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"The Albino Abnormality of the Central Visual Pathways and Its Development"

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The albino abnormality of the central visual pathways and its development.

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The pathway that carries nerve fibres from the eye to the brain is abnormal in all albino mammals. Many of the fibres that would take an uncrossed course in a normal animal take a crossed course in albinos. The misrouting occurs in the optic chiasm where a normal animal has a pattern of partial crossing that allows a single image in the left visual hemifield to produce excitation along two pathways going to the right cerebral hemisphere, one pathway coming from the left eye, the other from the right eye. Figures 1a and 1b show schematically that normally there is a mapped representation of the visual field in each cerebral hemisphere, and that the map coming from the left eye is in register with the map coming from the right eye. Figure 2 shows the relationships demonstrable in the central visual pathways of an animal having the albino abnormality.

One set of problems that can be addressed by studying this abnormality concerns the way in which the abnormal maps, produced in the brain by the misrouting, relate firstly to each other and secondly to the visual capacities of the animals that can be studied behaviourally. It has been found that although the abnormal fibres are misrouted in the optic chiasm they are not misrouted at their central terminal station, the lateral geniculate nucleus. This is indicated in Figure 2 which shows that fibres terminate in the appropriate (numbered) sector of the nucleus. However, because the fibres are on the wrong side, they produce a mirror reversal of one sector of the map. In the pathway from the lateral geniculate nucleus to the cerebral cortex the abnormal animals may show a suppression of the abnormal, fragmented (and partially reversed) map, or they may show a correction of the reversed sector. Either strategy produces a behaviourally adequate result and the two results are behaviourally distinguishable. The developmental processes that may lead to these two quite distinct solutions will be considered.

The mode of action of the albino gene upon the central visual pathways is not understood. The wild type gene at the albino locus produces tyrosinase, an enzyme necessary in the production of melanin, the pigment that colours skin and eyes. However, not all albinos lack tyrosinase. Some lack pigment because genes at quite different *loci* (some on different chromosones) are abnormal and these genes may be concerned with the "packaging" of the melanin or with the production of the strucures storing melanin, the melanosomes. It has been shown that any animal in which the melanin production in the retina is abnormal has abnormal visual pathways. The melanin of the skin is irrelevant, the nature of the gene action seems not to matter greatly, the important variable appears to be the degree of the melanin lack in the retina.

Melanin relates to the very early development of retinal cells and also relates closely to the early outgrowth of nerve fibres from the retina to the brain. How it influences the chiasmatic choice of the developing nerve fibres remains to be defined.

Some recent observations suggest that in normal development there is an interaction between the pathways coming from each eye, and that in the absence of this interaction an abnormal pathway like that of the albinos is produced. Presumably the interaction involves melanin. The evidence is that in a normal animal a very early monocular enucleation, done before any retinal fibres have reached their geniculate termination site, produces a surviving pathway that is essentially like that of an albino. A later enucleation done in a normal animal produces a very different type of surviving retinogeniculate pathway. A similar, very early enucleation done in an albino animal produces a result that is not distinguishable from the result produced by the early enucleation in a normal animal. Further, a later enucleation done in an albino produces the same result as the early enucleation. That is, the albino lacks an interaction between the two retinofugal pathways that is present normally and that produces the normal partial decussation. The nature of this interaction remains to be defined.

The organization and development of the optic nerve and the optic tract.

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The classical account of the optic nerve and optic tract has each carrying an orderly map of the visual field: the nerve carrying the map for the field of one eye, the tract carrying the two hemifields from the opposite side in register, one hemifield from each eye (fig 3). However, there is a rearrangement of fibres that occurs between the eye and the brain that makes the classical view untenable. Whereas behind the eye all nerve fibre classes, identifiable by fibre diameter, are mingled, and are arranged as a reasonably accurate map of the retina (that is, a reversed map of the visual field) in the optic tract the fibres are segregated according to diameter. Either nerve fibre diameters must change significantly as fibres pass from nerve to tract, or the nature of the mapping must change.

In our studies we accepted the generally held view that fibre diameters do not change and showed that there is not a single map of the visual field in the optic tract. Instead, each morphologically and functionally distinct retinal ganglion cell type, characterised by a particular range of fibre diameters, is mapped separately in the optic tract. The "beta cells", which have medium sized axons map most deeply, the uncrossed component lying slightly more superficial than the crossed component. The "alpha cells", which have the thickest axons map more superficially and the "gamma cells", having the finest axons, form a particular concentration most superficially next to the surface of the optic tract.

