



The Brain, Biology and Cognition (BBC)

Brain Damage

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Brain Damage

Important to study:

- 1.Helps understand how brain should work in healthy individual
- 2.Serves as basis for development of new treatment.

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



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Brain Tumors

- Mass of cells that grow independently of rest of body – cancer
- 20% are **meningiomas** – grow between meninges (3 membranes that cover CNS)
- All meningiomas are encapsulated: grow within own membranes (picked-up on CT)
- Usually benign, surgically removable, little risk
- However, most are **infiltrating** (grow diffusely through surrounding tissue)
- Malignant, difficult to destroy.
- About 10% **metastatic** – originate elsewhere (usually lungs) and carried to brain by bloodstream.

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Cerebrovascular Disorders



• Stroke:

- Sudden-onset cerebrovascular event
- Symptoms depend on area of brain affected but common consequences are amnesia, aphasia (language deficits), paralysis, & coma.
- Area of dead/dying tissue called infarct.
- Area surrounding infarct is penumbra.
- Two major types:
 - Cerebral hemorrhage (bleeding in brain)
 - Cerebral ischemia (disruption of blood supply)

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Cerebrovascular Disorders



• Cerebral hemorrhage (bleeding in brain)

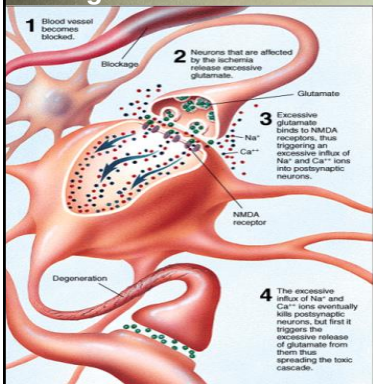
- Blood vessel ruptures and blood seeps to surrounding tissue.
- Aneurysm – balloon-like dilation that forms in wall of an artery at a point where elasticity of artery wall is defective; may be congenital (present at birth) or due to poison/infection.

• Cerebral ischemia (disruption of blood supply)

- Thrombosis – plug forms in brain, blocking flow
- Embolism – plug forms elsewhere and moves to brain
- Arteriosclerosis – wall of blood vessels thicken, usually due to fat deposits creating narrow channels.

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Damage Due to Cerebral Ischemia



- 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

The cascade of events by which the stroke-induced release of glutamate kills neurons

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Closed-Head Injuries

- Blow to head not penetrating skull:
- Brain collides with skull
 - Contrecoup injuries – contusions on side of brain opposite to blow
- Contusions – damage to cerebral circulatory system; produces internal hemorrhaging, which results in hematoma (localised collection of clotted blood – bruise)
- Concussions – disturbance of consciousness, no evidence of structural damage.
 - No apparent brain damage with single concussion, but evidence that cognitive, motor, & neurological effects last years (De Beaumont et al., 2009).
 - Multiple concussions may result in a dementia called “punch-drunk syndrome”

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Infections of the Brain

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- **Encephalitis** – inflammation of brain by invasion of microorganisms
 - Two common types of brain infection:
 - **Bacterial infections**
 - Abscesses, pockets of puss
 - May inflame meninges, creating meningitis
 - Treat with penicillin and other antibiotics
 - But does not reverse brain damage
 - **Viral infections**
 - Some preferentially attack neural tissues
 - Others attack neural tissue but do not have preference for it over other tissue.
 - Some can lie dormant for years

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n eurotoxins

- Damaged by exposure to variety of toxic chemicals.
- May enter through Gastrointestinal tract, lungs, or skin.
- **Toxic psychosis** – chronic insanity produced by a neurotoxin
- Mad Hatter: hat makers exposed to mercury when preparing felt
- Some antipsychotic drugs in 1950s produced a motor disorder called **tardive dyskinesia**
- Some neurotoxins are endogenous (produced by the body)
 - e.g., auto-immune disorders

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Genetic Factors

- Accidents during cell division leading to fertilised egg with abnormal or abnormal number of chromosomes.
- Most neuropsychological diseases of genetic origin are associated with recessive genes passed from parent.
- **Down syndrome:**
 - Extra chromosome 21 created in egg during ovulation – when fertilized, 3 instead of 2 of this chromosome exist
 - Characteristic disfigurement, mental health and other health problems result.



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Programmed Cell Death

All six causes of brain damage produce damage, in part, by activating **apoptosis**.

This can be of benefit, otherwise if damaged cells were just left in the brain they could swell, break off and travel around causing other problems.



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Neuropsychological Diseases

So far discussed causes of human brain damage.

What about diseases associated with brain damage.

