FIG. 1

MAJOR PROJECTIONS OF THE VISUAL SYSTEM

RETINA  LGN  VISUAL CORTEX

(OCULAR DOMINANCE COLUMNS)

R  L  R  R  L

M: MONOCULAR
B: BINOCULAR

(AXONS FROM LGN)
FIGURE 1. Postnatal development of ocular dominance columns in the cat as shown by transneuronal transport of [H]proline injected into one eye. These are darkfield autoradiographs of the visual cortex at four different ages, ipsilateral to the injected eye. Horizontal sections, midline at the top of each figure, anterior to the left. At 15 days of age the afferents are spread uniformly along layer IV, completely intermingled with the (unlabeled) afferents serving the contralateral eye. At later ages the afferents progressively aggregate into clumps—the anatomical basis for the physiologically defined ocular dominance columns. The gaps are occupied by unlabeled afferents serving the other eye. (From LeVay, S., M. F. Stryker, and C. J. Shatz [1978]. Ocular dominance columns and their development in layer IV of the cat’s visual cortex: a quantitative study. J. Comp. Neurol. 178:223–244. With permission of The Wistar Press.)
MONOCULAR DEPRIVATION LEADS TO A SHIFT IN OCULAR DOMINANCE COLUMNS

A. Movement across the retina
   - Contralateral light eye
   - Ipsilateral dark eye

B. Categories of responses given by single cells
   - Cortical cells

C. Normal area 17
   - Number of cells

C1. Area 17 after monocular closure of contralateral eye
   - Number of cells
   - Layer 4 cells
**FIG. 4**

**MONOCULAR DEPRIVATION LEADS TO MORPHOLOGICAL CHANGES IN LGN AXON TERMINALS**

**Fig. 1.** Coronal view of geniculocortical arbor reconstructed in kittens in which one eye had been occluded for 33 days. The terminal arborization of the deprived (D) eye shows a dramatic reduction in complexity as compared to that of the nondeprived (ND) eye. Cortical layers 3 and 4 are indicated by arrowheads.

**Fig. 2.** Coronal view of geniculocortical arbor reconstructed in kittens in which one eye had been occluded for 6 to 7 days. The borders of cortical layers 3 and 4 are indicated by arrowheads.
Fig. 5. Ocular-dominance histograms for cells in the left visual cortex of two kittens, not litter-mates, deprived by right-eye closure (A) from age 2 months to 3 months; (B) from age 2 months to 6 months. Coding as in Fig. 1. (From Wiesel & Hubel, 1963b.)

Fig. 6. Ocular-dominance histograms for cells in the left visual cortex of cats deprived by (A) right-eye lid suture at 4 months, eye opened at 7 months and recordings made at 15 years of age; (B) right-eye lid suture at 6 months, recording at 10 months; (C) right-eye lid suture in adult, recording 16 months later. Coding as in Fig. 1.
FIG. 6:
A BRIEF PERIOD OF DEPRIVATION CAN LEAD TO A PERMANENT REORGANIZATION OF O.D.C.'S

![Graph showing ocular dominance](image)

FIG. 7: STRABISMUS LEADS TO A LOSS OF BINOCULAR CELLS

![Graph showing ocular dominance distribution](image)
Figure 8: TTX leads to increase in binocular cells

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TTX Blocks Ocular Dominance Column Formation  
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TOTAL CELLS

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Figure 10: Comparison of ocular dominance findings for all cells and for layer IV cells in the 4 TTX animals subjected to retinal blockade beginning about 2 weeks and studied at about 6-8 weeks of age with those in normal animals about 2 weeks of age, about 5-6 weeks of age, and at adulthood. Ordinates plot the percentage of cells classified as strongly binocular (ocular dominance groups 2-5), equal binocular (ocular dominance group 3), and monocular (ocular dominance groups 1 and 7). Abscissas show the different groups of animals. The histogram bars represent the pooled data from each group: data from each individual animal are shown as a horizontal line. Vertical error bars span the range of data from individual animals in each group. Note that both the total sample and for the layer IV cells separately, the percentage of monocular cells increases as a function of age, and the percentage of strongly and weakly binocular cells declines as a function of age. Note also that the TTX group is even less monocular and more binocular than the 2 wk group.

CONTROL

BINDUCULAR TTX INJECTIONS

(LGN AXONS FAIL TO SEGREGATE)
**Fig. 9**

Cortical TTX injections prevent ocular dominance shifts following monocular deprivation.

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**Fig. 2.**

- **a** Histogram of ocular dominance distribution of 127 units recorded in four kittens after TTX treatment. Percent of units (ordinate) classified in each ocular dominance group (abscissa). Number of units in each category is written above appropriate bar. Cortical activity blockade completely prevented the ocular dominance shift that would normally have been seen after 1 week of monocular deprivation. As in normal kittens of this age there is a slight bias in favor of the contralateral eye, which is the deprived eye in the TTX treated kittens.

