Notes: Damage

PDF

_____ - localized damage, typically associated with a change in function/abilities
sometimes a literal hole - neurons die, area fills with cerebrospinal fluid

Cerebrovascular Disorders

problems with blood flow to the brain

_____
cardiopulmonary failures (heart attacks), near-drowning, strokes, carbon monoxide
generally 4-6 minute can result in permanent damage

sleep apnea can reduce blood oxygenation from 95% to ~50%

_____
swelling of the ventricles due to blockage of cerebrospinal fluid
swelling can disrupt blood flow and distort tissue

Stroke

U.S. Statistics

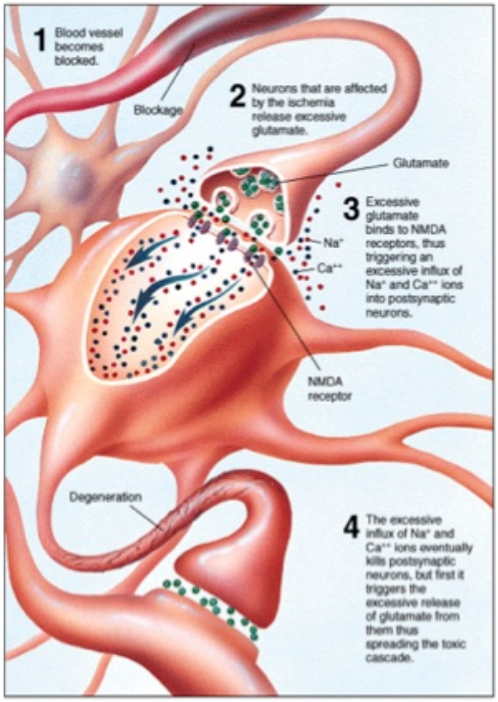
- ~800,000 per year
- 3rd leading cause of death (140,000 people per year)
- leading cause of adult disability
- average age: 70 years old (75% of stroke victims over 65 years old)
- Source: strokecenter.org

routes of harm:
- anoxia/hypoxia to affected tissue
- intracranial pressure and distorted tissue
- compromise of blood-brain-barrier

_____ - the area of dead/damaged tissue

cerebral _____
rupture of blood vessels
balloon like expanse in an artery: _____

cerebral _____
disruption of blood flow
thrombosis - a plug or clot that develops in place
embolism - a plug or clot that breaks free, travels through blood stream, lodges elsewhere
arteriosclerosis - narrowing of arteries by fatty plaques



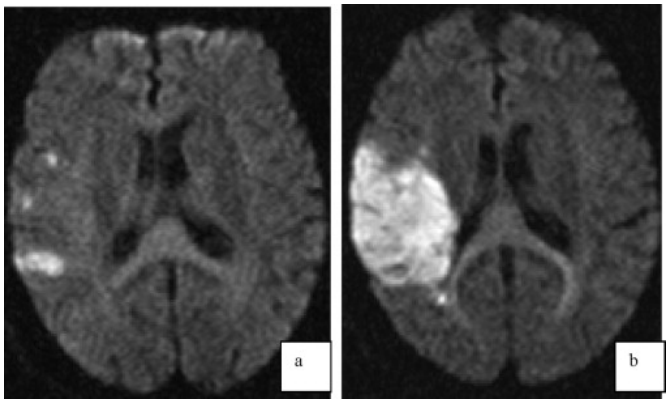
ischemic cascade
disruption of oxygen delivery causes energy crisis & failure to maintain cell homeostasis

fail to: _____
internal build up of Na+, permanent depolarization, glutamate release

fail to: clean up _____
causes over stimulation of post-synaptic neurons
influx and toxic buildup of _____ in post-synaptic neuron
over-stimulation of next post-synaptic neuron, cycle repeats

cell metabolism is catastrophically altered by _____
overexcited enzymes, breakdown of mitochondria and membrane

damage takes days to develop
some areas more sensitive than others: hippocampus



Diagnosing

_____ imaging - detect round, clean edge lesions of uniform density, noninvasive

_____ - inject contrast dye into venous/artery system, more detailed but invasive

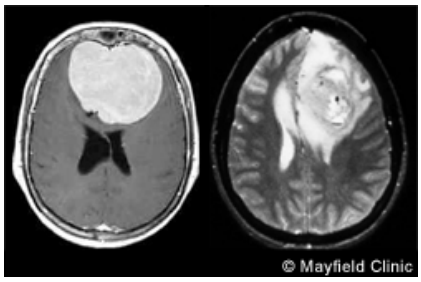
a) 4 hours after symptoms, b) 1 week after symptoms
Source: Weis-Müller et al, 2007

