

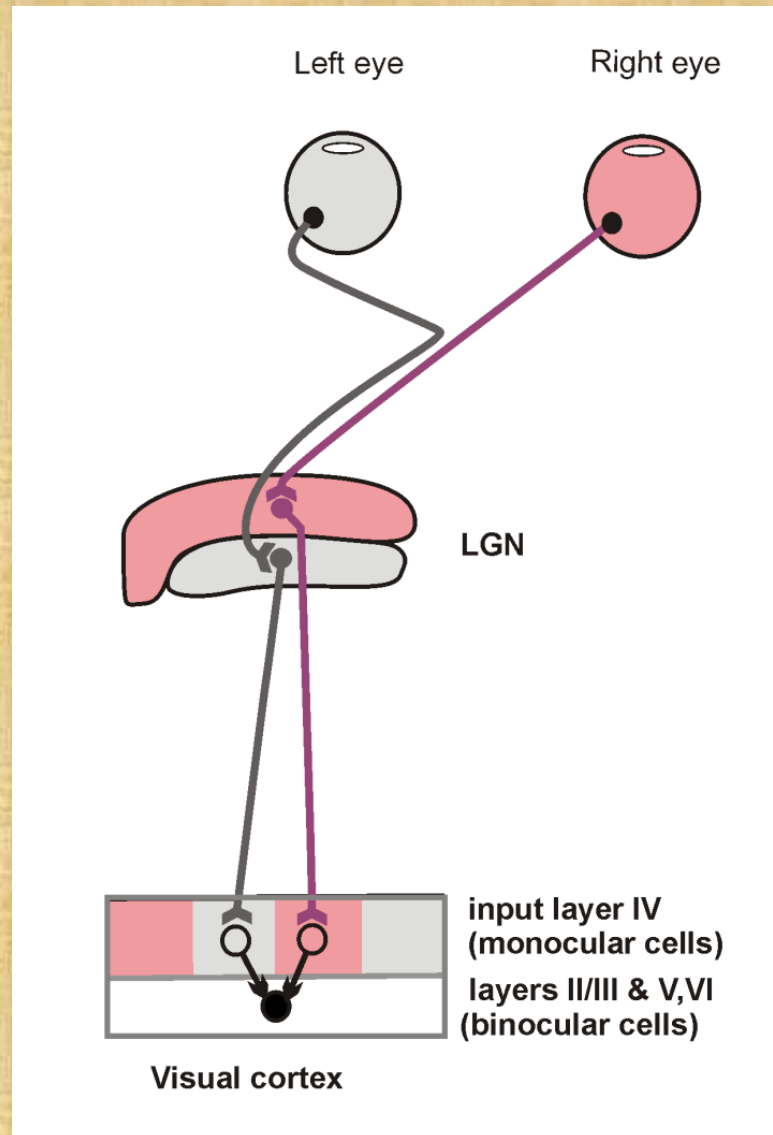
Organization of neuronal structures for binocular vision and the dynamics of their impairments in the case of amblyopia

