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Descending Motor Paths
• Multiple paths project from primary motor cortex to motor neurons of the spinal cord
• Act together to control voluntary movement

Sensorimotor Spinal Circuits
• Motor units are the smallest unit of motor activity
– A single motor neuron and all of the muscle fibers that it innervates
– All fibers contract together when neuron fires
– Acetylcholine is the neurotransmitter released at the neuromuscular junction
• Motor pool
– All of the motor neurons that innervate the fibers of a given muscle

Muscles
• Muscles can only contract to generate force
• Two types of fibres
– Fast twitch (white meat)
– Slow twitch (dark meat)
– Both present in a muscle, but vary in proportion
• Flexors and extensors act in antagonistic pairs
• Isometric and dynamic contraction
• Movement and action require coordinated movement
• Depends on multiple sources of feedback from the musculature and sensorimotor control

Receptor Organs of Tendons and Muscles
• Golgi tendon organs
– Embedded in tendons
– Tendons connect muscle to bone
– Detect muscle tension
• Muscle spindles
– Embedded in muscle tissue
– Detect changes in muscle length

Muscle Spindle Feedback Circuit
• Intrafusal muscle within each muscle spindle innervated by its own intrafusal motor neuron
– Keeps tension on the middle, stretch-sensitive portion of the muscle spindle to keep it responsive to changes in the length of the extrafusal muscle

Reflexes
• **Stretch Reflex:** monosynaptic, serves to maintain limb stability
– e.g. Patellar tendon reflex is monosynaptic
• **Withdrawal Reflex** is NOT monosynaptic
• **Reciprocal Innervation** – antagonistic muscles interact so that movements are smooth – flexors are excited while extensors are inhibited

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• **Recurrent Collateral Inhibition** – feedback loop through Renshaw cells that gives muscle fiber a rest after every contraction

Walking
• Requires a complex program of reflexes
• Integrates visual, somatosensory, and balance information
• Produces integrated series of limb movements and posture changes
• Despite complexity, can be coordinated by spinal cord in many species

Central Sensorimotor Programs
• Perhaps all but the highest levels of the sensorimotor system have patterns of activity programmed into them, and complex movements are produced by activating these programs
• Cerebellum and basal ganglia then serve to coordinate the various programs

Central Sensorimotor Programs Are Capable of Motor Equivalence
• A given movement can be accomplished various ways, using different muscles
• Central sensorimotor programs must be stored at a level higher than the muscle (as different muscles can do the same task)
• Sensorimotor programs may be stored in secondary motor cortex

Sensory Information That Controls Central Sensorimotor Programs Is Not Necessarily Conscious
• Evidence that patients could respond to visual stimuli of which they had no conscious awareness
• Evidence that patients could not effectively interact with objects that they consciously perceived
• **Ebbinghaus Illusion:** Conscious perception of disk size differs from motor response

The Development of Central Sensorimotor Programs
• Central sensorimotor programs may be hierarchically organized and capable of using sensory feedback without direct control at higher levels
• Programs for many species-specific behaviors established without practice

The Development of Central Sensorimotor Programs
• **Practice** can also generate and modify programs
– Response **Chunking**
  • Practice combines the central programs controlling individual response
– Shifting **Control to Lower Levels**
  • Frees up higher levels to do more complex tasks
  • Permits greater speed

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Development of the Nervous System
- Neural development consists of a series of processes
- Continue into adulthood and result in neural plasticity
- However, highest rates are earlier in development and through childhood/ puberty

Neural Development
• Disruption or alteration of development can result in lifelong impairments
• Depends critically on sensory input to drive development
– e.g. case of "Genie"; or development of ocular dominance columns

Phases of Development
• Induction of the neural plate – Neural proliferation
• Migration and aggregation
• Axon growth and synapse formation
• Neuron death and synapse rearrangement

Induction of the Neural Plate
- A patch of tissue on the dorsal surface of the embryo becomes the neural plate
- Development induced by chemical signals from the mesoderm (the "organizer")
- Visible three weeks after conception
- Three layers of embryonic cells

