KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

Module:
Biological Foundations of Mental Health

Week 4:
Biological basis of learning, memory and cognition

Dr Sam Cooke

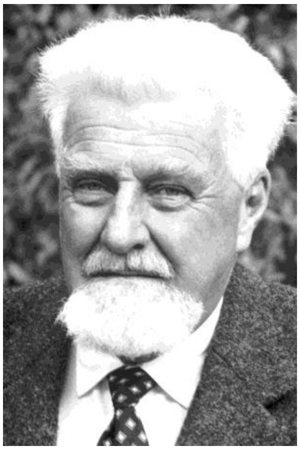
Topic 3:
The effects of activity, experience and deprivation on the nervous system
Part 4 of 5

Part 4

Part 4

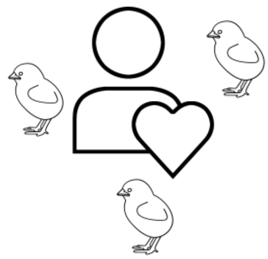
Critical periods: how does inhibition serve as a permissive factor for Hebbian plasticity?

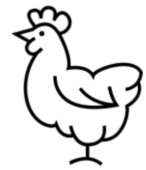
The critical period



Conrad Lorenz

Imprinting



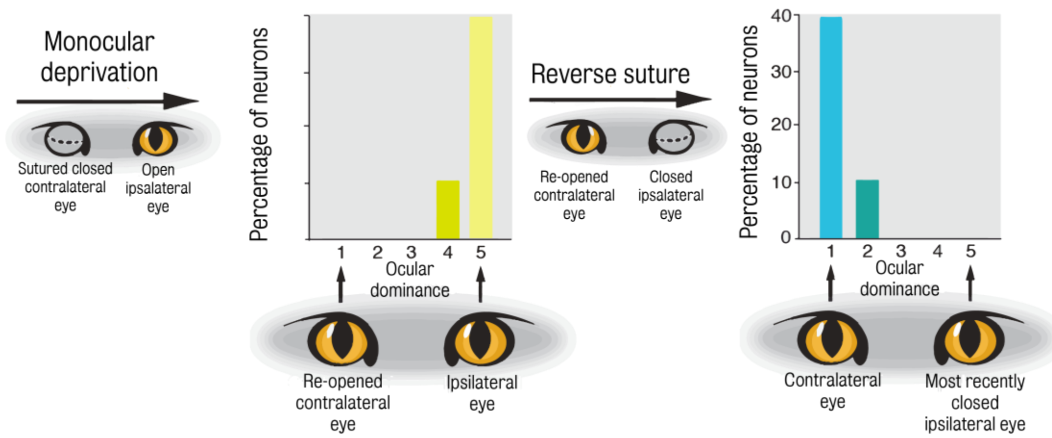


Persistent attachment formed if carer role was taken on by a human throughout a defined period of early post-natal development.

The critical period is a relatively brief time window during which defining plasticity is permitted

Ocular dominance shift in kittens

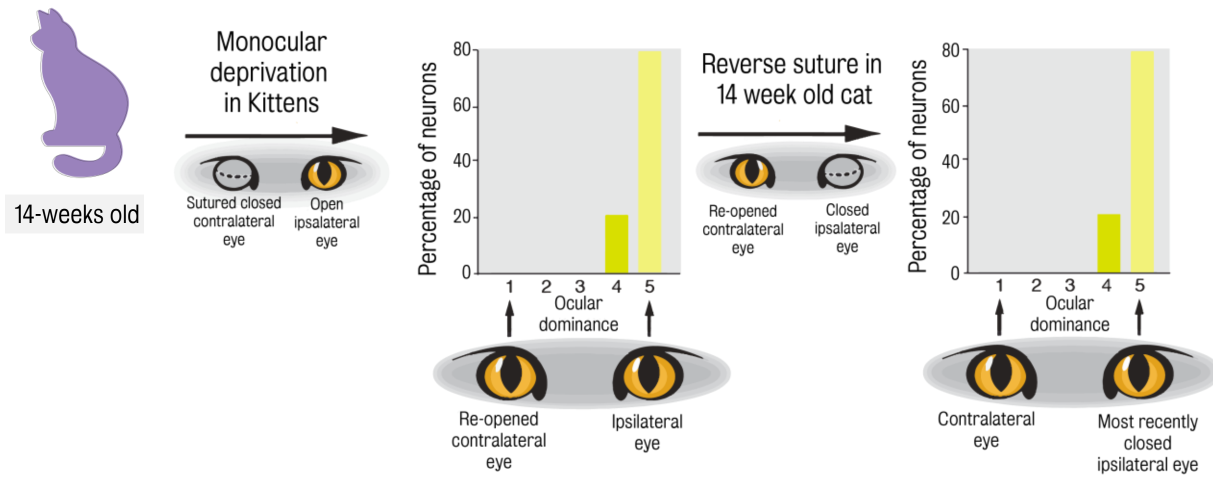
Five-weeks old



The ocular dominance shift **is reversible in kittens** through reversing the eye sutured.

