stereo vision (as in 3D cinemas) requires comparing slight differences between the image in the left and right eye

- Many people have poor stereopsis

- Why is this the case?

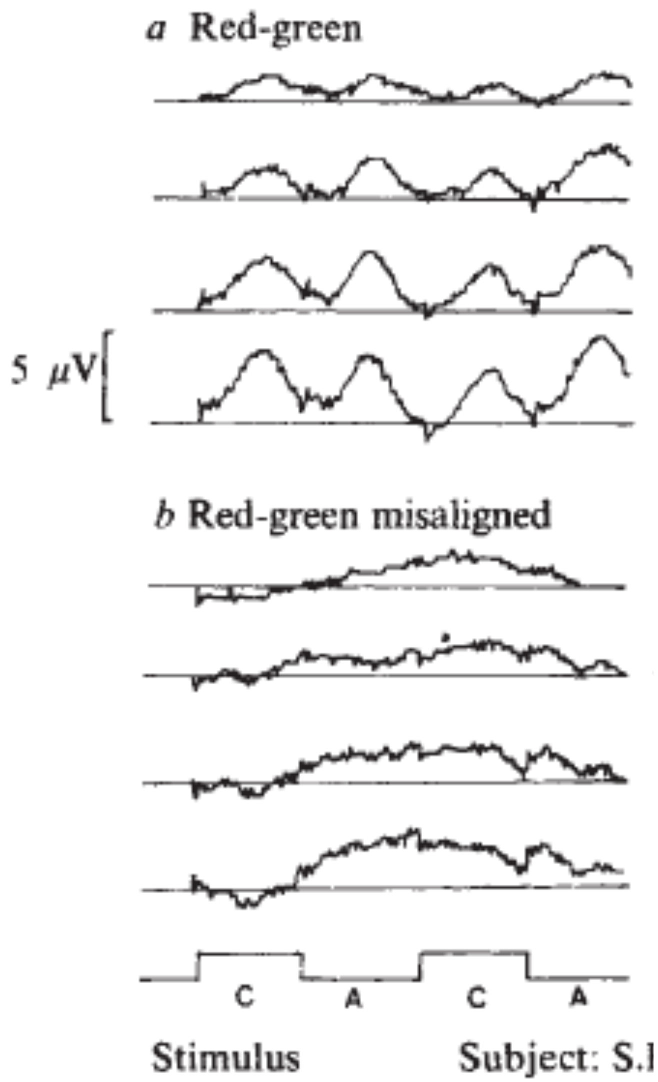
Random dot correlogram



anti-correlated ⟷ **correlated**

4 reversals/second

Random dot correlogram VEP

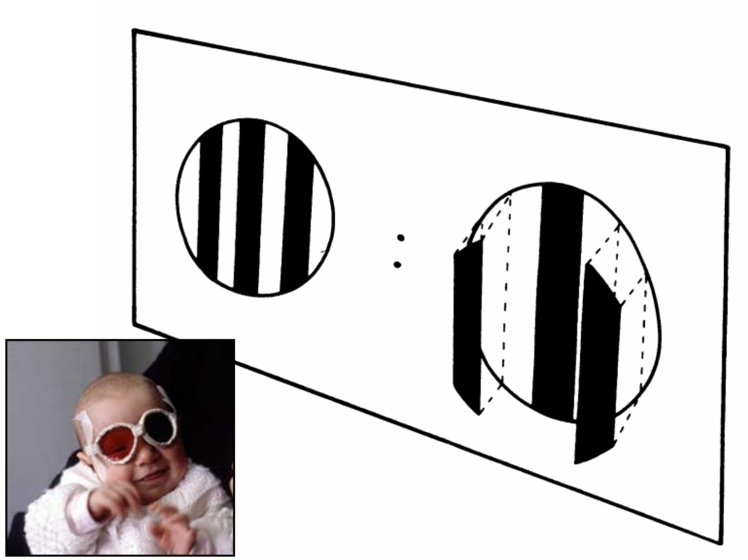


3 month infant

(Braddick et al, 1980)