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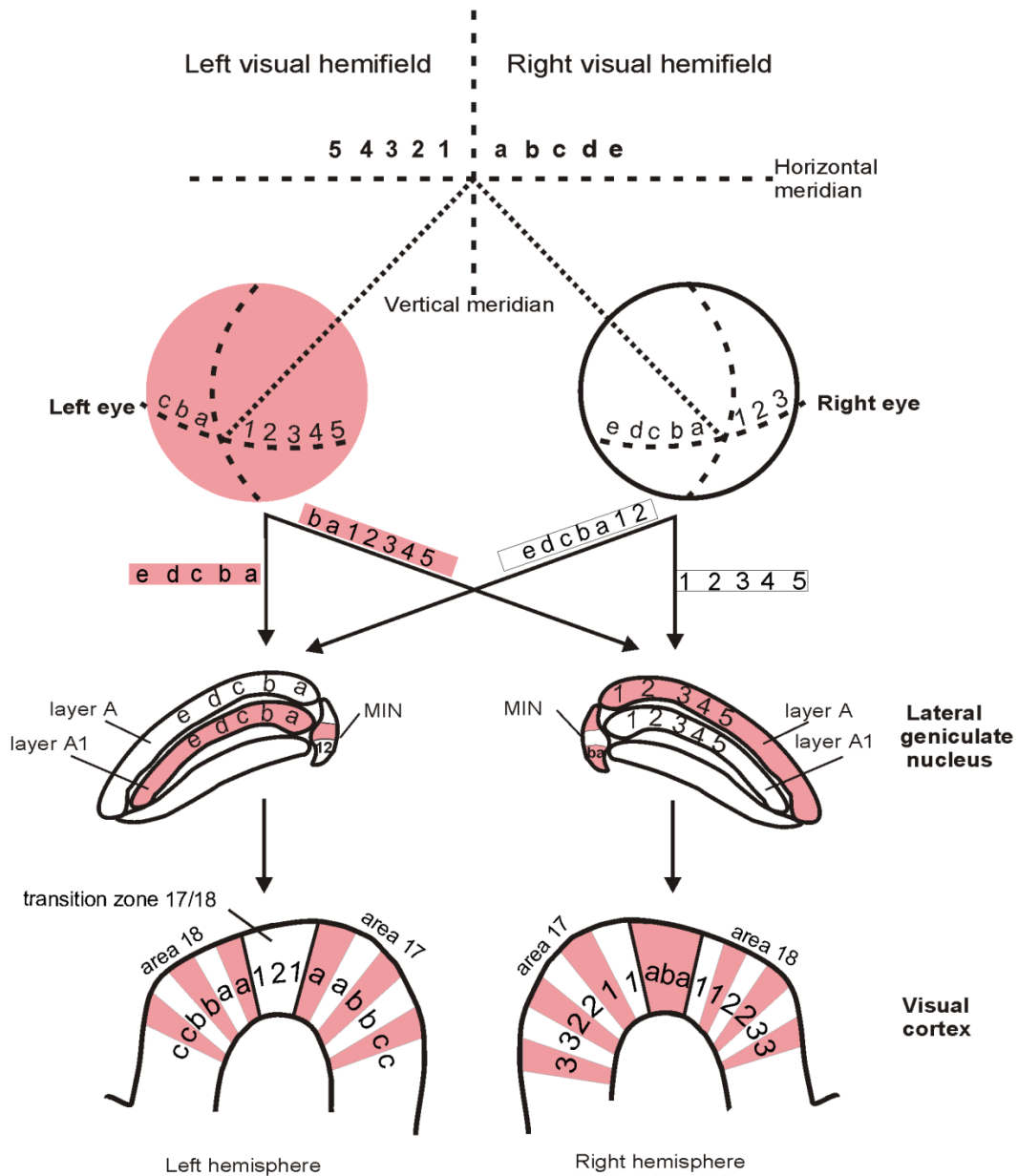
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Visual pathways from retinae to the cortex



Representation of 2D visual fields of the eyes in visual structures

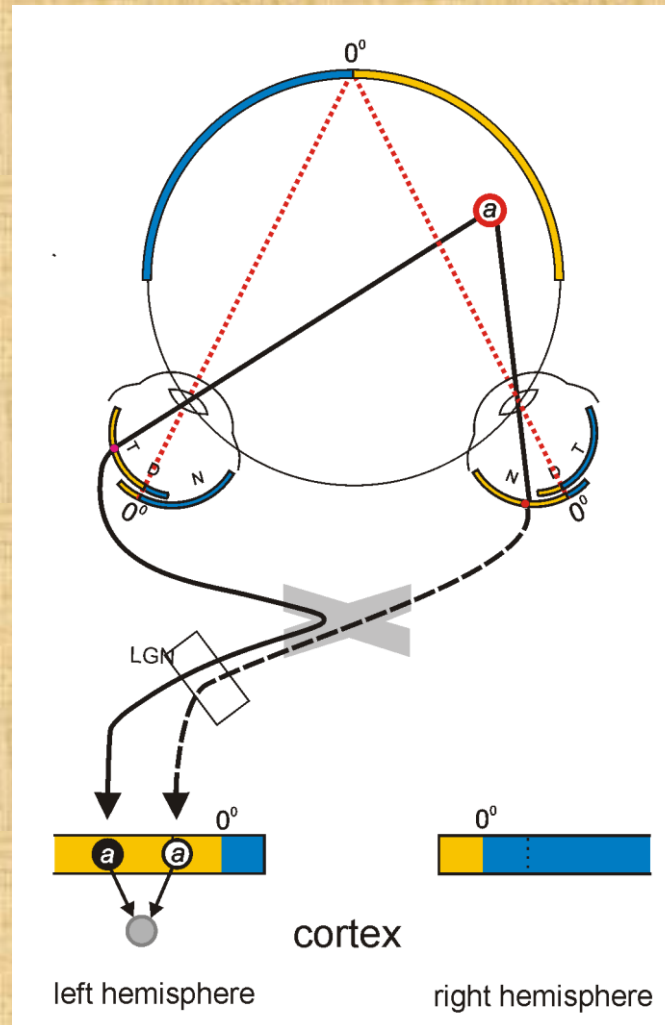
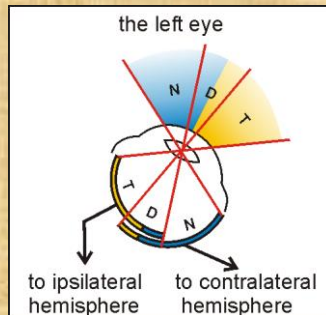