- **b** Histogram of ocular dominance distribution of 94 units recorded in three control kittens with vehicle solution infusions only. Most units were dominated by the open, ipsilateral eye, an effect which clearly differs from that seen with TTX infusions.
FIG. 10

SILENCING OF POSTSYNAPTIC RESPONSES BY INFUSION
OF A GABA AGONIST LEADS TO AN OCULAR
DOMINANCE SHIFT IN FAVOR OF THE DEPRIVED EYE.
(SELECTION AGAINST ASYNCHRONOUS ACTIVITY)

Fig. 2. Ocular dominance shift toward the closed eye in the cortex after long-term treatment with muscimol. (A) Schematic illustrating experimental procedures. (B) Ocular dominance histograms compiled from single-unit responses recorded in area 17. Results are plotted as if the eyelid suture was always ipsilateral to the hemisphere in which the recording was made. That is, ocular dominance of 1 indicates a cell driven exclusively by the open eye, and ocular dominance of 7 indicates a cell driven exclusively by the closed eye. Cells in category UR showed no visual responses. The upper histogram was compiled from responses recorded (total n = 226; UR, n = 71) within the muscimol-inactivated area of four kittens in which the visual cortex had been injected with muscimol solution for 4 weeks. The lower histogram was compiled from responses (total n = 135; UR, n = 0) in the control hemisphere of the same four kittens.
Fig. 11
INFUSION OF AN NMDA RECEPTOR ANTAGONIST PREVENTS OCULAR DOMINANCE SHIFTS CAUSED BY MONOC. DEPRIVATION

**Graphs:**

A. APV (50 nMol per hour)

- SEL 1
- SEL 2
- SEL 3

B. CONTROL

- SEL 1
- SEL 2
- SEL 3

C. Ocular Dominance

- RO 1
- RO 2
- RO 3

D. Ocular Dominance

- RO 1
- RO 2
- RO 3

**Diagram:**

- Thalamic Axon
- NMDA-R
- Cortical Neuron
- Ca2+
- Na+
- AMPA-R
**Figure 1.** Intracellular correlation of LTP in layer III field potentials following white matter stimulation in the presence of bicuculline methiodide (BMI). A. Drawing of the stimulation-recording configuration. Electrical stimulation (3) was applied to the white matter-layer VI border, and intracellular (EPSP) and extracellular (EP) responses were recorded in layer III. The pipette used for extracellular recording was filled with 1 x NaCl and 10 mM BMI. B. Record of one representative experiment. Theta burst stimulation (TBS) produced a lasting increase in the amplitude of the intracellular (solid circles) and the extracellular (open circles) responses to test stimulation. C. Intra- and extracellular traces collected before (1) and after (2) TBS on the experiment illustrated in A. D. Average of 16 experiments performed identically to that illustrated in B. In all cases, LTP of the EPSP correlates with LTP of the EPSP.

**Figure 3.** Effect of dark-rearing on LTP in V1 VIS. CTX.

**Figure 3.** Effect of dark-rearing on LTP evoked from the white matter in adult rat visual cortex. A. Time-response in visual cortical slices from 4- to 6-week-old dark-reared and control rats. B. Time-response in a normal lighted environment, V1 VIS. CTX. In this series, the experiments were performed in the same animal until all analyses had been performed. Data are expressed as in Fig. 1a-c; the difference between groups at 20 min post-TBS is significant at P < 0.02 (Mann-Whitney U test). C. The same as A, except that all experiments were performed in the lighted environment, V1 VIS. CTX. D. Cumulative histogram using all slices from dark-reared and control rats. These distributions are significantly different at P < 0.02 (Kolmogorov-Smirnov test).

**METHODS.** Pregnant strains rats were purchased from Charles River laboratories, and were housed in a lighted environment (12-h light/dark cycle). To provide care for animals in the dark, or to remove them for experiments, they were illuminated with white light and reared using infrared vision equipment. In the "blind" series of experiments, one dark-reared and one control rat was used each day, studied simultaneously on two slices. For each slice, LTP was first attempted with multiple layer stimulations, which were repeated at different locations on the same slices. If no plasticity was observed, the slice was not studied further. We used this criterion to ensure that only high-quality slices were used in the "blind" studies. The only criterion used for the nonblind study, however, was a stable baseline. To construct cumulative histograms, the percentage change in the response 20 min after TBS was calculated for each slice, and these values were rank-ordered to show the fraction of cases showing changes of various magnitudes.
Fig. 14
THE KINETICS OF NMDA-R CHANNELS CHANGE DURING DEVELOPMENT

