

The Brain, Biology and Cognition

Neurodevelopment

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Axon Growth and Synapse Formation



- **We begin as a zygote (single cell)**
 - This cell divides, then those divisions divide, etc.
- **Some cells turn to muscle, some to neurons, etc.**
- **All cells make go to appropriate sites and align to form a structure.**
- **Cells then establish relations with other cells.**
- **Five phases of neurodevelopment:**
 1. Induction of neural plate,
 2. Neural proliferation,
 3. Migration and aggregation,
 4. Axon growth and synapse formation,
 5. Neuron death and synapse rearrangement.

Axon Growth and Synapse Formation



- Once cells are aligned, axons and dendrites grow from them.
- They grow toward specific targets relevant to what they need to do through a growth cone:
 - A fingerlike cytoplasmic extensions that extend and retracts to find the correct route.
- Work of Sperry (1940s) on optic nerves of frogs led to:
 - Chemoaffinity hypothesis:
 - Each postsynaptic surface releases specific chemical that attracts a growing neuron

Axon Growth and Synapse Formation



- But fails to explain why axons follow same circuitous route to reach target in every member of a species rather than growing directly to it.
- Instead, growth cones influenced by other chemicals along the way or signals from adjacent cones.
- 1st growth cones to travel along a route are pioneer growth cones.
 - Follow correct route by interacting with guidance molecules.
- Then other growth cones follow the route.

Synapse Formation



- **Once axons reach relevant site, they must establish pattern of appropriate synapses.**
- **Formation of new synapses (synaptogenesis) requires glial cells:**
 - **High degree of cholesterol supplied by astrocytes.**
 - **Process, transfer, and store info supplied by neurons.**



Neuron Death and Synapse Rearrangement



- **Synapses that do not function appropriately are eliminated, which is fine because.....**
 - ~50% more neurons than are needed are produced.
- **Cell death can be:**
 - **Passive (necrosis)**
 - **Active (apoptosis – genetic programming inside neuron triggers it to die)**
- **Apoptosis is safer than necrosis**
 - **Because it does not promote inflammation**

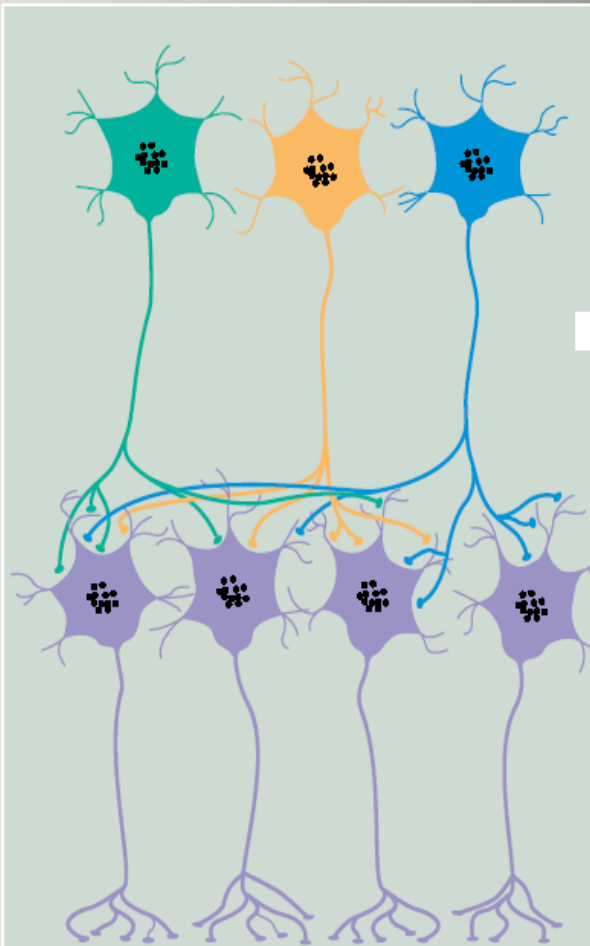


- **Some neurons die due to fulfilling their function**
- **Some die due to failure to compete for chemicals provided by targets:**
 - **More targets = fewer cell deaths**
 - **Destroying some cells increases survival of others**
 - **Increasing innervating axons = decrease in proportion that survives**
- **One type of chemical is Neurotrophins**
 - **promote growth and survival of neurons, guide axons, stimulate synaptogenesis.**
 - **It has a Nerve growth factor (NGF)**