View on the cortical surface



Visual cortex

Where the remote object **a** is represented through different eyes in the visual cortex?

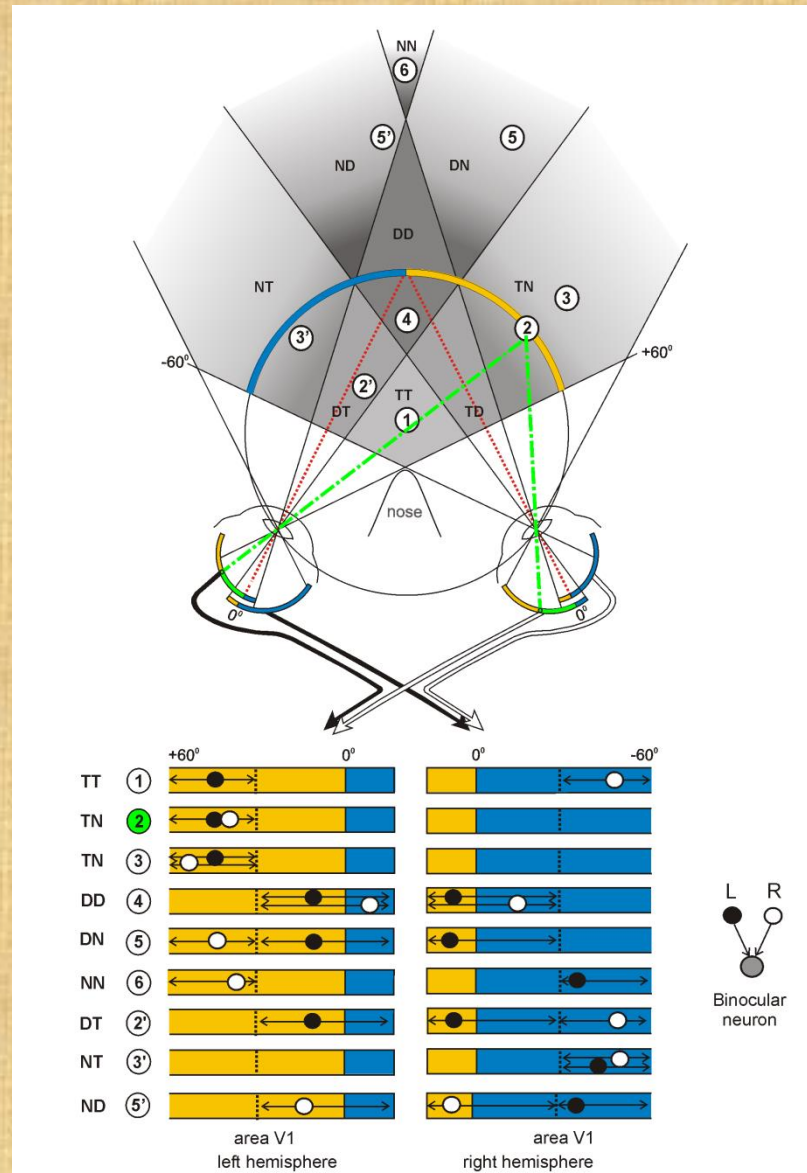


A circle passing through the fixation point (0 deg) and nodal points of the eyes, is Vieth-Muller circle (fixation plane). An object anywhere on this plane produces zero disparity.

Projections of object **a** through the left eye (black circle) and through the right eye (white circle) are shown on the diagram of flattened cortical surface, where horizontal meridian of visual field is represented.