Blakemore & Van Sluyters, 1973

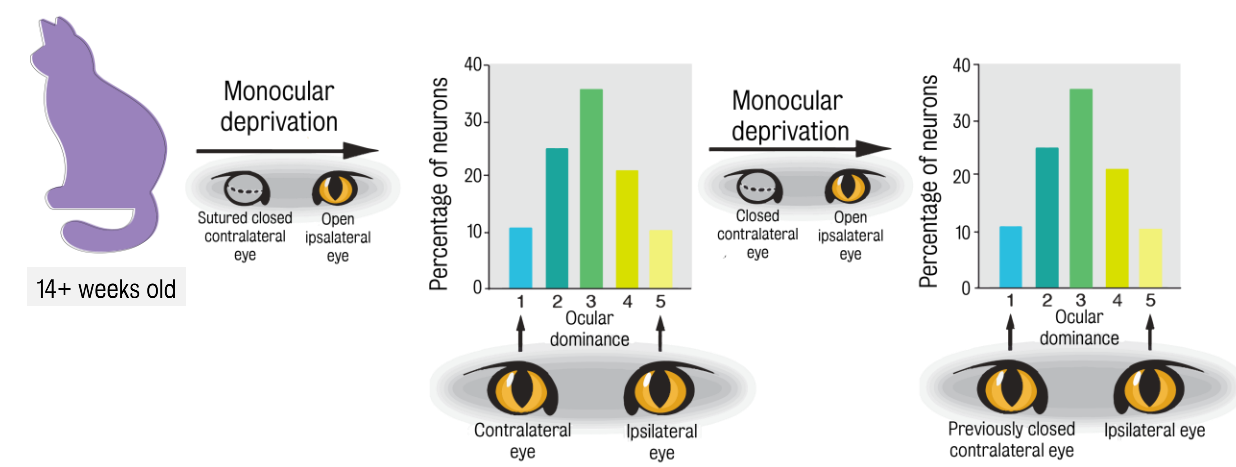
Lack of ocular dominance shift in adult cats



The ocular dominance shift occurring in kittens **is not reversible in cats** using reverse lid suturing.

Blakemore & Van Sluyters, 1974

Ocular dominance plasticity does not occur in adult cats

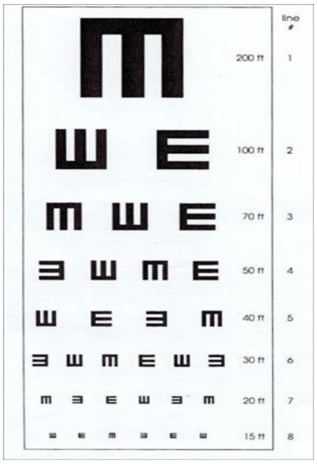


The capacity of the cortex for plasticity is lost after the critical period.

Hubel & Wiesel, 1969; Blakemore & Van Sluyters, 1974

Visual acuity

Does the permanent shift that compromises neural response to a visual stimulus in layer 2/3 also impair vision?



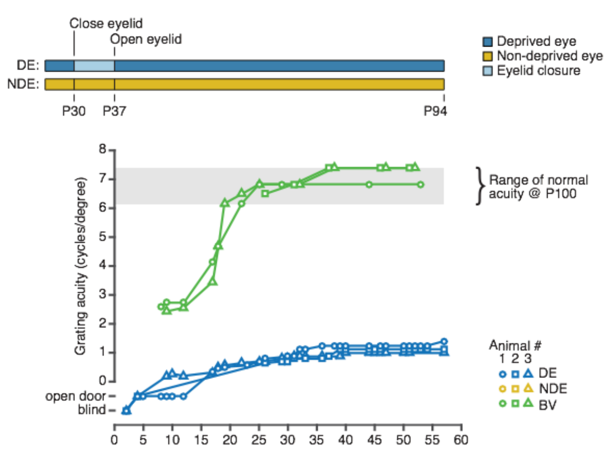
Snellen Chart

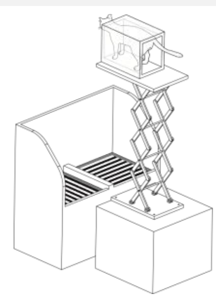
In humans, we test vision with a Snellen chart:

- stationary target and performer
- varying spatial frequency – resolving lines that are different distances apart
- determining visual acuity – reaching the threshold at which the letters M, W, E and the number 3 cannot be differentiated
- 20/20 vision – subject's vision at 20 feet matches normal vision at 20 feet

Restoration of binocular vision

Deficits occurring in kittens persist even when binocular vision is fully restored in adulthood.