Intracranial Tumors

morbid, uncontrolled growth of tissue
brain tumors make up 5% of all cancers
most common in early and middle adulthood
because CNS neurons do not typical undergo mitosis (reproduce),
  tumors usually do not originate from neurons

_____ (from "glial" cells)
  infiltrative tumors
  difficult surgery, unlikely to remove completely, often reoccurring
  40-50% of brain tumors

Benign (left) vs malignant (right) tumors



Source: www.mayfieldclinic.com/PE-BrainTumor.htm

_____ (originating in the meninges)
  usually benign, wrapped in a membrane
  easier to surgically remove
  slow growing, can become quite large
  cause problems by displacing tissue,
    but brain can sometimes adapt for years
  about 15-20% of brain tumors

_____
  originating from elsewhere in the body
  typically closer to cortical surface but can be anywhere
  difficulty surgery, poor prognosis because already spreading
  15% of brain tumors

pituitary tumors
  pituitary gland is a major interface between nervous and endocrine system
  can result in excessive growth hormones, resulting in giantism
  15% of brain tumors

symptoms: headaches, nausea, seizures, disruption of cognitive function
has effects by disrupting neural tissue, vascular compression, endocrine interference
typically diagnosed using CT or MR imaging

Traumatic Brain Injury (TBI)

U.S. Statistics
- 2 million per year
- 4th leading cause of death (1st in persons aged 1-44 years)
- 50% of trauma deaths are secondary to TBI (35% of these gunshot wounds)
- 92% mortality rate for gunshot wound
- Source: Vinas & Pilitis, 2006

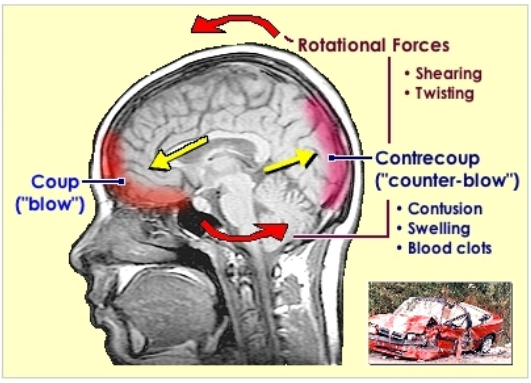
_____ head injury
- penetration of the skull
- death typically caused by disruption of blood flow (ischemic cascade)

_____ head injury
- impact or sudden acceleration, but skull was not fractured
- adolescents & young adults: accidents, defuse damage
- 65 and older: falls, focal damage

Closed Head Injuries

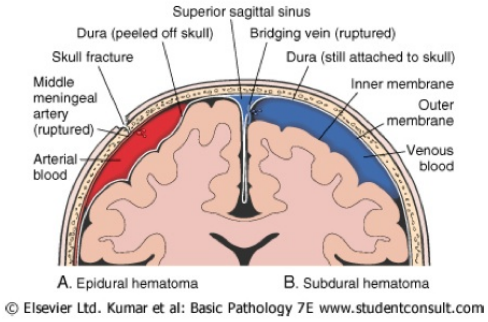
_____
- a "mild" TBI
- altered consciousness for 2-30 minutes
- no evidence of vascular damage
- symptoms: cognitive, somatic (dizzy, nausea), emotional
- not considered a medical event until ~1980s
- increasing awareness of potential for long term damage, especially with repetition

Damage



_____ of axons
damage is not immediate
subsequent neuron death
difficult to detect with imaging
over long term, shows up as decreased volume
(enlarged ventricles)