– Ectoderm (outermost)
– Mesoderm (middle)
– Endoderm (innermost)
• Neural plate cells: embryonic stem cells
– Have unlimited capacity for self renewal
• Can become any kind of mature cell
– **Totipotent** – earliest cells have the ability to become any type of body cell
– **Multipotent** – with development, neural plate cells are limited to becoming one of the range of mature nervous system cells

Neural tube
• Eventually develops into the nervous system
• Failure of tube to fully close can result in neural tube defects

Neural Proliferation
• Neural plate folds to form the neural groove, which then fuses to form the neural tube
• Inside will be the cerebral ventricles and neural tube
• Neural tube cells proliferate in species-specific ways: three swellings at the anterior end in humans will become the forebrain, midbrain, and hindbrain
• Proliferation is chemically guided by the organizer areas – the roof plate and the floor plate

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Migration

• Once cells have been created through cell division in the ventricular zone of the neural tube, they migrate
• Migrating cells are immature, lacking axons and dendrites
• Two types of neural tube migration
– Radial migration (moving out) – usually by moving along radial glial cells
– Tangential migration (moving up)
• Two methods of migration
– **Somal** – an extension develops that leads migration, cell body follows
– **Glial-mediated migration** – cell moves along a radial glial network
• Most cells engage in both types of migration

Neural Crest

• A structure dorsal to the neural tube and formed from neural tube cells
• Develops into the cells of the peripheral nervous system
• Cells migrate long distances

Aggregation

• After migration, cells align themselves with others cells and form structures
• Cell-adhesion molecules (CAMs)
– Aid both migration and aggregation
– CAMs recognize and adhere to molecules
• Gap junctions pass cytoplasm between cells
– Prevalent in brain development
– May play a role in aggregation and other processes

Axon Growth and Synapse Formation

• Once migration is complete and structures have formed (aggregation), axons and dendrites begin to grow
• **Growth cone** – at the growing tip of each extension, extends and retracts filopodia as if feeling its way
• **Chemoaffinity hypothesis** – postsynaptic targets release a chemical that guides axonal growth, but this does not explain the often circuitous routes often observed
• Mechanisms underlying axonal growth are the same across species
• A series of chemical signals exist along the way – attracting and repelling
• Such guidance molecules are often released by glia
• Adjacent growing axons also provide signals
• **Pioneer growth cones** – the first to travel a route, interact with guidance molecules
• **Fasciculation** – the tendency of developing axons to grow along the paths established by preceding axons
• **Topographic gradient hypothesis** – seeks to explain topographic maps

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Synapse Formation
• Formation of new synapses
• Depends on the presence of glial cells – especially astrocytes
• High levels of cholesterol are needed – supplied by astrocytes
• Chemical signal exchange between pre- and postsynaptic neurons is needed

Neuron Death and Synapse Rearrangement
• ~50% more neurons than are needed are produced – death is normal
• Neurons die due to failure to compete for chemicals provided by targets
– The more targets, the fewer cell deaths
– Destroying some cells increases survival rate of remaining cells
– Increasing number of innervating axons decreases the proportion that survives

Life-Preserving Chemicals
• **Neurotrophins** – promote growth and survival, guide axons, stimulate synaptogenesis
– Nerve growth factor (NGF)
• Cell death during development is usually programmed: apoptosis, not passive: necrosis

Synapse Rearrangement
• Neurons that fail to establish correct connections are particularly likely to die
• Space left after apoptosis is filled by sprouting axon terminals of surviving neurons
• Ultimately leads to increased selectivity of transmission

Neural Production
• Involves **overproduction** of neurons and connections
• Then **selective attrition**

Postnatal Cerebral Development in Human Infants
• Postnatal neural development is a result of
– Synaptogenesis
– Myelination – sensory areas and then motor areas. Myelination of prefrontal cortex continues into adolescence
– Increased dendritic branches
• Overproduction of synapses may underlie the greater plasticity of the young brain

Development of the Prefrontal Cortex
• Believed to underlie age-related changes in cognitive function
• No single theory explains the function of this area
• Prefrontal cortex plays a role in working memory, planning and carrying out sequences of actions, and inhibiting inappropriate responses (executive function)