Binocular disparity / stereopsis

- Infants like looking at 3D objects (on right) rather than 2D objects (on left)
- We can therefore work out when infants start to notice differences in depth caused by stereo vision

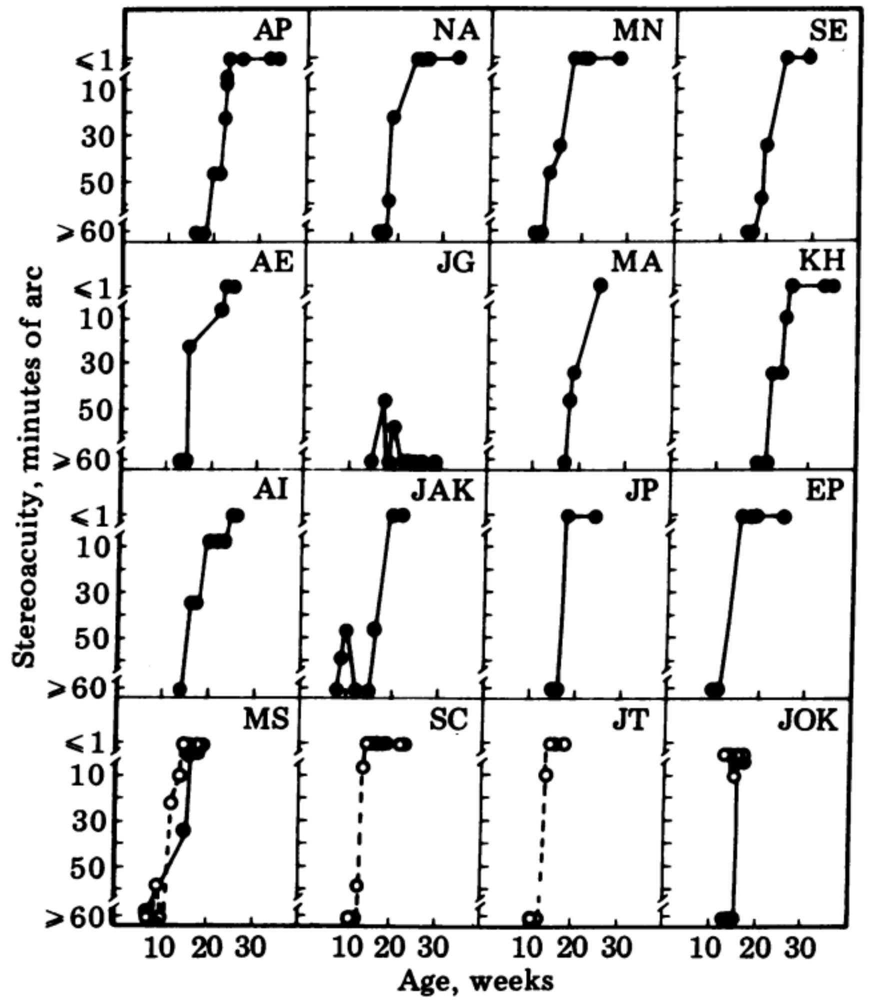


If stereo vision is present, left stimulus will have depth – otherwise it appears flat
Held 1980

