Functional Studies of Visual System Development in Mice

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Before fully-assembled

**Neural Circuits vs. Electronic Circuits**

Connections in developing neural circuits can be shaped in an *experience-dependent* manner.
Experience-Dependent Neural Development and Critical Periods

A Critical Period for Language Development
A critical period is defined as the time during which a given behavior is especially susceptible to, and indeed requires, specific environmental influences to develop normally.

Once this period ends, the behavior is largely unaffected by subsequent experience (or even by the complete absence of the relevant experience).

Conversely, failure to be exposed to appropriate stimuli during the critical period is difficult or impossible to remedy subsequently.
Critical Period in Visual System

(A) Normal adult

(B) Monocular deprivation in kitten

(C) Monocular deprivation in adult

Ocular dominance group

Period of deprivation (months)

0 38

Birth 2.5 38

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Hubel & Wiesel, 1960s
Amblyopia ("lazy eye“): loss of one eye's ability to see details.

Strabismus ("cross-eyed"): the eyes are misaligned and point in different directions.
Ocular Dominance Plasticity and Critical Period

- First discovered by Hubel and Wiesel (1963).
- A widely-studied model system for cortical developmental plasticity.
- Helped the understanding and treatment of human amplyopia.
Ocular Dominance Plasticity and Critical Period

• However, what purpose does this period of heightened plasticity serve during normal development?

• Cortical OD does not change during the critical period.

• OD plasticity is only induced by an imbalance of inputs.
Orientation Selectivity in Visual Cortex
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Wang et al. (2010) Neuron, 65:246-256
Critical Period Plasticity Matches Binocular Orientation Preference in the Visual Cortex

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A Sequence in Binocular Matching

WT

Eyes Open

P14 P20 P26 P32

Plasticity

Simple Complex

BDNF-O/E

Eyes Open

P14 P20 P26 P32

Plasticity

X

?
A Sequence in Binocular Matching

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Advancing visual system development to rescue?
Mouse Visual System Development in Enriched Environment

- Larger cage
- More mice per cage
- Toys
- Rearranged every 1-2 days
- Placed in EE 3-4 days before birth
- 1-2 litters of pups at a time
WHY is Experience-Dependent Neural Development Needed?

Critical Period Plasticity wires up neural circuits for information association/integration, where sensory/motor/social experience provides the common input?

- Binocular matching, but not monocular tuning maturation, requires visual experience.
- Multisensory integration: e.g., matching visual and auditory spaces in sound localization.
- Language development: sensorimotor learning.
- Cognitive and social development: learning and association.
A “Critical Period” Cause for Human Neurodevelopmental Disorders?

Rett syndrome:
• affects ~1/10,000 girls during early childhood.
• normal ~6-18 month development followed by stagnation and rapid regression.
• severe autistic features: abnormal socialization, communication difficulties, sensory integration dysfunctions.
• caused by mutations in x-linked MECP2, which encodes methyl-CpG-binding protein-2, a critical regulator of gene expression that binds methylated DNA.

• MeCP2−/− mice recapitulate many aspects of behavior deficits and their developmental progression (Chen et al 2001; Guy et al 2001)

• **Deficit in critical period plasticity?**
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