_____ - at site of impact
countrecoup - opposite of impact, due to rebound
most common in frontal and temporal lobes



_____ - damage to circulatory system
produces a hematoma (bruise)
even trivial tears can cause problems weeks later

_____
swelling of tissue

_____
caused by hematoma or edema
downward compression of brain
pressure on brainstem, cranial nerve, cerebral arteries

Symptoms

loss or altered consciousness
Glasgow Coma Scale - assess eye opening, motor response, verbal response
low scores 6 hours after injury indicates 35-50% chance of death within 6 months

post-traumatic anterograde amnesia
difficulties forming new memories
lasting longer than 3 weeks indicates poor prognosis

difficulties with divided attention, behavioral control, planning, abstract planning

Sports Related Injuries

football, boxing, rugby, horseback riding

dementia pugilistica
- tremors, difficulty speaking, abnormal reflexes
- related to the number of matches (Mortimer & Pirozzolo, 1985)

subtle but long-term cognitive differences
- number of concussions (ranging from 0-7) in amateur soccer players was inversely correlated with
  - performance on planning and memory tests
  - Matser et al, 1999
- rugby players with single mild head injury (<20 minutes of altered consciousness, amnesia < 24 hours)
  - changes in visual attention task still present 1 year later
  - Cremona-Meteyard & Geffen, 1994

Other

Infection

_____ - inflammation of brain due to the invasion of a microorganism
- bacterial - syphilis, Lyme disease, malaria
- viral - rabies, mumps, herpes encephalitis
- cause deficits by interfering with cell function and producing an inflammatory response

Toxins

Drugs: alcohol, marijuana, LSD, MDMA
- Difficult to disambiguate neurological effect of the drug from:
  - cognitive deficits associated with a person's increased likelihood to take drugs
  - cognitive deficits associated with risky or neglectful drug-related behaviors

Lead, organic solvents, pesticides (organophosphates)
- Some improvement after leaving harmful environment, but usually lasting effects

Neuron damage & regeneration

_____ - the ability of neuron configurations, and therefore the brain, to change with time and recover

critical to development, learning and recovery

Damage

_____

programmed cell death

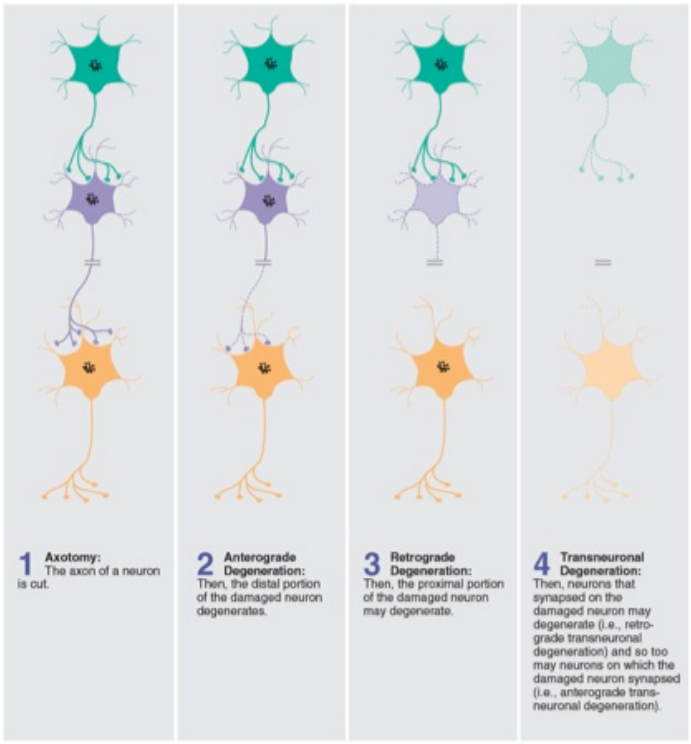
slow, orderly disintegration of cells, no inflammation, doesn't disturb neighboring cells

(Full review: Apoptosis in neurodegenerative disorders, Nature Reviews Mol Cell Bio, Mattson 2000)