Early visual experience & Plasticity

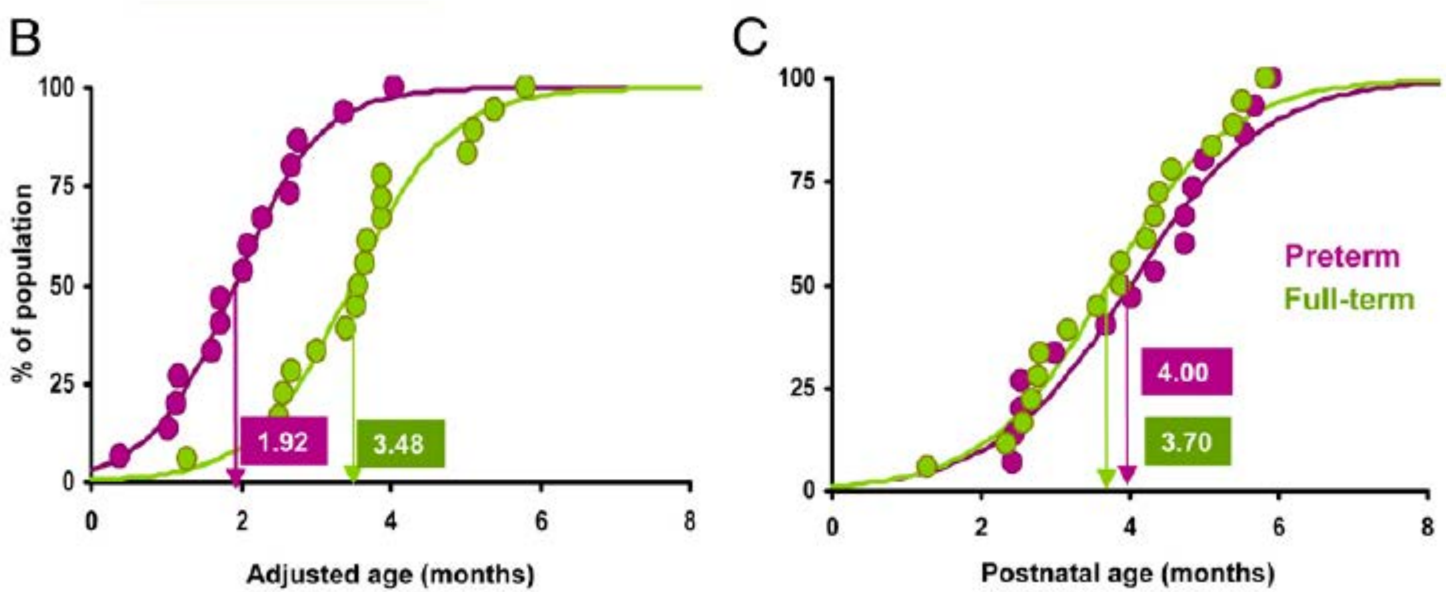
- Stereo vision develops super quickly over a few days when infants are between 2.5-5 months old
- There is a very specific and brief sensitive period
- Therefore, people with uncorrelated eye input in infancy (even after correction) are very vulnerable to poor stereo vision later in life

Results from 16 babies tested longitudinally (Held, 1980)



What controls the onset of binocularity?

Jando et al (2012): correlogram response in infants born full-term ● and preterm ● (mean 31 wks gestation)