Scheme of projections of dot-objects (1, 2, 3...) located in different parts of visual space

TT, DD, ... – visual space sectors related to Temporal, Nasal parts of retina and the zone of Naso-Temporal overlap (NTO)



The distance between cortical loci representing the inputs from the left and right eyes varies systematically with the distance between the dot-object and the Vieth-Muller circle (plane of fixation). It is clear that monocular neurons are located in these loci.

The farther the dot-object is located from this circle, the the larger the distance between the corresponding loci in the cortex (dot 3 and 5).

Dot-objects, located in the central part of visible space, fall onto the NTO zone of one or both retinae. Therefore they are represented twice, in both hemispheres (dot 4).

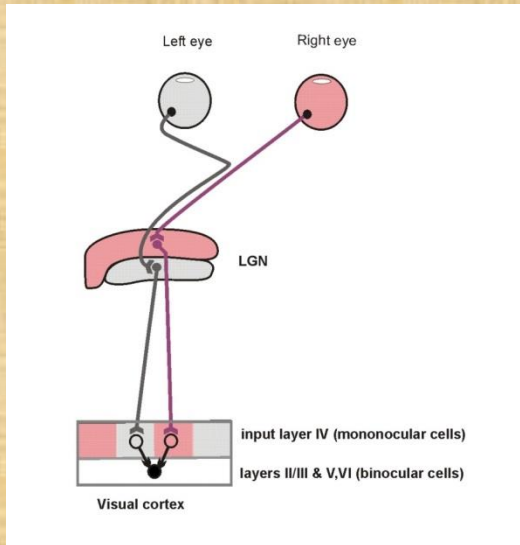
Spatial position of objects in visible space is reconstructed by Binocular neurons generated by convergence of monocular neurons driven by the left and right eyes. Each binocular neuron is tuned to a specific position in space.

Such fantastic organization of neuronal pathways and connections between them may be changed if information supplied by two eyes mismatch. Abnormal binocular experience in early childhood may produce amblyopia reducing visual acuity and stereovision, changing visuo-motor behaviour.

Amblyopia may be caused by abnormal alignment of eyes (strabismus), or by the difference in eyes refractive power, or by deprivation due to cataract, ptosis.

- Amblyopia resulting from cataract develops due to light intensity attenuation and visual-pattern deprivation.
- In the case of eye deviation (strabismus) the luminance of retinal images is not reduced but there is a difference in their spatial patterns. Depending on the angle between visual axes of the eyes, the objects are perceived as doubles or information from the eyes is contradictory. To prevent such contradiction, one eye is favoured while the information from the other eye is suppressed.

Therefore, the mechanisms of development of deprivational and disbinocular amblyopia can be different, and they are not yet fully understood.