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Effects of Early Experience

- **Permissive experiences:** those that are necessary for information in genetic programs to be manifested
- **Instructive experiences:** those that contribute to the direction of development
- Effects of experience on development are time-dependent

– Critical period
– Sensitive period

Early Studies of Experience and Neurodevelopment

• Early visual **deprivation**
– Fewer synapses and dendritic spines in primary visual cortex
– Deficits in depth and pattern vision
• **Enriched environment**
– Thicker cortexes
– Greater dendritic development
– More synapses per neuron

Competitive Nature of Experience and Neurodevelopment

• Ocular Dominance Columns example:
• Monocular deprivation changes the pattern of synaptic input into layer IV of V1 (but not binocular deprivation)
• Altered exposure during a sensitive period leads to reorganization
• Active motor neurons take precedence over inactive ones

Effects of Experience on Topographic Sensory Cortex Maps

• Cross-modal rewiring experiments demon- strate the plasticity of sensory cortexes – with visual input, the auditory cortex can see
• Change input, change cortical topography – shifted auditory map in prism-exposed owls
• Early music training influences the organization of human auditory cortex – *fMRI* studies

Effects of Experience

• Use it or Lose it
• Twitches and movements at fetal stages may even be required for normal sensorimotor development

Experience Fine-Tunes Neurodevelopment

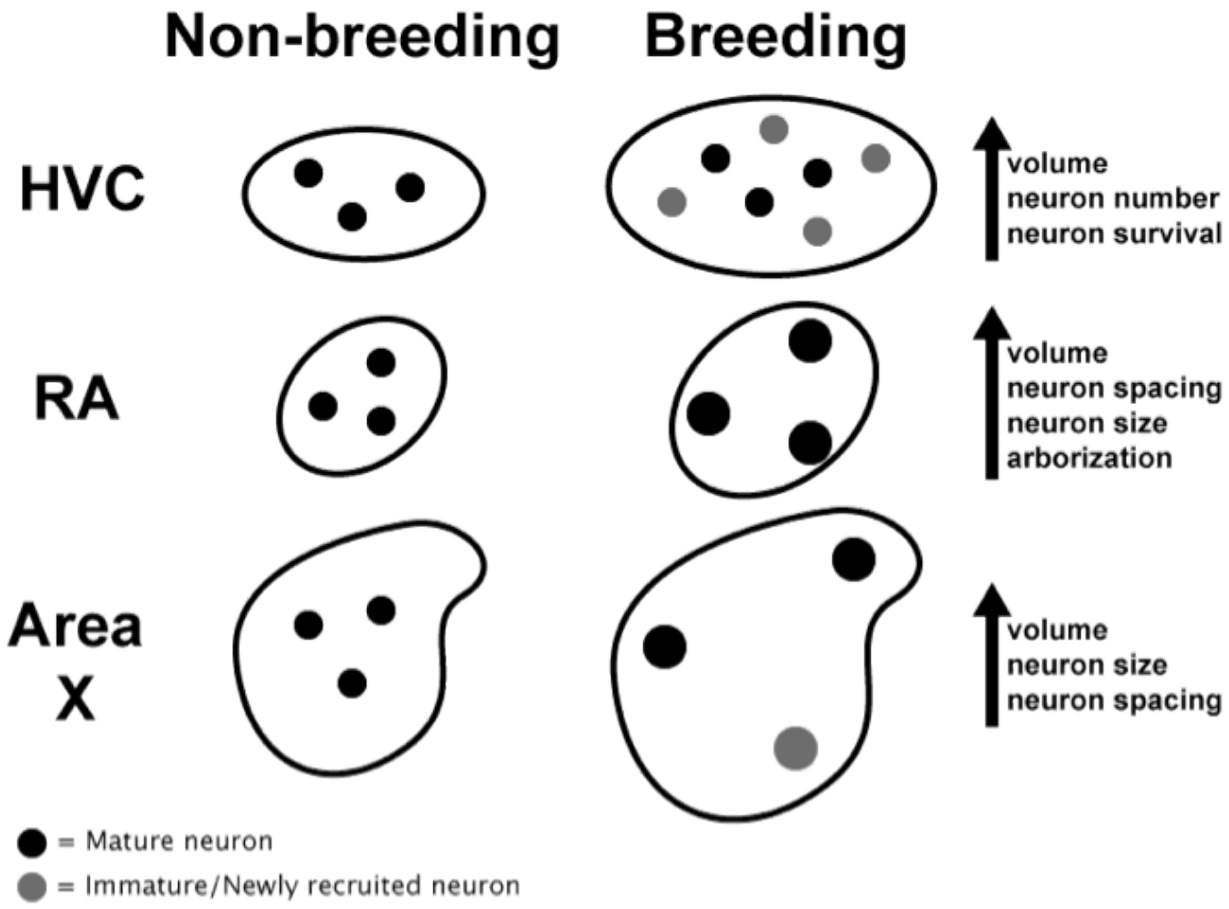
- Neural activity regulates the expression of genes that direct the synthesis of CAMs
- Neural activity influences the release of neurotrophins
- Some neural circuits are spontaneously active and this activity is needed for normal development