- **data line up for time post-birth, i.e. experience dependent**

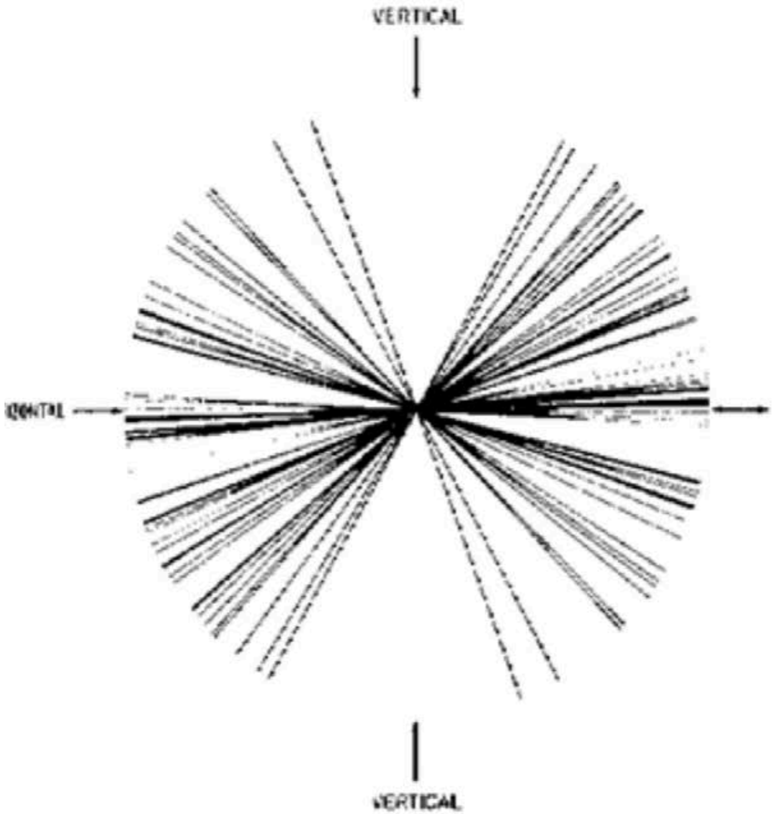
Another example of postnatal plasticity

Experience-based tuning of orientation sensitivity

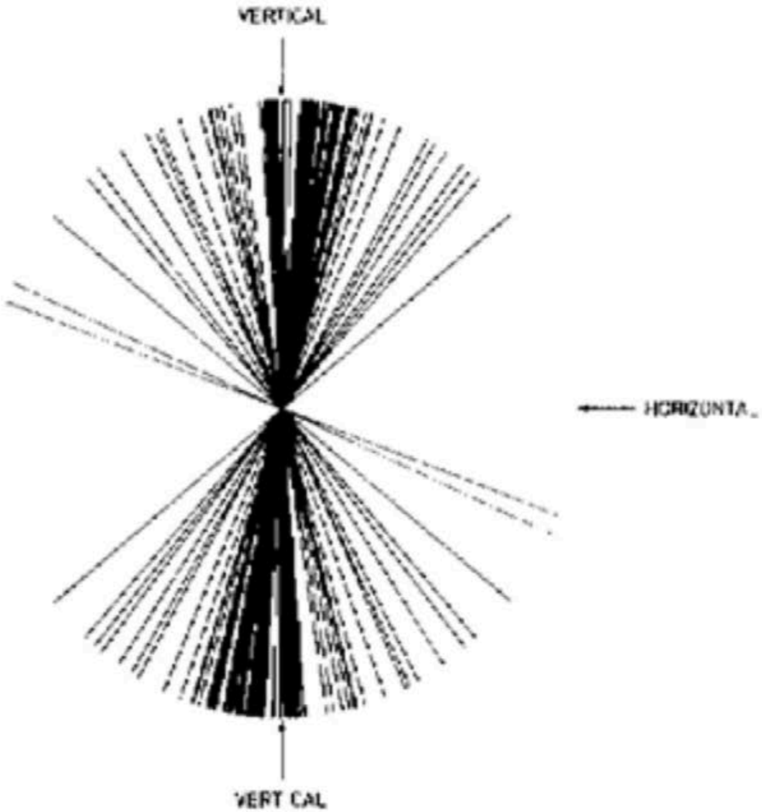
Blakemore & Cooper

Experience-based tuning of orientation sensitivity

Horizontally reared



vertically reared



Blakemore & Cooper

Experience-based interpretation of ambiguous visual input

Light from above prior

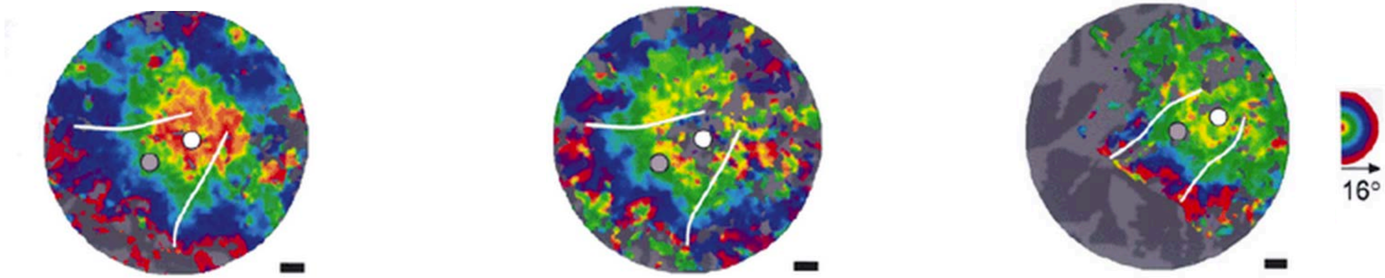
we assume the light comes from above so perceive this footprint as concave