_____

sudden, disorderly cell death

causes inflammation, disrupts neighboring cells



_____ degeneration

damage between cut and synaptic terminals

this is the distal portion of the neuron

_____ degeneration

damage between cut and cell body

this is the proximal portion of the neuron

_____ degeneration

when a neuron dies, other neurons that are

post-synaptic, or

pre-synaptic

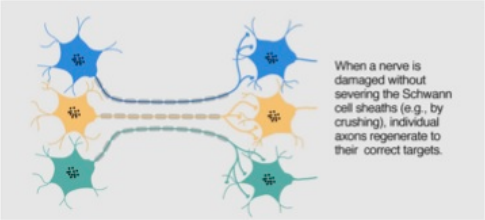
may also die

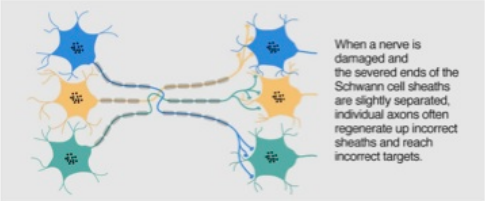
Regeneration

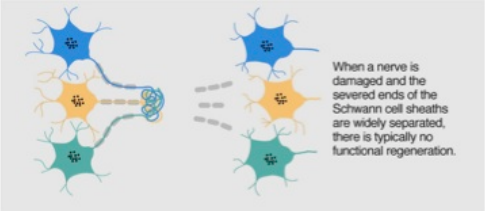
Unsuccessful in mature mammals and higher vertebrates

CNS - virtually non-existent

PNS - unlikely but possible







Regeneration in PNS

requires original _____ to be intact

neurotropic factors - chemicals that encourage tissue growth

CAMs - cell adhesion molecules, provide guidance

new growth may connect to incorrect targets

It is not the neurons themselves, but the environment

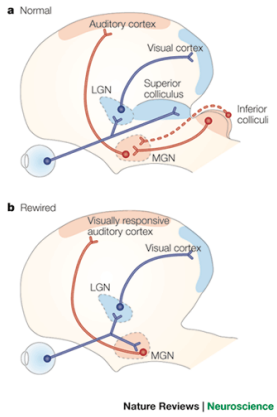
CNS neurons transplanted to PNS will regenerate

PNS neurons transplanted to CNS will not regenerate

Reorganization

Example 1: Reorganization in V1 following retinal lesions

In adult monkeys, remapping can occur within hours (Botelho et al, 2012)



Example 2: Rewiring neurons from the eye to the auditory cortex

In the developing ferret, input to MGN (auditory) is removed

MGN then "attracts" input from retinal ganglion cells

Visual stimuli produce activity in the auditory cortex

Source: Sur & Leamey, Nature Reviews Neuroscience, 2001

Example 3: In newly blinded individuals, auditory and somatosensory input is processed in formerly visual areas

Example 4: Phantom limb

somatosensory cortex that previously received input from amputated arm begins responding to neighboring input

Example: touching a patient's cheek can feel like touching the amputated arm

Treatment & Recovery

_____ - return of original function in a damaged area

Example: after a stroke affecting the hand motor area, that tissue recovers and hand function returns

_____ - performing a function by newly learned methods using non-damaged areas

Example: after a stroke affecting the hand motor area, neighboring tissue learns to operate the hand

1. Reducing degeneration

apoptosis inhibition

nerve growth factors

estrogen (Review: Brann et al, 2007)

- females have better incidence/outcomes in neurological pathologies
- administration of estrogen improves post-stroke outcomes in rodents

2. Promoting regeneration

can be induced in CNS neurons by Schwann cells (Xu et al, 2004)

physical activity promotes adult neurogenesis in rodent hippocampus

3. Transplant

fetal substantia nigra cells for treating monkeys with Parkinson's disease-like symptoms

- limited success with humans

embryonic stem cells in rat damaged spinal cord improved mobility

4. Rehabilitative training

for hands, restrict the functioning limb to maximize use of impaired hand

for spinal cord injuries, facilitated walking