Neuroplasticity in Adults

• The mature brain changes and adapts
• **Neurogenesis** (production of new neurons) widespread. More widespread in other vertebrates

– Seen in olfactory bulbs and hippocampuses of adult mammals – adult neural stem cells created in the ependymal layer lining in ventricles and adjacent tissues
• Enriched environments and exercise can promote neurogenesis

Adult neurogenesis
• Originally discovered in rodents but discounted
• Research on birdsong demonstrated that it is a real phenomenon, and that new cells become parts of functioning neural circuits



Adult Neurogenesis
• Following work on songbirds, research on mammals validated earlier studies and has proven that adult-generated neurons become part of functioning neural circuits

Effects of Experience on the Reorganization of the Adult Cortex
• **Tinnitus** (ringing in the ears) – produces major reorganization of primary auditory cortex
• Adult musicians who play instruments fingered by left hand have an enlarged representation of the hand in the right somatosensory cortex
• Skill training leads to reorganization of motor cortex

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Disorders of Brain Development
• Autism
• Williams Syndrome

Disorders of Brain Development
• Autism
– Complex disorder widely considered as a spectrum of disorders
• Core symptoms
– Reduced ability to interpret emotions and intentions of others
– Reduced social communication
– Preoccupations with single activity/object
• Core symptoms displayed in most, but not all cases (in varying forms)

Autism Spectrum Disorder
• A group of related disorders ranging in symptoms
• E.g. Asperger's syndrome may be considered a mild autistic disorder with preserved cognition and language abilities
• Early signs
– Delayed language development
– Delayed social interaction
• Overall most prevalent childhood neurological disorder
– Increasing prevalence
  • Increasing numbers or better detection and awareness?

Autism: A Heterogenous disorder
• Deficits are often quite specific
• E.g. mental impairment, but unimpaired art, music and memorization
• Reveals modular nature of cognition with specific deficits

Autistic savants
• **Savant:** intellectually impaired but displaying amazing highly specific abilities
– About 10% of autistic individuals have some savantism
• E.g. naming day of week of any date – see text for examples
• Savant abilities seem to emerge spontaneously

Autism and Genetics
• Clearly underlying genetic contribution, but large environmental influences
• Sibling with autism: 5% risk (versus approx 1⁄2% risk at large)
• Identical twin with autism: 60% risk
• Classic case of interactionism: inherited predisposition to develop autism in particular environments

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Neural Mechanisms of Autism
• Understanding of brain structures involved in autism is still limited, so far implicated:
– Cerebellum
– Amygdala
– Frontal cortex
• Two lines of research on cortical involvement in autism:
– Abnormal response to faces in autistic patients
  • Spend less time than non-autistic subjects looking at faces, especially eyes
  • Low fMRI activity in fusiform face area
– Possibly deficient in mirror neuron function

Williams Syndrome
• Similar to autism in heterogeneity
• However, very different impairments
• Highly sociable, empathic and talkative, sometimes gifted musically
• Severe impediment in spatial reasoning and abilities, very low IQ
• Much rarer (1 in 7,500)
• Typically cardiac health issues
• Evidence for a role of chromosome 7 (as in autism)
• General thinning of cortex at juncture of occipital and parietal lobes, and at the orbitofrontal cortex
• "Elfin" appearance – short, small upturned noses, oval ears, broad mouths