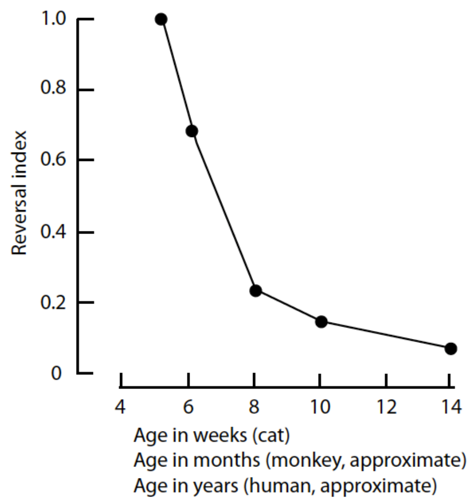


No functional recovery can occur if the visual experience does not return to normal prior to closure of the critical period.

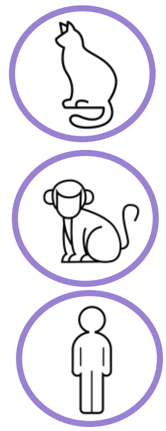
Duffy & Mitchell, 2013

Opportunity for recovery from MD

The visual cortical critical period varies in time and longevity between species.



Closure of the critical period for vision:



Eight to nine weeks

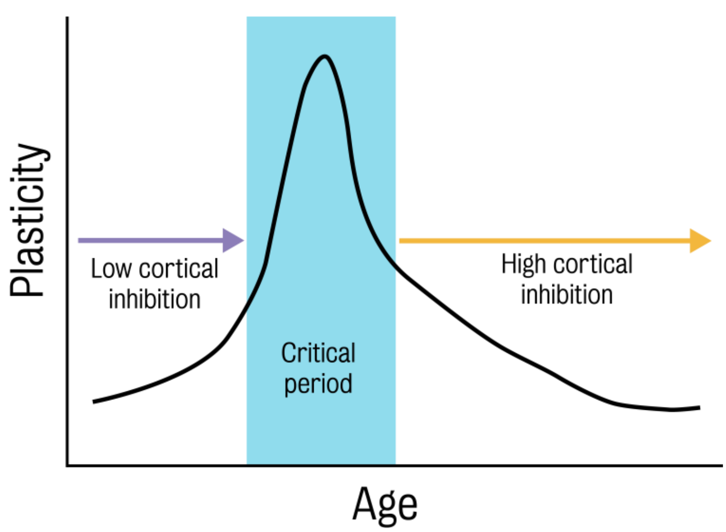
Eight to nine months

Eight to nine years

Hubel & Wiesel, 1969; Blakemore & Van Sluyters, 1973

The level of cortical inhibition determines the onset and offset of the critical period

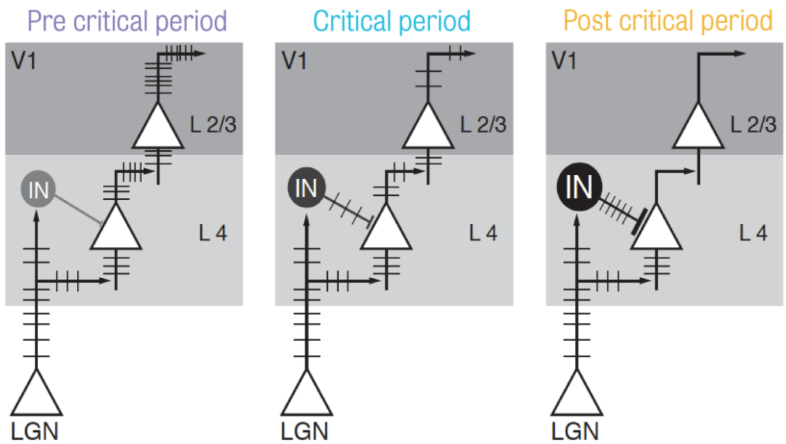
Cortical inhibition is a central factor in the onset and offset of the critical period.