- **Epilepsy**
- **Parkinson's disease**
- **Multiple sclerosis**
- **Alzheimer's disease**



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Epilepsy



- Primary symptom is seizures
- But not all who have seizures have epilepsy
- Epileptics have seizures generated by brain dysfunction
- Affects about 1% of population
- Difficult to diagnose due to diversity and complexity

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Epilepsy



- Types of seizures
 - **Convulsions** – motor seizures: tremors, rigidity, loss of balance and consciousness.
 - Others involve subtle changes of thought, mood, cognition, or behavior
- Causes
 - Brain damage
 - Faulty Genes – over 70 linked so far
 - Faults at inhibitory synapses, particularly GABA where neurons end up just firing in synchronized bursts.
- Diagnosis
 - EEG – **electroencephalogram**
 - Why?.....Seizures associated with high amplitude EEG spikes during an attack.

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Epilepsy



- Some experience psychological change before a convulsion – auras
 - A smell, thought, hallucination, feeling
 - Aura's nature suggests epileptic focus
 - Warns of impending seizure
- Once diagnosed, usually assigned to either:
 - Partial epilepsy – does not involve whole brain
 - Generalized epilepsy – involves entire brain

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Partial Seizures divided into:



Simple	Complex
• Symptoms primarily sensory, motor or both • Known as Jacksonian after neurologist Hughlings Jackson • Symptoms spread as epileptic discharge spreads	• Restricted to temporal lobes • Patient engages in compulsive and repetitive behaviors (automatisms) • More complex behaviors seem normal • Although conscious, they do not recall seizure.

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Generalized Seizures can be:



- **Grand mal**
 - Loss of consciousness
 - Loss of Equilibrium
 - Violent Tonic-clonic convulsions
 - Rigidity (tonus)
 - Tremors (clonus)
- **Petit mal**
 - Not associated with convulsions
 - Disruption of consciousness associated with cessation of ongoing behavior
 - EEG of petit mal seizure is different from other types: bilateral symmetrical 3 per second spike and wave discharge.

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Treatment



- **Medication:**
 - Antiepileptic drugs
 - But have side effects
 - Some patients are drug resistant
- **Brain Surgery (in extreme severe cases)**
- **Ketogenic diet**
 - High fat, low carbohydrate, controlled protein diet
- **Other Cognitive and Behavioural interventions**
 - Need to consider lifestyle, age, seizure frequency, and specific diagnosis when deciding best course of treatment.

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Interactive Task



Complete the H5P Quiz titled Brain Damage and Epilepsy within this week's tile on the module Moodle page

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Parkinson's Disease



- Movement disorder, middle- old age, males more prevalent.
- Tremor at rest, muscular rigidity, difficulty initiating movement, slowness of movement, pain and depression.
- Also display cognitive deficits
- No single cause (faulty genes, brain damage)
- Degeneration of the substantia nigra; neurons release dopamine to striatum of basal ganglia
- Autopsies reveal **Lewy bodies** (protein clumps) in substantia nigra
- Treated temporarily with L-dopa (synthesis of dopamine)
- Deep brain stimulation** of **subthalamic nucleus** reduces symptoms, but effectiveness slowly declines over months or years

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Multiple Sclerosis



- **Progressive disease that attacks CNS myelin, leaving areas of hard scar tissue (sclerosis).**
- **Autoimmune disorder.**
- **Periods of remission common.**
- **Symptoms = visual disturbances, muscle weakness, numbness, tremor, and loss of motor coordination (ataxia).**
- **Can include cognitive and emotional change.**
- **Evidence for genetic and environmental causes – particularly an interaction.**
- **Role of vitamin D implicated.**

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Alzheimer's Disease



- **Definitive diagnosis at autopsy.**
 - Neurofibrillary tangles: thread tangles of protein in neural cytoplasm
 - Amyloid plaques: clumps of scar tissue of degenerating neurons and a protein called amyloid
 - Both prevalent in medial temporal lobe structures (amygdala and hippocampus - role in memory).
 - Both prevalent in inferior temporal, posterior parietal, and prefrontal cortex (complex cognitive functions).
 - Genetic component & acetylcholine decline is early sign

Figure 10.12 in the Pinel book

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Animal Models of Human Neuropsychological Diseases



- Human neuropathology experiments not always possible - Animal models used instead:
- Kindling model of epilepsy
 - Experimentally induced seizure activity
- Transgenic mouse model of Alzheimer's
 - Genes that accelerate synthesis of human amyloid injected in to newly fertilized mouse eggs.
- MPTP model of Parkinson's
 - Drug-induced damage comparable to that seen in PD