Reorganisation of visual cortex with solely rod inputs

normal control
rods + cones

normal control
rods

achromatopsia
rods



Baseler et al., 2011)

Cross-modal plasticity

Cataract is clouding of the lens

www.projectprakash.org

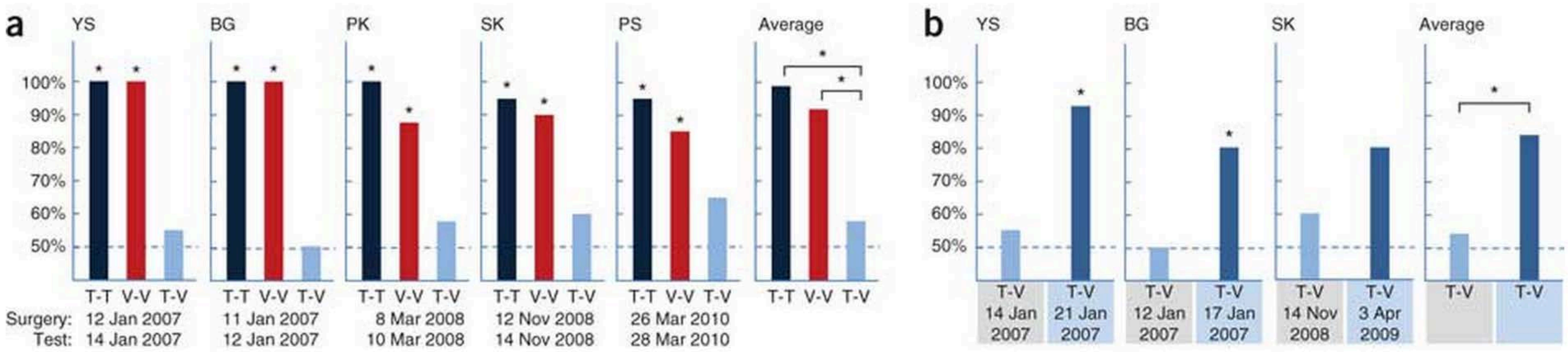
Cataracts

- Infants born with cataracts have specific long term problems with vision (Maurer, 2005)
  - Faces
  - Acuity if >10 days
  - Movement

- Later removal results in more severe problems

- But after removal some vision always restores
  - Molyneux's problem, 1688

Acquiring visual recognition via touch



Held et al., 2010

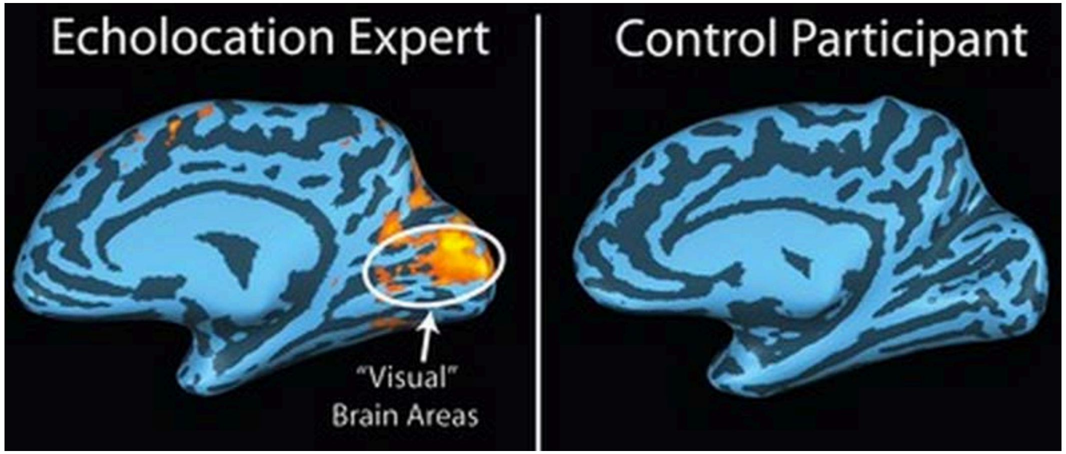
- When cataracts removed first no understanding of touch from vision, so no direct “innate” correspondence between touch and vision.

