

Lecture 39 – Early Experience and the Fine Tuning of Synaptic Connections -- Mason

Themes:

There is a connection between neural development and learning – K. Lorenz' work on "imprinting"
The immature brain is highly plastic, with developing circuits molded by patterns of electrical activity.

I. Effects of social deprivation

A. Neglected or abandoned young children often have difficulty learning to speak.

B. Observations of Spitz

1. young children raised in two different institutions, one with open cribs, a lively environment and extensive interaction with the mother, the other where cribs were shielded, there was no intimate interaction with the mother or other caregiver, and little opportunity for other social interaction

2. by first birthday, children in latter institution showed susceptibility to disease; they were not walking or talking properly at 2-3 years old

C. Experiments of the Harlows

1. infant monkeys raised in isolated cages subsequently showed severely abnormal behavior: no social interactions, "autistic" rocking, self-mutilation, lack of sexual curiosity, no maternal behavior

2. most severe components of this syndrome not seen when surrogate inanimate mother available

3. other components eliminated by contact with normal peer

4. isolation devastating for infant, but not older child or adult, so there is "critical period" during which developing system is particularly susceptible to environmental deprivation

II. Experience and the Visual System

A. Pattern recognition

Children or chimps receiving only diffuse light input during early childhood subsequently have difficulty in pattern recognition.

B. Ocular dominance

1. Some neurons above and below the input layer 4C in the primary visual cortex (V1) respond to input only from one eye, but the majority are binocular, which contributes to depth perception.

2. Hubel and Wiesel found that suturing one eye closed for as little as a week during first few months postnatally (critical period) almost completely eliminated the responsiveness of V1 cells to visual input through the eye that had been closed, resulting in lasting blindness in that eye.

3. Neurons in layer 4C receive input directly from the lateral geniculate nucleus (LGN) and are monocular. They are organized in ocular dominance columns that alternate across V1. Closing one eye during the critical period causes the columns representing the open eye to expand to encompass neighboring territory formerly representing the closed eye. This results from increased branching of LGN axons representing the open eye and shrinkage of the arbors of LGN axons representing the eye that had been closed.

4. Closing both eyes does not affect ocular dominance, so the balance of inputs is the crucial factor.

5. Ocular dominance columns are influenced by visual input during the critical period.

6. Monocular segregation by layer in the LGN develops *in utero* and is dependent on spontaneous electrical activity.

7. Possible mechanism for winner-take-all synapse elimination (Fig. 56-12):

-Synchronous firing by multiple axons representing one eye causes sufficient postsynaptic depolarization to open NMDA receptor channels.

-This causes release of neurotrophic factor from the postsynaptic cell and the factor can only efficiently be taken up by nerve endings that have just released transmitter and thus have high levels of endocytosis.

-The neurotrophic factor promotes growth, while the branches from the other eye wither.

This mechanism, which resembles LTP, explains how an initial relatively small bias towards one eye can be progressively reinforced until there is complete dominance.

III. Topics/Controversies in Recent Research (*not in the text book; discussion as time permits*)

A. Are cortical ocular dominance columns set up prenatally in the absence of neural activity?

Does neural activity play a role in the formation of ocular dominance columns from the initial steps, or are the columns set up by other mechanisms (innate molecules that guide and match fibers to terminate in specific columns), with activity "finishing off" the final details of connectivity?

(*JC Crowley and LC Katz, 2002, Ocular dominance development revisited, Curr Op Neurobiol 12: 104-109*)

B. Dendritic Spines (sites of excitatory synaptic input on large neurons) are highly motile:

These structures are dynamic, changing shape and, possibly, synaptic contacts.

Increased dynamism in enriched environments; perturbed in deprived contexts.

Does morphological plasticity continue? At reduced levels?

(*T Bonhoeffer and R Yuste, 2002, Spine motility: Phenomenology, mechanisms, and function. Neuron 35, 1019-1027;*

JT Trachtenberg et al. 2002 Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. Nature 420, 788-794.

C. Experience and changes in connections later in life?

1. Reactivation of plasticity in the adult by degradation of the extracellular matrix

(*Pizzorusso et al. 2002 Reactivation of ocular dominance plasticity in the adult visual cortex Science 298 1248-1251*).

2. Changes in steroid hormone levels induce dendritic alterations, and loss of synapses

(*JR Gray and J C Weeks, 2003 Steroid-induced dendritic regression reduces anatomical contacts between neurons during synaptic weakening and the developmental loss of a behavior. J. Neurosci. 23: 1406-1415*).

3. Barn owls and auditory localization: instructed learning and innate connections;

learning in adult is affected by appropriate juvenile experience.

(*EI Knudsen, 2002 Instructed learning in the auditory localization pathway of the barn owl, Nature 417: 322-328*)

Relevant reading: chapter 56 in "Principles"