



The Brain, Biology and Cognition (BBC)

Brain Damage

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Brain Damage

Studying brain damaged individuals is important:

1. It helps us understand how the brain should work in a healthy individual
2. Serves as basis for the 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

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

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Cerebrovascular Disorders

Stroke:

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

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Cerebrovascular Disorders

- Cerebral hemorrhage (bleeding in the 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 the 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 that does not penetrate skull:
- Brain collides with skull
 - Contrecoup injuries – contusions on side of brain opposite to the blow
- Contusions – involve damage to cerebral circulatory system; damage produces internal hemorrhaging, which results in a hematoma (localized collection of clotted blood - bruise forms)
- Concussions – disturbance of consciousness and no evidence of structural damage.
 - While there is no apparent brain damage with a single concussion, there is substantial evidence that cognitive, motor, & neurological effects can last years (De Beaumont et al., 2009).
 - Multiple concussions may result in a dementia referred to as “punch-drunk syndrome”

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Infections of the Brain

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- **Encephalitis** – inflammation of the brain by an 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 a preference for it over other tissue.
 - Some can lie dormant for years

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neurotoxins

- Damaged by exposure to variety of toxic chemicals.
- May enter circulation through Gastrointestinal tract or lungs, or through the skin.
- **Toxic psychosis** – chronic insanity produced by a neurotoxin
- Mad Hatter – hat makers often had toxic psychosis due to mercury exposure when preparing felt used to make hats
- 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 fertilized 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 the egg during ovulation – when fertilized, 3 instead of 2 of this chromosome exists
 - Characteristic disfigurement, mental health and other health problems result.

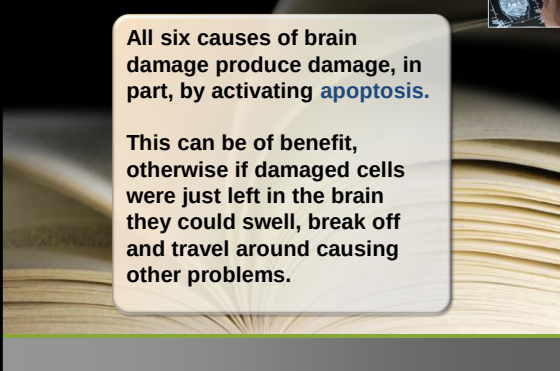


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Programmed Cell Death

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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Interactive Task

Complete the H5P Quiz titled Brain Damage on the module Moodle page



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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 the population
- Difficult to diagnose due to the diversity and complexity of epileptic seizures

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Epilepsy



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

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Epilepsy

- Some epileptics experience psychological changes before a convulsion – known as auras
- Such as a smell, thought, hallucination, feeling
 - Aura's nature suggests the epileptic focus
 - Warns epileptic of an impending seizure
- Once diagnosis is given, it's usual to assign the epilepsy to one of 2 categories:
 - Partial epilepsy – does not involve whole brain
 - Generalized epilepsy – involves the entire brain



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Partial Seizures are divided into:

Simple

- Symptoms are primarily sensory or motor or both
- Known as Jacksonian seizures after neurologist Hughlings Jackson
- Symptoms spread as epileptic discharge spreads



Complex

- Often restricted to the temporal lobes (temporal lobe epilepsy)
- Patient engages in compulsive and repetitive simple behaviors (automatisms)
- More complex behaviors seem normal & although conscious they do not have recollection of 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
- Instead there is a disruption of consciousness associated with cessation of ongoing behavior
- The EEG of a petit mal seizure is different from other types: it is a bilateral symmetrical 3 per second spike and wave discharge.



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Treatment

- **Medication:**
 - Antiepileptic drugs
 - But have to 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 of epilepsy when deciding on the best course of treatment.

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Interactive Task

Complete the H5P Quiz titled Epilepsy on the module Moodle page

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Parkinson's Disease

- Movement disorder of middle and old age & more prevalent in males.
- 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)
- Associated with 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).
- An autoimmune disorder.
- Periods of remission are common.
- Symptoms include 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 between the two.
- Role of vitamin D implicated.