- But with very little experience, correspondences could be learnt

- **Touch experience helps to rapidly learn to interpret vision**

Resources for vision used by other senses

- Typical expectation is that blind individuals hear better and have more sensitive auditory and tactile senses because "unused" visual cortex can be recruited

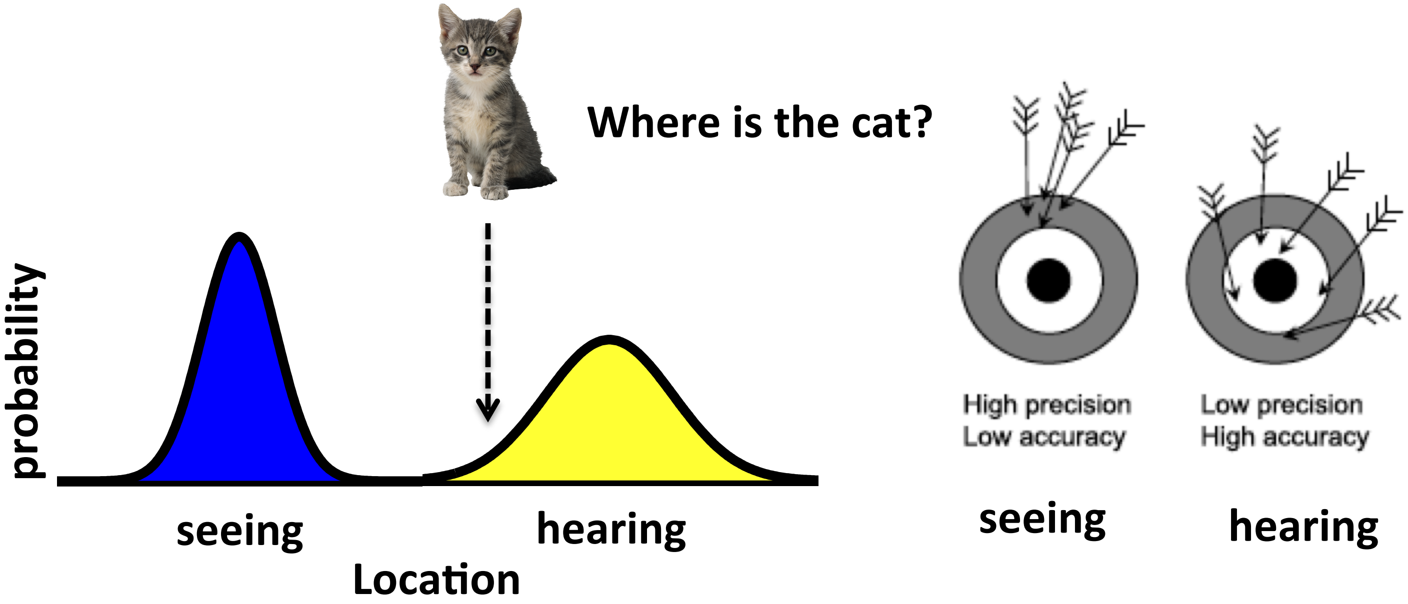


Thaler et al. 2011

Visual cortex areas activated in expert detect a difference between a click without and a click with an echo

- However, if we assume senses are needed to calibrate each other, we would expect that other senses are not always enhanced:

Calibration of vision by other senses



- As late cataract removal illustrates, when vision comes on, the brain doesn't immediately have direct knowledge of the world
- It is not obvious how signals in our neurons relate to the actual properties of the world - estimates are noisy and might be biased, especially when our body is still growing
- senses may be calibrated (aligned) to each other during development

Calibration for size vs. orientation perception?

Size Orientation

- Visual system has "direct" access to orientation
  - Neurons that are sensitive to orientations are present at the very low levels of the visual system
  - Hands do not have orientation specific touch sensors
- Visual system no direct access to (true) size
  - Projected size varies with distance, so need to compare to environment to judge true size (object constancy)
  - Hands are much better at this

Calibration for size vs. orientation perception?