Brain Damage (text 10.1)
• Brain damage can result from developmental disorder, or from a variety of causes in adulthood

Causes of Brain Damage
• Brain tumors
• Cerebrovascular disorders
• Closed-head injuries
• Infections of the brain
• Neurotoxins
• Genetic factors

Brain Tumors
• A tumor (**neoplasm**) is a mass of cells that grows independently of the rest of the body – a cancer
• 20% of brain tumors are meningiomas – encased in meninges
– Encapsulated, growing within their own membranes
– Usually benign, surgically removable
• Most brain tumors are infiltrating
– Grow diffusely through surrounding tissue
– Malignant, difficult to remove or destroy

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• About 10% of brain tumors are metastatic
– They originate elsewhere, usually the lungs

Cerebrovascular Disorders
• **Stroke** – a sudden-onset cerebrovascular event that causes brain damage
– **Cerebral hemorrhage** – bleeding in the brain
– **Cerebral ischemia** – disruption of blood supply
• Third leading cause of death in the U.S. and most common cause of adult disability

Cerebrovascular Disorders
• **Cerebral Hemorrhage** – blood vessel ruptures
– Aneurysm – a weakened point in a blood vessel that makes a stroke more likely; may be congenital (present at birth) or due to poison or infection
• **Cerebral Ischemia** – disruption of blood supply
– **Thrombosis** – a plug forms in the brain
– **Embolism** – a plug forms elsewhere and moves to the brain
– **Arteriosclerosis** – wall of blood vessels thicken, usually due to fat deposits

Damage Due to Cerebral Ischemia
• Does not develop immediately
• Most damage is a consequence of excess neurotransmitter release – especially glutamate
• Blood-deprived neurons become overactive and release glutamate
• Glutamate overactivates its receptors, especially NMDA receptors leading to an influx of Na+ and Ca2+

Damage Due to Cerebral Ischemia
• lnflux of Na+ and Ca2+ triggers
– The release of still more glutamate
– A sequence of internal reactions that ultimately kill the neuron
• Ischemia-induced brain damage
– Takes time
– Does not occur equally in all parts of the brain
– Mechanisms of damage vary with the brain structure affected

Closed-Head Injuries
• Brain injuries due to blows that do not penetrate the skull – the brain collides with the skull
– **Contrecoup injuries** – contusions are often on the side of the brain opposite to the blow
• **Contusions** – closed-head injuries that involve damage to the cerebral circulatory system; hematoma (bruise) forms
• **Concussions** – when there is disturbance of consciousness following a blow to the head and no evidence of structural damage
• While there is no apparent brain damage with a single concussion, multiple concussions may result in a dementia referred to as “punch- drunk syndrome”

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• Cumulative concussions – depression or anxiety
– Higher risk for future concussions

Infections of the Brain
• Encephalitis – the resulting inflammation of the brain by an invasion of microorganisms
– Bacterial infections
  • Often lead to abscesses, pockets of pus
  • May inflame meninges, creating meningitis
  • Treat with penicillin and other antibiotics
– Viral infections
  • Some preferentially attack neural tissues
  • Some can lie dormant for years

Syphilis
• Sexually transmitted via genital sores
• After dormancy bacteria (**spirchetes**) attack several tissues including the brain resulting in dementia
– General paresis

Neurotoxins
• May enter general circulation from the GI tract or lungs, or through the skin
• **Toxic psychosis** – chronic insanity produced by a neurotoxin

Genetic Factors
• Most neuropsychological diseases of genetic origin are associated with recessive genes
– e.g., PKU

Down Syndrome
• Down syndrome
– 0.15% of births, probability increases with advancing maternal age
– Extra chromosome 21 during meiosis
– Characteristic facial development, impaired mental development and other health problems

Programmed Cell Death
• All causes of brain damage discussed above produce damage, in part, by activating apoptosis
– Not just necrosis
• Interaction between inherited factors and environmental effects that activate cell signaling paths