This layered arrangement is formed during development because newer fibres tend to grow near the surface of the brain. This can be shown by studying the "birthdates" of retinal ganglion cells or by differentially labelling the oldest fibres.

The change from a "retinotopic" arrangement in the nerve behind the eye to the "chronotopic" arrangement seen in the tract occurs in the nerve close to the optic chiasm. Studies of early development at the time that the nerve fibres are entering the tract show that there is a change in the nature of the glial (supporting) cells coincident with the change in fibre arrangement. It appears that the advancing growth cones tend to be directed towards the surface of the glial processes that characterize the central parts of the optic nerve and the optic tract.

Although these studies were undertaken on the assumption that fibre diameters do not change as the fibres pass from nerve to tract (see above) recent studies demonstrate that this assumption, too, is false. It should be noted that the false assumption stimulated the studies described above but that these studies did not have their foundation in the false assumption. We now have the interesting problem of defining how axon diameters are determined in development: it would appear that there must be an interaction between axons and glial cells and that this interaction differs according to the type of glia involved.

The organization and development of the optic nerve and the optic tract

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Light from the right binocular zone falls on the left temporal hemiretina and the right nasal hemiretina. Because fibers from the nasal hemiretina of each eye cross to the opposite side at the optic chiasm, the left optic tract carries axons from the left temporal hemiretina and the right nasal hemiretina, and therefore contains a complete representation of the right hemifield of vision.

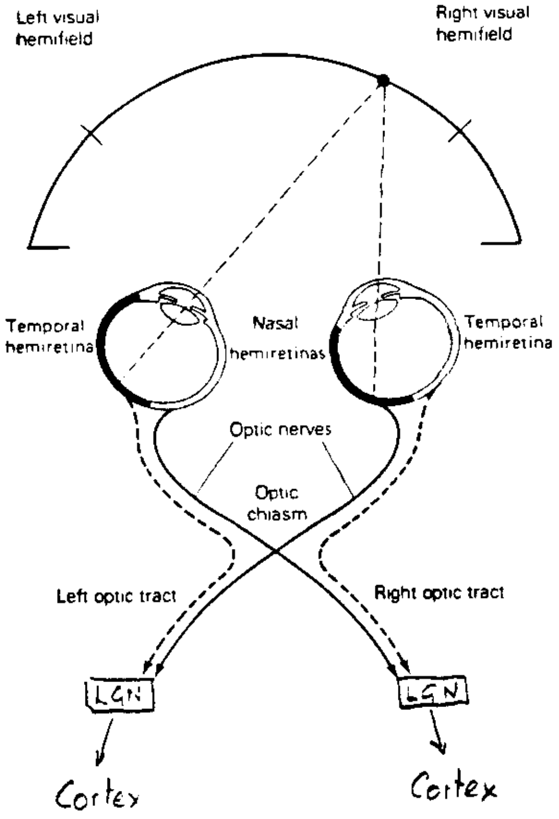


Figure 1A

The arrangements of retinofugal fibres in the optic nerves and optic tracts of a mammal

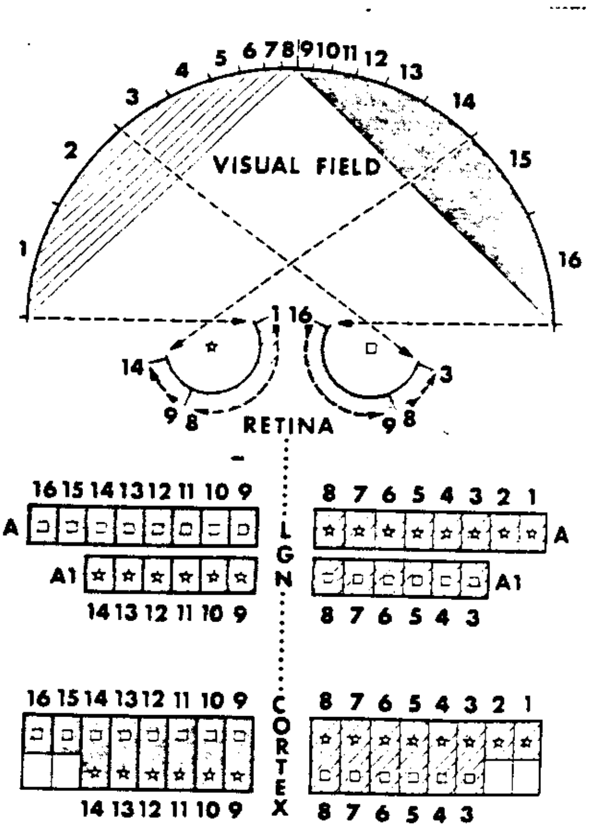


Figure 1B

The representation of the visual field and the retina as orderly maps within the lateral geniculate nucleus and the cortex