Size Orientation

- Size: which of two blocks is bigger?
- Orientation: which of two blocks is rotated further?

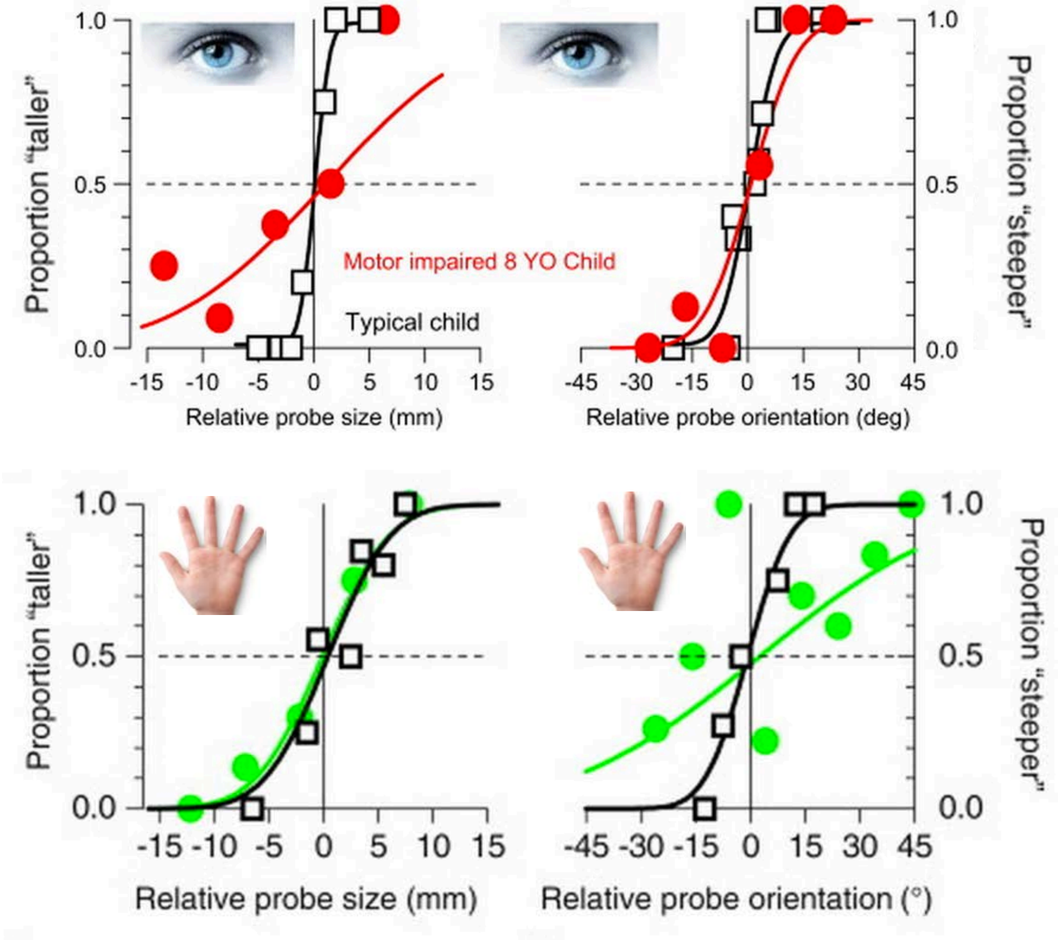
- Blind children used touch (Gori et al. 2012)
- motorically impaired children used vision (Gori et al. 2012)

Size vs. orientation judgment

size task **orientation task**

Motor impairment

Visual impairment



Implication:
Need touch to calibrate visual size - not orientation - recognition

Implication:
Need vision to calibrate tactile orientation – not size - recognition

- A flat slope means that you need large size/orientation differences between the stimuli to correctly judge which block was larger/steeper
- So, a steep slope means you can pick up small differences in size or orientation

Thank you for your attention!