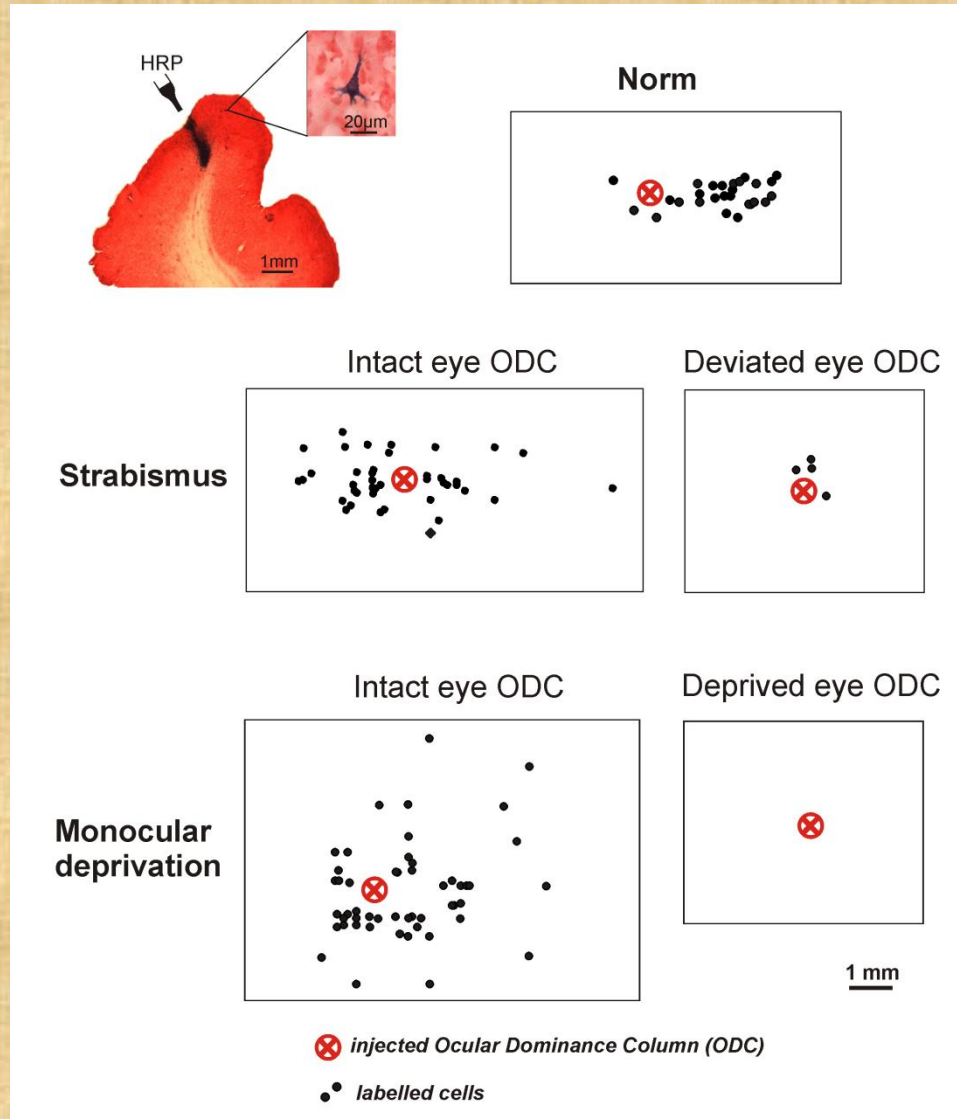


Since amblyopia is caused by mismatch of information supplied by two eyes, the initial changes must occur in the structure where visual pathways from the left and right retinæ converge and binocular cells are formed. Such structure is Primary visual cortex.

In animal models of amblyopia: Visual cortical neurons become strongly dominated by the non-deviated and non-deprived eye, and the proportion of binocular neurons greatly decreases [Hubel, Wiesel, 1965; Van Sluyters, Levitt, 1980; Freeman et al., 1982; Mower et al., 1982; Kalil et al., 1984; Sireteanu et al., 1993].

Moreover, there are changes in neuronal connections within visual cortex [Löwel, Singer, 1992; Löwel, Engelmann, 2002].

Distributions of labelled cells in cortical area 17 after neuronal marker (HRP) injection into the single Ocular Dominance Column (*view on flattened cortical surface*)



Long-range horizontal connections of **intact eye** ODCs increase in strabismic and monocularly deprived cats. (The zones of labelled cells are larger than in normal cats).

Long-range connections of **squinted** eye ODCs are shorten and absent in the most of **deprived** eye ODCs.

Using this method we were not able to find significant differences between deprivation and strabismus.

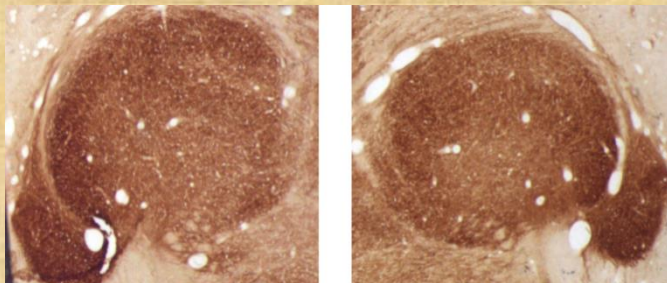
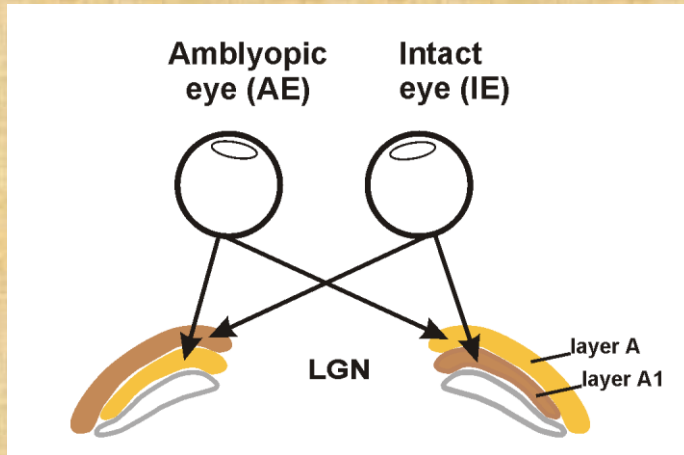
What happens in the **dorsal lateral geniculate nucleus (LGN)** when developing deprivation and disbinocular amblyopia?