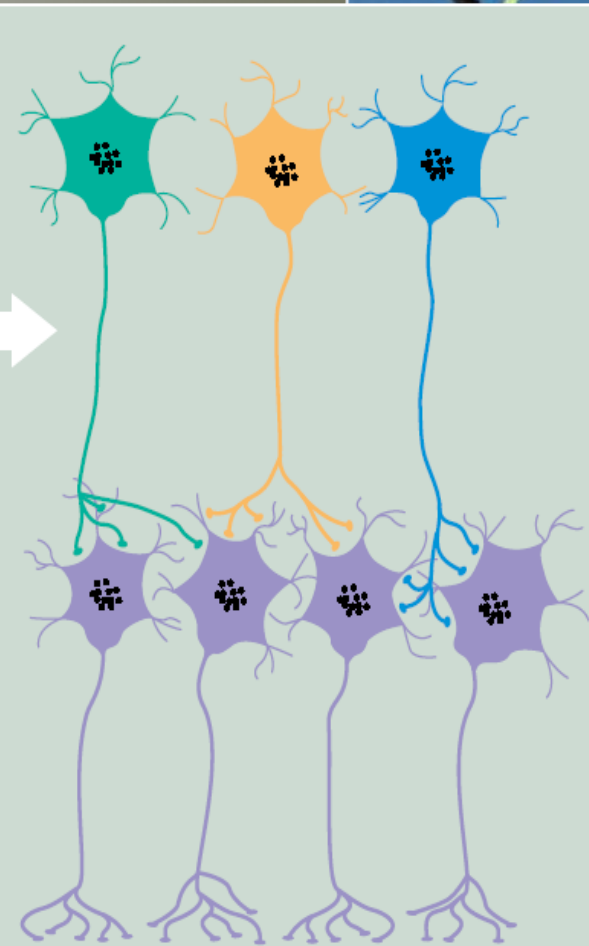
Life-Preserving Chemicals



- **Neurons failing to establish correct connections are likely to die.**
- **Space left after apoptosis is filled by sprouting axon terminals of surviving neurons**
- **Ultimately leads to increased selectivity of transmission**



A diffuse pattern of synaptic contact is characteristic of early stages of development.



A more focused pattern of synaptic contact is present after synapse rearrangement.



Human brain develops slower than other species.

Postnatal growth is consequence of:

- Synaptogenesis
- Myelination: sensory then motor areas.
 - Continues to adolescence for prefrontal cortex
- Increased dendritic branches
- Overproduction of synapses may underlie greater plasticity of young brain





Prefrontal Cortex Development

- **Longest period of development.**
- **Underlies age-related changes in cognitive function.**
- **No single explanation for function of this area.**
- **Role in:**
 - **Working memory,**
 - **Planning and carrying out sequences of actions,**
 - **Inhibiting inappropriate responses,**
 - **Rules for social behavior.**

Effects of Experience on the Early Development, Maintenance, and Reorganisation of Neural Circuits



- **Neurodevelopment occurs through interactions between neurons & environment:**
 - **Environment = all structures/events inside and outside the organism that can affect the neuron.**
- **Permissive experiences: necessary for information in genetic programs to be manifested**
- **Instructive experiences: contribute to the direction of development**
- **Effects of experience on development are time-dependent:**
 - **Critical period: Must happen within certain time**
 - **Sensitive period: Can affect outside certain time**

Early Studies of Experience & Neurodevelopment



- **Early visual deprivation**
 - Rats brought up in darkness had fewer synapses and dendrites in primary visual cortex than normally reared rats, and as adults had poor depth and pattern vision.
- **Enriched environment**
 - Rats brought up in complex group cages had:
 - Thicker cortexes
 - Greater dendritic development
 - More synapses per neuron



