

Lecture 22 - Deprivation and Binocular Vision Anomalies

(Steinman Chapter 9; Schwartz Chapter 17; Adlers Chapter 24)

INTRODUCTION TO VISUAL DEPRIVATION

Very important research about visual development was done by David **Hubel** and Torsten **Wiesel** beginning in 1959, and for their work, they were awarded the Nobel prize for medicine in 1981 (Fig. 1) They were interested in the development of the visual system and the effect of visual deprivation early in the life of cats and monkeys.

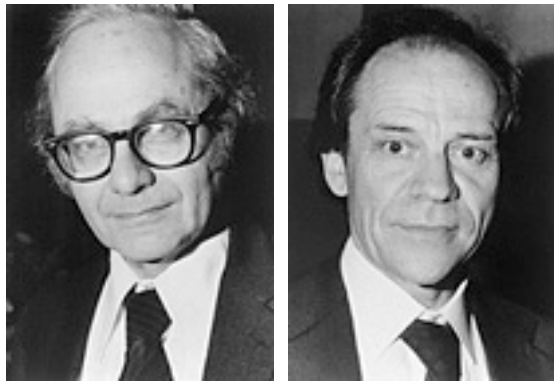


Figure 1. Nobel laureates in physiology or medicine in 1981, Hubel (L) and Wiesel (R); “for their discoveries concerning information processing in the visual system” (<http://nobelprize.org/medicine/laureates/1981/>)

Ocular dominance histograms

When recording from neurons in the visual cortex of a normal adult cat, they found that 80% were binocular; that is, they received some input from both eyes. The relative influence of either eye varied. Some neurons were more strongly dominated by the right eye, some more strongly influenced by the left eye, and some seemed to be equally influenced by either eye. They classified each cell into one of seven “ocular dominance” categories, which described the degree to which each cell was influenced by either the contralateral or ipsilateral eye (Fig. 2 left; similar to **Steinman Fig. 9-9**).

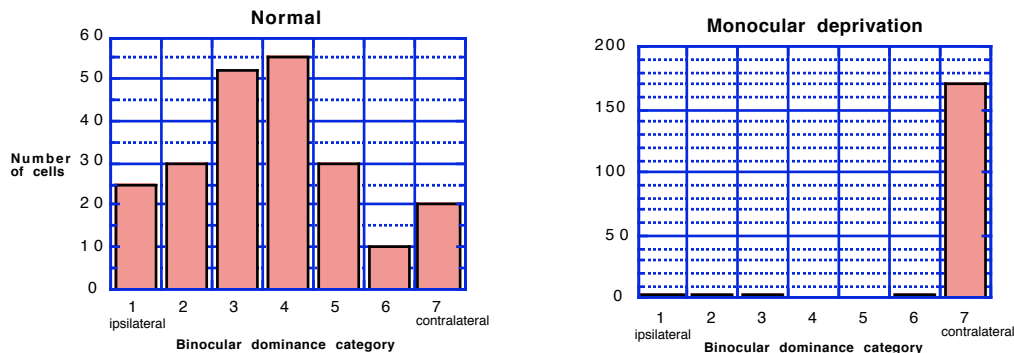


Figure 2. Ocular dominance histograms showing the results of Hubel and Wiesel’s experiments.

Group 1 neurons were influenced by the ipsilateral eye only (monocular); group 7 cells by the contralateral eye (monocular), and groups 2-6 showed different degrees of binocularity. Group 4 cells, in the middle of the **ocular dominance histogram**, were equally sensitive to input from both eyes.

At birth, they found that the ocular dominance distribution of a kitten’s area V1 neurons was similar to that of the adult cat, shown in Figure 2-left. During the early stages of life, however, the ocular dominance

characteristics of these neurons were very susceptible to change, depending on the quality of visual input they received from both eyes. This is referred to as **plasticity**.

Monocular occlusion

They sutured the eye lids on one side closed shortly after birth and let the kitten mature, so the cat was allowed to use only one eye during this period. After this, they tested many neurons in the visual cortex and discovered that, though the cortical cells looked normal histologically, their function had radically changed. Now 90% of the cells were monocularly driven by the opened eye and were insensitive to input from the deprived eye. This is illustrated by the **ocular dominance histogram** in Figure 2-right (similar to **Steinman Fig. 9-10**). When forced to use the deprived eye, the kittens acted as if they were blind.