What is the dynamics of activity changes in crossed and uncrossed pathways originating from each retina ?

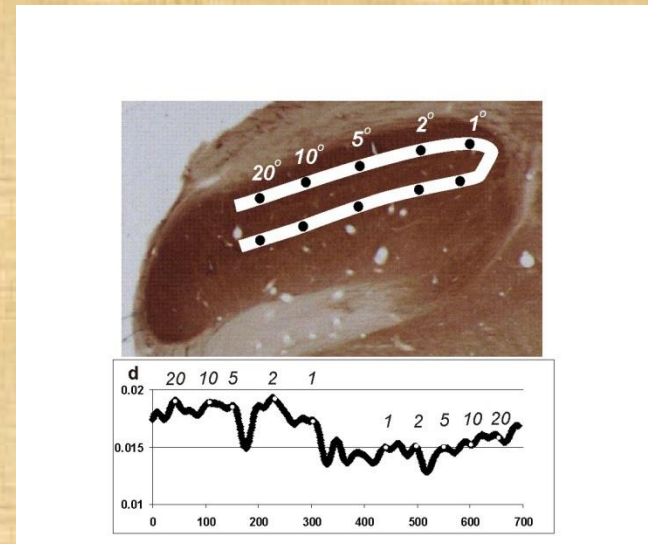
To answer these questions the monocularly deprived kittens and kittens with unilateral convergent strabismus were reared in normal environment to different ages (from 1 to 5 months).

Methods

The method of histochemical staining for cytochrome oxidase was used for estimation of functional activity in eye-specific A-layers of LGN. *Cytochrome oxidase is a mitochondrial enzyme involved in energy production, and its activity correlates with neurons' functional activity. The more active zones are stained in darker tones.* Therefore the optical density was measured on the images of stained LGN-sections. Measurements were done in projection columns representing 1, 2, 5, 10 and 20 deg along the horizontal meridian of visual field. The Michelson contrast K between optical density in A-layers was determined according to the formula shown.