Fig. 1. Kinetic changes of NMDA-EPSCs from layer IV neurons. (A and B) Five superimposed EPSCs (top left) followed by the average of 20 consecutive events (bottom right) obtained from a stellate cell of (A) a 12- and (B) a 35-day-old rat. In (A), the single exponential curve of the decay is superimposed on the average current (bottom right). In (B), the poor single exponential fitting is followed by the superimposed double exponential curve with fast and slow components also shown (bottom right). Spontaneous NMDA-EPSCs at -50 mV holding potential are also shown in the top left panels of (A) and (B). Bottom traces (left) are the average of 30 events with the superimposed single exponential curve. The average decay of miniature NMDA-EPSCs from six neurons of 12-day-old rats is 221 ± 84 ms (n = 145) and from six neurons of 35-day-old rats is 45.9 ± 17 ms (n = 182). The amplitudes (range, 5 to 45 pA) and rise times (range, 4.8 to 10.5 ms) did not significantly differ with age; f, fast component; s, slow component. (C) Developmental decrease of the slow component contribution to NMDA-EPSC at -50 and +50 mV (inset) holding potentials. Lines connect the averages (diamonds) of the experimental points (circles). One-way analysis of variance (ANOVA) with subsequent comparison by the Duncan multiple range test showed that the slow component contributions to EPSCs from rats at different ages were statistically different (P < 0.05) between 12- to 14-day-old rats and rats older than 16 days. The label "adult" refers to two 4-month-old rats. (D) Time constants of the fast and slow exponential decays at -50 mV holding potential. Filled circles represent the \( \tau_f \) and empty circles the \( \tau_s \). The only statistically significant difference was for the \( \tau_s \) of 9-day-old rats (P < 0.05, ANOVA followed by the Duncan test).
Fig. 15. Developmental changes in NMDA receptor-mediated postsynaptic responses.

Fig. 2. Kinetic changes of NMDA channel currents activated by 4 ms application of L-glutamate in (A) a 12-day-old rat and (B) a 35-day-old rat. Two consecutive responses (top) and the average current (bottom) of 20 consecutive L-glutamate applications shown with a superimposed double exponential curve with fast and slow components are shown independently. The open-tip current used to measure the duration of the drug application pulse is shown above each of the two channel current traces. The amplitude calibration bar does not apply to these traces. The single channel current amplitude did not differ at the two ages considered [-50 mV holding potential, 2.7 ± 0.51 pA at 12 to 14 days after birth (n = 9) and 2.7 ± 0.45 pA at 30 to 35 days after birth (n = 15)]. (C) Developmental decrease of the slow kinetic component to NMDA-EPSC (same data as in Fig. 1) and average NMDA channel currents. Differences between young (12 to 14 days) and old (30 to 35 days) rats were statistically significant (P < 0.05, ANOVA followed by the Duncan test). (D) Time constants of the fast and slow exponential decays of average NMDA channel currents.
FIG. 16
DARK-REARING PROLONGS THE CRITICAL PERIOD
AND DELAYS CHANGES IN NMDA RESPONSES

Fig. 3. Effects of dark-rearing and TTX intracerebral treatment on the developmental change of NMDA-EPSCs. (A) Five overlapping EPSCs from 25-day-old rats reared in the three different conditions (left) followed by the ensemble average of 20 consecutive events with superimposed double exponential curve (middle) and double exponential fittings (right). (B) Developmental decrease of the slow component of NMDA-EPSC in control and dark-reared rats. Statistical analysis of control versus dark-reared animals at different ages showed significant differences in rats older than postnatal day 22 ($P < 0.05$, two-way ANOVA followed by the Duncan test). (C) The time courses of the fast and slow exponential decays of the EPSCs in dark-reared rats.

DEVELOPMENTAL SWITCH IN NMDA-
COMPOSITION

NR1/NR2B $\rightarrow$ NR1/NR2A $\rightarrow$ Ca$^{2+}$
THE NEUROTROPHIN BDNF MAY MEDIATE Activity-Dependent Plasticity in the Cortex

1. Activity regulates BDNF expression

![Fig. 17](image)

**Fig. 17.** The neurotrophin BDNF may mediate activity-dependent plasticity in the cortex.

2. BDNF potentiates synaptic responses

3. BDNF infusion prevents ocular dominance segregation

**Figure 2.** Potentiation of field responses by BDNF. A. Examples of field responses of layer 4/5 to test stimulation of layer 4/5, recorded at the time points indicated by corresponding letters in B. Arrows indicate the postsynaptic component of responses. Initial upward (negative) peaks are potentials evoked monosynaptically by layer 4/5 stimulation. B, C. Plots of the amplitude and rising slope of the postsynaptic component of field potentials against time, respectively. BDNF at 200 ng/ml was applied to the slice during the period indicated by horizontal bar. In B, the amplitude of the postsynaptic component from the preceding positive (downward) to negative peak was measured and expressed as the percentage of the mean of 60 responses before the application of BDNF. In C, the slope of the rising phase (from 10 to 90% point) of the postsynaptic component was measured and expressed in the same way as in B.
A possible mechanism by which neurotrophins mediate activity-dependent plasticity in the visual system. In this model, the production of neurotrophins by the post-synaptic cell is regulated by trans-synaptic activity, and the response of a thalamic axon to the target-derived trophic factors is proportional to its level of activity.