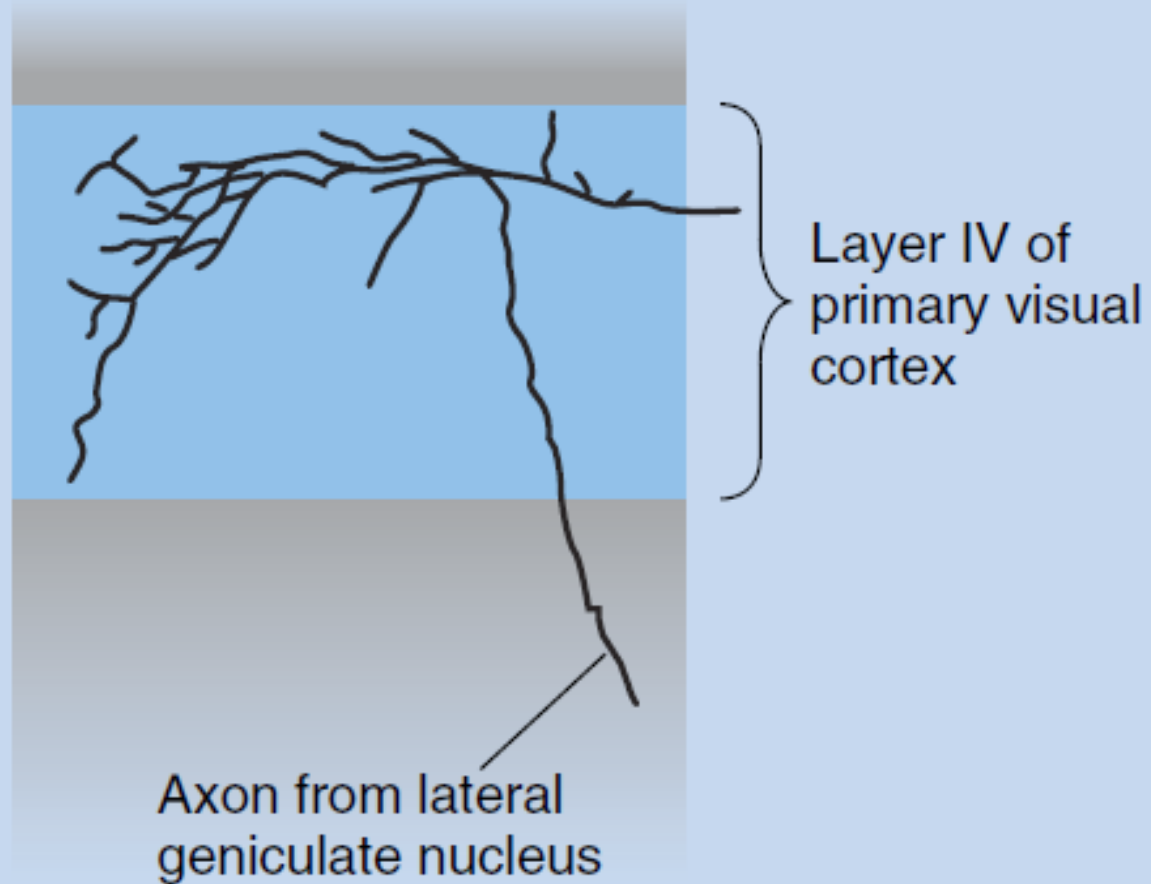
Competitive Nature of Experience and Neurodevelopment



Nondeprived eye



Deprived eye



The effect of a few days of early monocular deprivation on the structure of axons projecting from the lateral geniculate nucleus into layer IV of the primary visual cortex. Axons carrying information from the deprived eye displayed substantially less branching. (Adapted from Antonini & Stryker, 1993.)

Experience Fine-Tunes Neurodevelopment



- So, should we experience everything as soon as possible?
 - Not necessarily (or possible).
- Research into neurodevelopment involves taking away from what would normally be part of our lives.
- Also, neurons spontaneously fire and interact with environment before nervous system finishes developing.
- These patterns of neural activity fine-tune neural development.
- Experience also influences gene expression.