Inhibition develops late in the cortex relative to excitatory circuits.

The critical period represents **a sweet-spot** between too little and too much inhibition.

How can inhibition be a key determinant in whether or not Hebbian plasticity occurs?

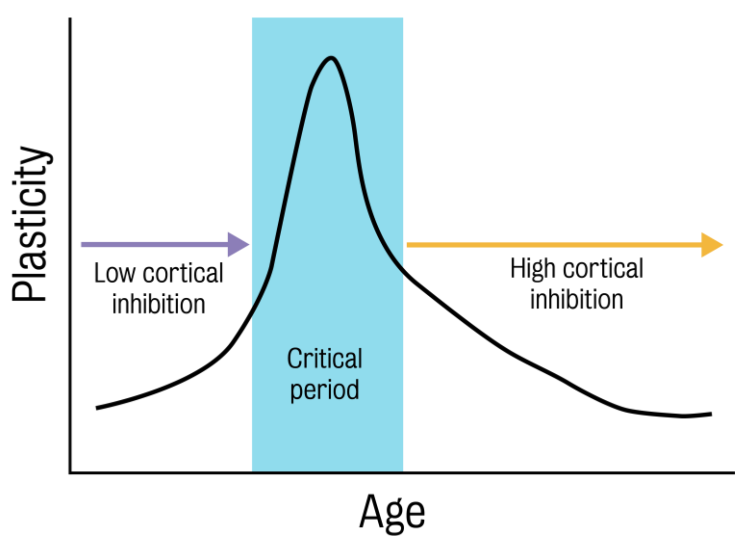


Hebbian plasticity cannot operate to integrate signals due to noise when there is too little inhibition.

After maturation of inhibition during the critical period, only the strongest visual inputs can drive enough cortical activation to initiate plasticity.

GABAergic inhibition is required to open the critical period and increased inhibition closes it.

The capacity for change still exists in cortical circuits if inhibition can be modified



(Fagiolini et al. 2004)

Increased inhibition in very young mice using Valium precociously opens the critical period.

(Fagiolini & Hensch, 2000)

Genetic reduction of inhibition (Gad65 knockout) allows juvenile ocular dominance plasticity in the adult animal.

(Davis et al., 2015)

Grafting immature inhibitory neuron precursors into visual cortex of adult mice recovers juvenile ocular dominance plasticity.

Summary

- critical periods define the time window during which the effects of sensory experience or deprivation on the nervous system are most pronounced, usually occurring quite early in post-natal development.
- critical periods vary for brain regions and sensory modalities, eg a critical period for plasticity in somatosensory cortex opens and closes earlier than for the visual cortex. Higher order regions of cortex, such as prefrontal cortex, have even later critical periods.
- critical periods vary from species to species, eg the critical period for ocular dominance plasticity closes much earlier for mice than cats, and earlier for cats than primates.
- several lines of evidence indicate that inhibitory neurons play a key role in critical period duration, with development of inhibition opening the critical period and maturation of cortical inhibition closing it. Increasing inhibition can prematurely open the critical period and reducing inhibition can re-open the critical period after it has closed.
- Inhibition is believed to serve as a permissive factor for Hebbian plasticity by reducing overall activity at the opening of the critical period, thereby reducing 'noise' and allowing differentiation of correlated and uncorrelated activity. However, too much inhibition can prevent sufficient post-synaptic activity to allow Hebbian plasticity to occur, thereby closing the critical period.

References

[1] Blakemore C. and Van Sluyters C. (1973) Experimental creation of unusual neuronal properties in visual cortex of kitten. Nature. 246(5434):506-8

[2] Davis M. et al. (2015) Inhibitory Neuron Transplantation into Adult Visual Cortex Creates a New Critical Period that Rescues Impaired Vision. Neuron. 86(4):1055-1066.

[3] Duffy K. and Mitchell D. (2013) Darkness alters maturation of visual cortex and promotes fast recovery from monocular deprivation. Curr Biol. 23(5):382-6.

[4] Fagiolini M. and Hensch T. (2000) Inhibitory threshold for critical-period activation in primary visual cortex. Nature. 404(6774):183-6.

[5] Fagiolini M. et al. (2004) Specific GABAA circuits for visual cortical plasticity. Science. 303(5664):1681-3.

[6] Hubel D. and Wiesel T. (1969) Anatomical demonstration of columns in the monkey striate cortex. Nature. 221(5182):747-50.

[7] Kirkwood A. and Bear M. (1994) Hebbian synapses in visual cortex. J Neurosci. 14(3 Pt 2):1634-45.

End of part 4