Binocular occlusion

Figure 3-left (redrawn from **Adler's 8th ed., Fig. 24-36**; similar to **Steinman Fig. 9-13**) shows the ocular dominance histogram when the kittens had binocular occlusion early in life. In terms of ocular dominance, most of the neurons had a distribution similar that of a normal cat. The cells were not completely normal, however. Many of the cells did not show normal sensitivity for specific orientations, and many were unresponsive to any light stimulation.

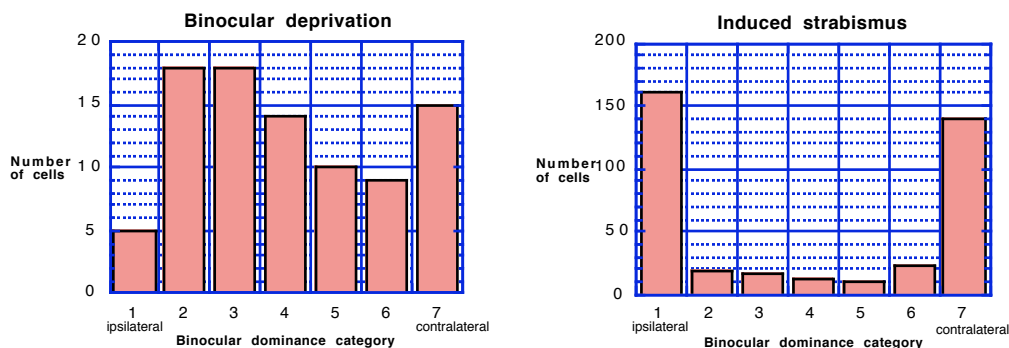


Figure 3. More ocular dominance histograms showing the results of binocular deprivation (left) and induced strabismus (right).

Surgically induced strabismus

In order to induce a large exotropia, Hubel and Wiesel cut the medial rectus muscle of kittens shortly after birth. This induced a large exotropia. The ocular dominance of their cortical neurons was studied 3 months to a year later, and results are shown in Figure 3-right. The vast majority of cells were monocularly driven (groups 1 and 7), while the number of cells that could respond to stimulation from both eyes (binocular cells) was severely reduced.

Note that, in this case (induced strabismus), neither eye was deprived of vision. Each had access to monocular vision, but binocular fusion was impossible. It seemed that the normal development of binocular cortical cells required fusible binocular input from both eyes during this developmental period. That is, as we discussed before, **high quality, highly correlated images to both eyes**.

They found a similar result when alternately occluding one eye on alternate days following birth. An opaque contact lens was placed on one eye one day, then switched to the other eye the next day, and this was continued for several weeks. These kittens also had mostly monocularly driven neurons and few binocular cells (See **Steinman Fig. 9-17**).

THE SENSITIVE OR CRITICAL PERIOD

Hubel and Wiesel used different forms of binocular deprivation at different times during the development of the kittens and found that the cortical neurons were affected only if the deprivation came between the 4th and 12th weeks of life. Within this **sensitive or critical period**, the visual system was highly vulnerable to

deprivation. After this time period, susceptibility gradually dropped off. After about 4 months of age, even extended periods of deprivation had no effect on the visual cortex.

If the kittens were visually deprived during the critical period only, but allowed normal binocular visual input after the end of this period, their visual cortex never recovered normal binocularity. On the other hand, it is possible for the visual cortex to recover some binocular function if the formerly good eye (opened eye) is occluded and the formerly sutured eye is opened (**reverse occlusion**). In order to be effective, however, this must be started as early as possible within the critical period.

MONKEY RESEARCH

Subsequent research used monkeys, since they are more similar to humans in the anatomical structure of their visual system than cats. At birth most of the first order neurons in layer IVC of the visual cortex receive input from both eyes, but within the first few weeks, neurons segregate into distinct ocular dominance regions. Then, as with humans, the first order neurons become essentially monocular, while the binocular neurons are found at higher levels in the visual system.

Binocular deprivation

In order to test the influence of binocular deprivation, Regal raised monkeys in total darkness between 2 weeks of age, up to about 3-6 months. This caused deterioration of the visual cortex below the level it previously had at birth. Afterwards the monkeys behaved as if they were blind. In the following weeks they were able to recover some visual function, but they never returned to the normal level.

Monocular deprivation

Von Noorden tested monkeys monocularly deprived during various times in their development, and found that even relatively short periods of monocular occlusion (2-4 weeks at about 4-8 weeks of age) caused severe irreversible amblyopia. Even after years of normal un-occluded vision, those eyes were not able to recover. If reverse occlusion were performed following the critical period, no recovery was possible.