LGN sections stained for cytochrome oxidase



$$K = (d_{IE} - d_{AE}) / (d_{IE} + d_{AE})$$

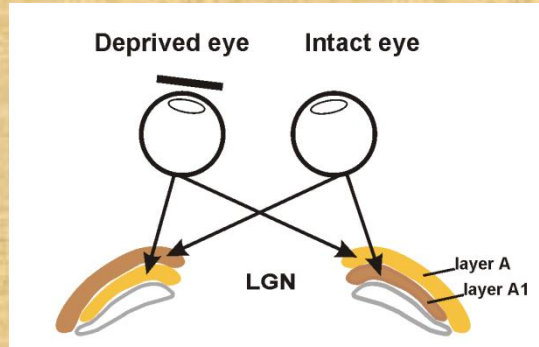
d – optical density

IE – intact eye

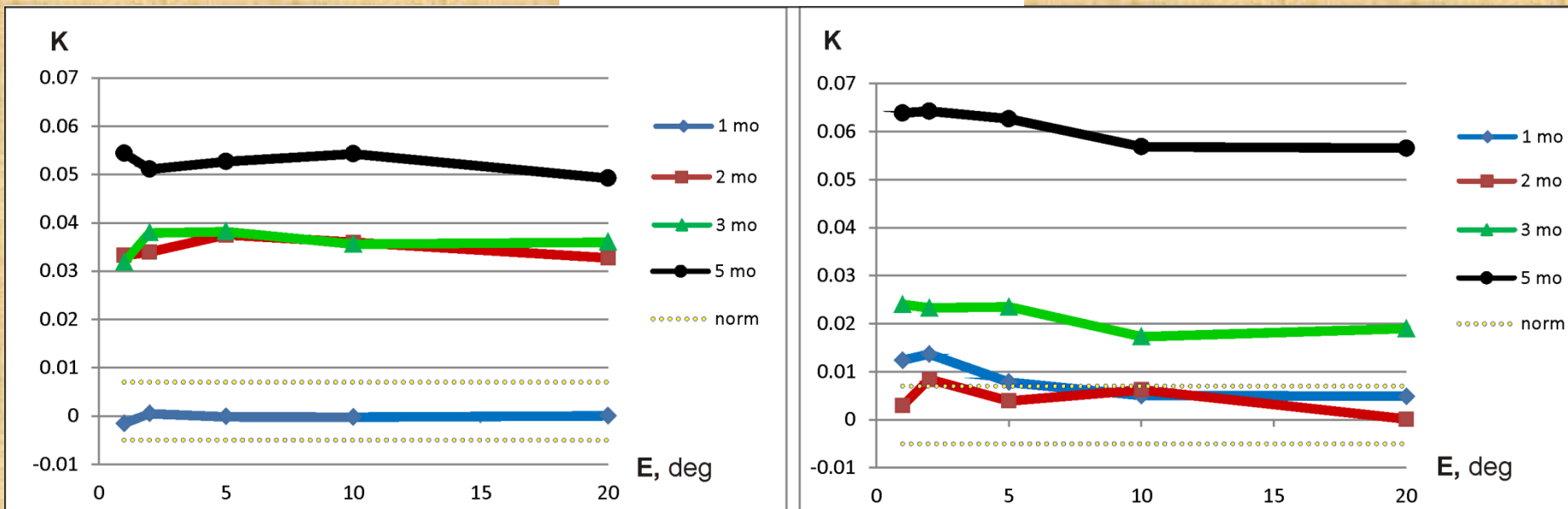
AE – affected eye

Dynamics of K changes in monocularly deprived kittens

$$K = (d_{IE} - d_{DE}) / (d_{IE} + d_{DE})$$

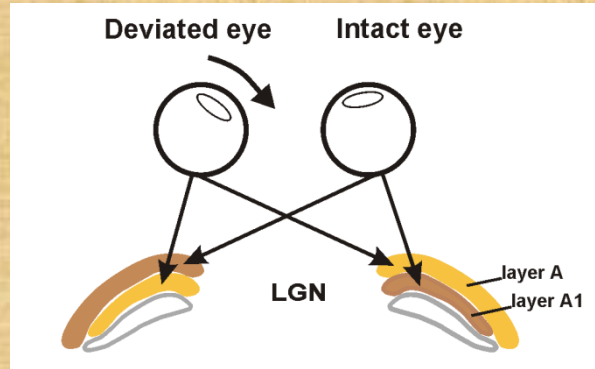


K - contrast between optical density in A-layers of LGN;
E - eccentricity along the projection of central horizontal meridian of the visual field