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Alzheimer's Disease



- Definitive diagnosis only at autopsy – must observe neurofibrillary tangles & amyloid plaques.
- Neurofibrillary tangles: threadlike tangles of protein in neural cytoplasm
- Amyloid plaques: clumps of scar tissue composed of degenerating neurons and a protein called amyloid
- Both often prevalent in medial temporal lobe structures such as amygdala and hippocampus (role in memory).
- Both often prevalent in inferior temporal cortex, posterior parietal cortex, and prefrontal cortex (involved in complex cognitive functions).
- Thought to have a major genetic component
- Decline in acetylcholine levels is early sign of AD

Figure 10.12 in the Pinel book

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Interactive Task



Complete the Worksheet on the Neuropathology of Alzheimer's Disease on Moodle

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Animal Models of Human Neuropsychological Diseases

- Experiments on neuropathology not always possible with humans - Animal models are often utilized, for example:
- Kindling model of epilepsy
 - Experimentally induced seizure activity
- Transgenic mouse model of Alzheimer's
 - Genes that accelerate synthesis of human amyloid are 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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Neural Degeneration

1 Axotomy:
The axon of a neuron is cut.

2 Anterograde Degeneration:
Then, the distal portion of the damaged neuron degenerates.

3 Retrograde Degeneration:
Then, the proximal portion of the damaged neuron may degenerate.

4 Transneuronal Degeneration:
Then, neurons that synapsed on the damaged neuron may degenerate (i.e., retrograde transneuronal degeneration) and so too may neurons on which the damaged neuron synapsed (i.e., anterograde transneuronal degeneration).

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Neural Regeneration in the PNS

When a nerve is damaged without severing the Schwann cell sheaths (e.g., by crushing), individual axons regenerate to their correct targets.

When a nerve is damaged and the severed ends of the Schwann cell sheaths are slightly separated, individual axons often regenerate up incorrect sheaths and reach incorrect targets.

When a nerve is damaged and the severed ends of the Schwann cell sheaths are widely separated, there is typically no functional regeneration.

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Cortical Reorganization Following Damage in Humans

- Cortical reorganization in animals prompted research to search for similar effects in humans
- Studies have used brain-imaging to examine the cortices of blind individuals.
- These studies indicate there is continuous competition for cortical space by functional circuits.
- Because there is no visual input to the cortex in those who are blind, the auditory and somatosensory cortex therefore expand and info regarding sound or touch is then processed in former visual areas

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Mechanisms of Neural Reorganization

- How does this neural reorganization work?
- Two mechanisms have been proposed.....

1. Strengthening of existing connections
 - Support for this comes 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.
- But difficult to study because other compensatory changes occur – gradual improvement could reflect learning new cognitive strategies.
- **Cognitive Reserve** (roughly equivalent to education and intelligence) plays a role.
 - Cognitive recovery following damage can seem to occur.
 - However, patients may not recover lost brain function, instead their prior cognitive abilities may assist in allowing them to accomplish tasks in alternative ways (Kapur, 1997).

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Neuroplasticity and the Treatment of Nervous System Damage



- So what sort of treatments can be administered following brain damage?
- Reducing brain damage by blocking neurodegeneration through neurochemicals
- Promoting recovery by promoting regeneration through directing growth of axons by Schwann cells
- Promoting recovery by transplantation (fetal tissue or stem cells)
- Promoting recovery by rehabilitative training

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Promoting Recovery by Rehabilitative Training



- Successful in monkeys with lesion to hand area of the motor cortex following an induced stroke.
- 5 days after damage, monkey participated in hand training by plucking hundreds of tiny food pellets, which reduced cortical damage in surrounding areas.
- Following this a rehabilitative program called Constraint-induced therapy was created based on the idea that neurons compete with each other for synaptic sites and neurotrophins with the losing neurons dying.
- The procedure involves tying down functioning arm of a stroke patient for 2 weeks while impaired arm receives intensive training, which creates a competitive situation that leads to recovery from the increase in the area of motor cortex that controls that arm.



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Promoting Recovery by Rehabilitative Training

- On this principle the benefits of cognitive and physical exercise have shown:
- Correlations in human studies between physical/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 the experience of limb that has been amputated.
- Ramachandran's hypothesis: phantom limb caused by reorganization of the somatosensory cortex following amputation
- Amputee feels a touch on his face and also on his phantom limb (due to their 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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