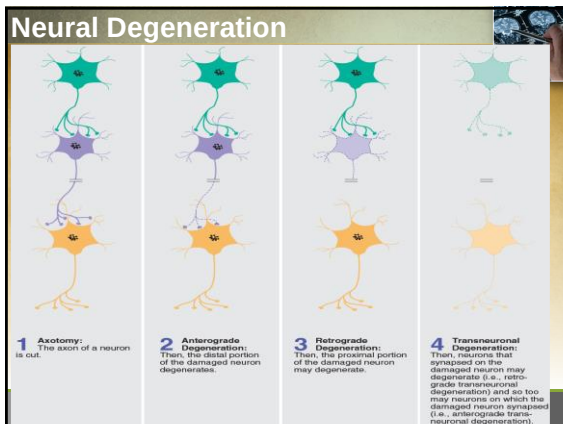
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Neuroplastic Responses to Nervous System Damage

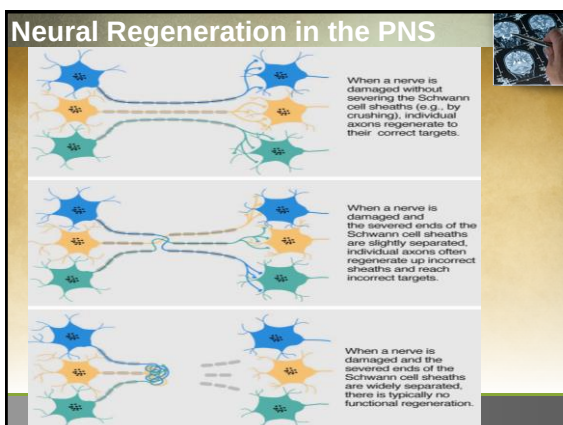


- **Degeneration** – deterioration
- **Regeneration** – regrowth of damaged neurons
- **Reorganization**
- **Recovery**

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Cortical Reorganization Following Damage in Humans

- Brain-imaging used to examine cortices of blind individuals.
- Shows continuous competition for cortical space by functional circuits.
- As there is no visual input to cortex, auditory and somatosensory cortex expand and info regarding sound/touch is processed in former visual areas

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Mechanisms of Neural Reorganization



- How does this work?
- Two mechanisms proposed.....

1. Strengthening of existing connections

- Support from 2 observations:
 - A. Reorganization happens too quickly to be explained by new growth
 - B. Rapid reorganization does not involve changes of more than 2 millimeters across the cortical surface.

2. Establishment of new connections

- Indirect evidence from fact that magnitude of long-term reorganization can be too great to be explained by changes in existing connections



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Recovery of function after brain damage



- Can occur if lesion is small and patient is young.
- Difficult to study as other compensatory changes occur – gradual improvement could reflect learning new cognitive strategies.
- **Cognitive Reserve** (roughly equivalent to education and intelligence) plays a role.
 - Patients may not recover lost brain function, instead prior cognitive abilities assist in allowing them to accomplish tasks in alternative ways (Kapur, 1997).

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Neuroplasticity and the Treatment of Nervous System Damage



- What treatments can be administered following brain damage?
- Reducing further damage by blocking neurodegeneration through neurochemicals
- Promote regeneration through directing growth of axons by Schwann cells
- Transplantation (fetal tissue or stem cells)
- Rehabilitative training

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Promoting Recovery by Rehabilitative Training



- Monkeys with lesion to hand area of motor cortex following induced stroke.
- 5 days after damage, monkey participated in hand training
- Pluck hundreds of tiny food pellets, which reduced cortical damage in surrounding areas.
- Program called Constraint-induced therapy created based on idea neurons compete for synaptic sites and neurotrophins, with the loosing neurons dying.
- Involves tying down functioning arm of stroke patient for 2 weeks while impaired arm receives intensive training, which creates competitive situation that leads to recovery from increase in area of motor cortex that controls that arm.



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Promoting Recovery by Rehabilitative Training



- Correlations in human studies between physical and cognitive activity and resistance or recovery from neurological injury and disease
- Rodents raised in enriched environments designed to promote cognitive and physical activity are resistant to induced neurological conditions (epilepsy, models of Alzheimer's, Huntington's, etc.)
- Physical activity promotes adult neurogenesis in rodent hippocampus.



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Phantom Limbs: Neuroplastic Phenomena



- Phantom limb: amputees continue to have experience of amputated limb.
- Ramachandran's hypothesis: phantom limb caused by reorganization of somato-sensory cortex following amputation
- Amputee feels a touch on face and on phantom limb (due to proximity on somatosensory cortex)
- Amputee with chronic phantom limb pain gets relief through visual feedback: view in mirror intact hand unclenching as seen in mirror box



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