Neuroplasticity in Adults



- Changing or adaptation of neurons
- Neurogenesis seen in olfactory bulbs & hippocampus of adult mammals
- Adult neurogenesis seen in adult rats living in enriched environments (toys, wheels, other rats).
 - Produced 60% more new hippocampal neurons than adult rats living in non enriched environments.
- Enriched environments and exercise can promote neurogenesis

Effects of Experience on Reorganization of Adult Cortex



- **Tinnitus** (ringing in ears) – produces major reorganization of primary auditory cortex
- Adult musicians who play instruments with left hand have enlarged representation of hand in right somatosensory cortex
- Skill training leads to reorganization of motor cortex



Neurodevelopment: Autism



- **Core symptoms:**
 - Differences in ability to interpret emotions
 - Differences in capacity for social interaction
 - Occupation with single subject or activity
- **Heterogenous disorder** – differences vary
- Considered a spectrum disorder (ASD)



Neurodevelopment: Autism



- Exceptional abilities – e.g., rote memory, jigsaw puzzles, musical ability, artistic ability
- **Autistic Savants** – poor intellectual abilities but display specific cognitive or artistic abilities.
 - ~1/10 autistic individuals display savant abilities
 - Perhaps consequence of compensatory functional improvement in one area following differences in development to another

Neural Mechanisms of Autism



Understanding of brain structures involved in autism is still limited, but so far implicated are:

- Cerebellum
- Amygdala
- Frontal cortex



Neural Mechanisms of Autism



Two lines of research on cortical involvement in autism:

- Difference in response to faces in some autistic population
 - Spend less time than non-autistic individuals looking at faces, especially eyes
 - Low fMRI activity in fusiform face area
- Possibly deficient in mirror neuron function



Neurodevelopment: Williams Syndrome

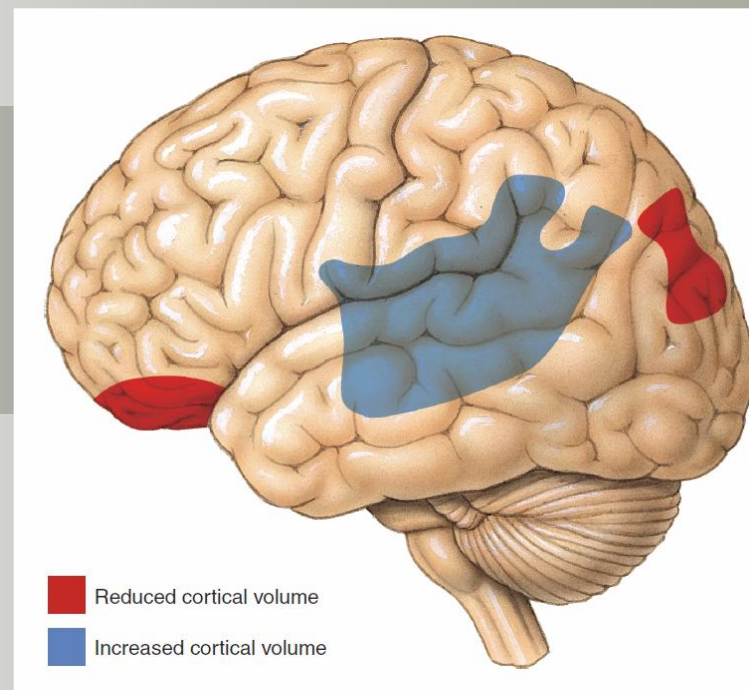


- Uneven pattern of abilities and disabilities
- Sociable, empathetic, talkative – exhibit language skills, music skills, and enhanced facial recognition
- Profound impairments in spatial cognition
- Usually have heart disorders associated with mutation in a gene on chromosome 7 – absent in 95%

Neurodevelopment: Williams Syndrome



- **General thinning of cortex at juncture of occipital and parietal lobes, and orbitofrontal cortex.**
- **Lack of development here may be related to impairment of spatial cognition and hyper sociability**
- **Thickness of cortex in superior temporal gyrus is normal and linked to high levels of language and music processing.**
- **Characteristic appearance: short, small upturned noses, oval ears, broad mouths**



Two areas of reduced cortical volume and one area of increased cortical volume observed in people with Williams syndrome.