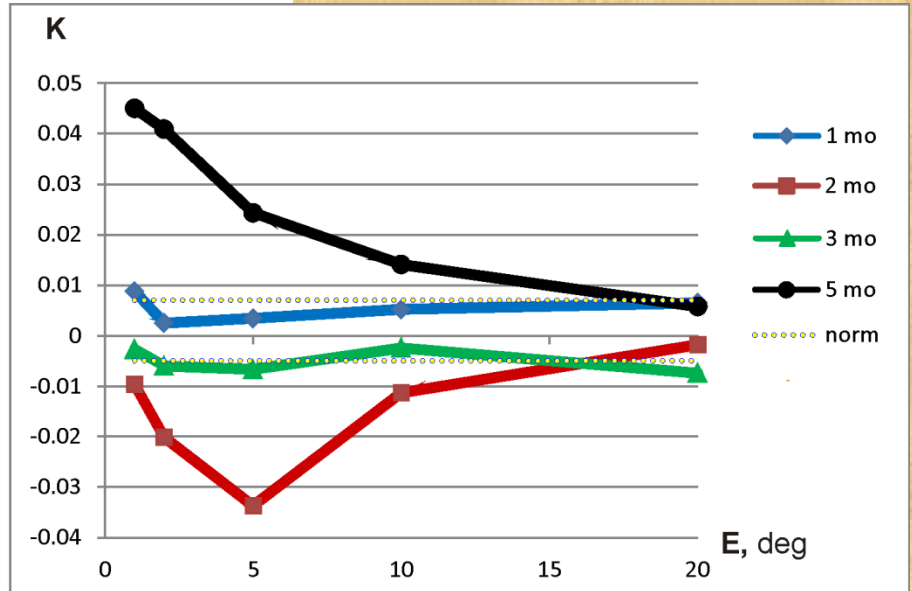
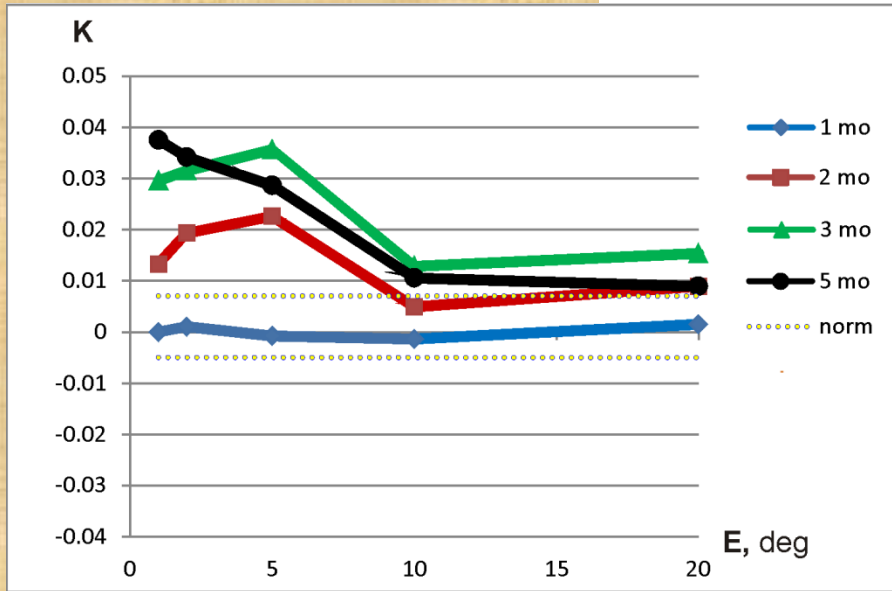
In LGN of both hemispheres the relative decrease of activity in deprived eye layer was obtained along the whole projection of the visual field, but it happens earlier for layer innervated by uncrossed pathway from deprived eye than for deprived layer innervated by crossed pathway.

Dynamics of K changes in strabismic kittens



$$K = (d_{IE} - d_{DE}) / (d_{IE} + d_{DE})$$

$K > 0$ - intact eye dominates,
 $K < 0$ - deviated eye dominates



Alterations of activity were mostly confined to the LGN zone of central part of visual field representation. At the age of 2 months the activity in both LGNs was higher in layers, which receive retinal inputs via crossed pathways, **despite the fact that one eye was deviated**. Activity in LGN layer innervated via uncrossed pathway from deviated eye decreases earlier than in the layer innervated via crossed pathway from the same eye.

CONCLUSIONS

- The observed differences in development of deprivation and disbinocular amblyopia strongly suggest the different mechanisms implicated in them.
- Alterations of LGN layers activity are observed in the projection of the entire visual field in deprived animals, but only in the projection of central 10-15 degrees in strabismics. Moreover, these changes develop earlier with deprivation than with strabismus. We suggest that during development of congenital strabismic amblyopia the initial period of alternating fixation is preceding the suppression of squinting eye.
- Nevertheless, in both cases of amblyopia a relative decrease of activity in LGN layer innervated by uncrossed pathway from impaired eye is observed earlier than in layer innervated by crossed pathway from the same eye. So evolutionary older crossed pathways are less plastic.
- We speculate that intense stimulation of nasal visual hemifield (temporal hemiretina) of the impaired eye in pre-surgical period of corrections might be useful to delay the initially developing disorders in uncrossed pathways.

Thank you for attention

Experimental information

Groups of animals	Norm				Monocular deprivation				Unilateral strabismus			
	1	2	3	5	1	2	3	5	1	2	3	5
Age (months)	1	2	3	5	1	2	3	5	1	2	3	5
Number of animals	5	4	5	3	4	4	4	3	4	3	4	3
Number of LGN sections (L+R)	27	36	37	18	23	47	27	15	24	34	22	15
Number of Contrast measurements	416	327	359	116	437	501	573	283	513	473	627	215

In total : 4840 measurements of contrast in the 325 sections of LGN from 46 kittens.