The organization of the retinogeniculocortical pathways in a normal cat. The visual field is shown as a numbered sequence, and the representations of the visual field within the lateral geniculate nucleus (LGN) and the cortex are shown as corresponding sequences. The left hemifield and its central representation are shown by wide stripes, the right hemifield by narrow stripes. Geniculocortical regions that receive from the left eye are shown by stars and those that receive from the right eye are shown by squares. (Modified from Guillery et al. 1974.)

Figure 2

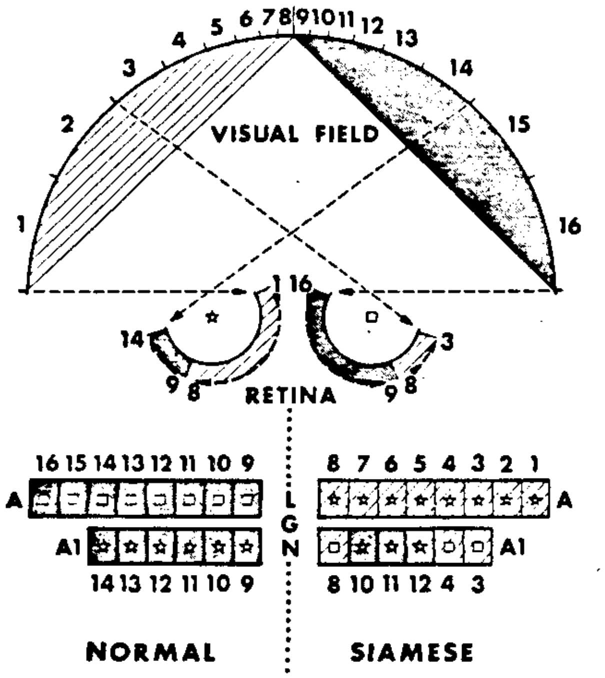
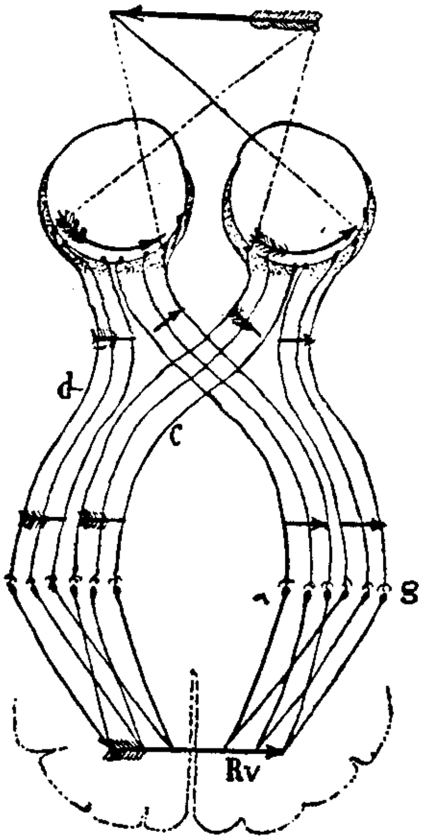


Figure 2. The organization of the retinogeniculate pathway in a normal cat (left side of figure) and in a Siamese cat (right side). Conventions as in Figure 1. In the Siamese cat, the abnormal segment of lamina A1 is shown by 10*, 11* and 12*



— Schéma du chiasma des voies optiques et de la projection visuelle centrale chez l'homme. — On y voit que le faisceau direct est nécessaire chez les animaux à champ visuel unique.

Figure 3

This schema, produced by Santiago Ramon y Cajal, shows the two partial maps in the optic tracts (en route to g) represented as end to end partial arrows. Later work suggested that the two partial arrows are in register. I shall discuss a different pattern of mapping