Histological studies show that monocular occlusion at 6 weeks following birth causes the ocular dominance regions corresponding to the non-deprived eye to expand, while the cortical cells in the ocular dominance columns for the closed eye shrink (**Adlers Fig. 24-47**). Recall that segregation into right and left ocular dominance columns occurs during the developmental period. Beyond 6 weeks of age monocular occlusion causes less and less of an effect on the development of ocular dominance regions among the first order neurons in layer IVC, but there is some effect on the ocular dominance of the higher order (binocular) neurons. In the fully mature monkey monocular deprivation has no effect on the neurons in layer IVC or higher levels.

Reverse suturing, if started early enough (for example, at 3 weeks), can cause the right and left ocular dominance columns to return to more equal sizes for neurons in the parvocellular layer (IVC- β) but not for the magnocellular neurons. Recall that the parvocellular tract is important for processing high spatial frequency, or high resolution (good VA) visual information. Reverse suturing at 6 weeks allows a less complete recovery and after 1 year, reverse suture has no effect. Although reverse suturing can help correct maldevelopment of ocular dominance, other aspects of vision were permanently damaged, since the first few weeks of life are so important for the development of monocular functions such as visual acuity or sensitivity to certain orientations.

Instead of reverse suturing, simply leaving both eyes open did not help the formerly deprived eye (actually the visual cortex) to recover from amblyopia.

Quoting from Bishop (Adler's 8th ed. Chapter 24, p. 670):

Simply reopening the deprived eye after a period of monocular deprivation causes no detectible change in the ocular dominance of the cortical cells and, on average, on expansion of the dominance columns in layer IVC for the initially deprived eye. Therefore the recovery seen

after reverse suture depends not just on the restoration of normal activity in the axons from the newly opened eye but also on the establishment of a competitive advantage on the part of the newly opened eye by becoming more active than the eye that has just been closed.

Induced strabismus in monkeys

Surgically induced strabismus in young monkeys caused abnormal development in the visual cortex, though the results were somewhat different depending on whether it was caused by esotropia or exotropia. In esotropia, the deviated eye becomes amblyopic, while in exotropia the monkeys develop alternating fixation and normal monocular visual acuity in both eyes. In those monkeys, visual cortex neurons become unnaturally polarized into right or left dominance, with few binocularly responsive cells. In addition to fewer binocular cells, there were a large number of cells in both esotropia and exotropia that were unresponsive to any stimulus.

Crawford and von Noorden also found that, following esotropia, neurons in the LGN were smaller than usual, especially in the parvocellular layers. The magnocellular layers were affected only after a longer period of esotropia.

After a brief period of esotropia, reverse suturing helped restore the normal ocular dominance balance, but the originally deprived neurons were still abnormal in other ways.

Another way to induce strabismus is to have monkeys wear large amounts of prism. In those studies, the optically induced strabismus also causes a loss in the number of binocular neurons.

Monocular Cycloplegia

Another technique used to study the development of vision in monkeys was extended cycloplegia of one eye using atropine. This was designed to produce anisometropia. As expected, animals raised this way also became amblyopic.

NEUROLOGICAL BASIS FOR DEVELOPMENTAL AMBLYOPIA

Scientists believe that monocular deprivation leads to amblyopia due to changes in the visual cortex. No effect is seen in the retina, and changes in the LGN seem to be secondary to retarded development in the visual cortex. Quoting from Bishop (Adler's 8th ed., p. 672):

Many of the diverse effects of visual deprivation can be linked together by the idea that during the sensitive period the afferent paths from the two eyes compete for control over the cortical cells. Although the actual mechanism of this binocular competition is still unknown, it is proposed that geniculocortical axons arising from adjacent geniculate laminae compete with each other for synaptic sites on binocular cortical neurons. Hubel and his colleagues have further proposed that, in the normal postnatal development of the visual system, competition between the geniculate terminals in areas occupied by sets from both eyes leads to their segregation from one another, the process occurring by a simultaneous retraction of the two sets so that each strip or column comes to be dominated by one eye or the other.

Recall that at birth, layer IVC neurons are still binocular and immature with respect to monocular receptive field features. With development, layer IVC neurons segregate into ocular dominance columns and the first binocular interactions occur at the next level up. Along with the development of binocular vision, neurons must also mature in their ability to process other aspects of spatial vision. The higher order neurons, which will eventually respond to binocular disparity are also immature at this stage.