Section 4.3 Addiction – Ischemia – Stroke

- Addiction
- Ischemia
- Stroke
Thought for the day:

"I have often wondered how so many teachers manage to spend a year with a group of students and never reveal who they are, what kind of lives they have led, where their ideas come from, what they believe in, or what they want for themselves, for their students, and for the world."

--Howard Zinn

- (Credit to Michael Williams, Brazoswood H.S.)
Neurotransmitters

- Review three handouts (in order):
  - Neurotransmitters
  - Generic Effects of Drugs
  - Neurotransmitter “Hall of Fame”
EVERYTHING CAN BE HIGHLY MEANINGFUL OR TOTALLY ABSURD, DEPENDING ON THE CHEMICALS CURRENTLY INFLUENCING YOUR BRAIN.

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Physiology of Addiction

- Addiction is defined as “a state of dependency upon a drug.”
- This dependency may have both psychological and/or physiological components. In other words, you may just think you need the drug or you may actually need the drug.
Example: Nicotine – The endless cycle

- Nicotine is absorbed into the blood at the lungs and carried to the brain where it mimics ACh and binds to nicotinic receptors.

- This triggers the release of excitatory hormones epinephrine and norepinephrine more commonly known as adrenaline and noradrenaline. The user feels energized and more alert.
Example: Nicotine – The endless cycle

• Within 30 minutes your nicotine levels drops and your energy level drops. By now you’re probably facing a bit of “stress” in your day. So you light up again to “relax.”
Example: Nicotine – The endless cycle

- This time the nicotine triggers the release of a stress-reducing hormone cortisol and the brain’s own pleasure producing NTs – dopamine and probably glutamate.

- The user feels calmer and more relaxed but only for about 30 minutes and the then the craving is back.
Example: Nicotine – The endless cycle

- The craving is back because the presence of nicotine has prompted the brain to \( \uparrow \) the \# of nicotinic receptors for ACh and \( \downarrow \) production of your own ACh.
Example: Nicotine – The endless cycle

- Therefore, you actually do “need” the nicotine. When these receptors don’t get “their fair share” of the drug nicotine the brain experiences “withdrawal symptoms” and you experience impaired function.
Example: Nicotine – The endless cycle

- The user (addict) actually needs the nicotine just to feel normal.

- Nicotine is 2X as addictive as heroin.
Nicotine

- Does it enhance mental capacity?
Does it enhance mental capacity?

- As the complexity of mental tasks increases, nonsmokers outperform smokers by wider and wider margins... even though the smoker *feels* like he is performing quite well.

- As a “bonus” - More than half of those who smoke cigarettes will die from a preventable smoking related illness.
Effect of Addiction on Neurotransmitters

- See page 424 in book

- Drugs such as Cocaine suppress dopamine levels long term.
  - User cannot experience pleasure without the drug
  - Glutamate facilitates learning and addiction.
  - Doomed to long term suppressed brain activity levels.

- See diagram on 424.
Neurotransmitters

- Chemicals used for neuronal communication with the body and the brain
- 50 different neurotransmitters have been identified
- Classified chemically and functionally
Chemical Classes of Neurotransmitters

- Acetylcholine (ACh) – Best understood
- Biogenic amines – Norepinephrine, Dopamine, Seratonin
- Amino acids – glycine, glutamate, GABA
- Peptides – Endorphins, Somatostatin
- Novel messengers: ATP and dissolved gases NO and CO
Neurotransmitters: Acetylcholine

- First neurotransmitter identified, and best understood
- Released at the neuromuscular junction
- Synthesized and enclosed in synaptic vesicles
- Degraded by the enzyme acetylcholinesterase (AChE)
- Released by:
  - All neurons that stimulate skeletal muscle
  - Some neurons in the autonomic nervous system
Neurotransmitters: Biogenic Amines

- Include:
  - Catecholamines – dopamine, norepinephrine (NE), and epinephrine
  - Indolamines – serotonin and histamine
- Broadly distributed in the brain
- Play roles in emotional behaviors and our biological clock
Synthesis of Catecholamines

- Enzymes present in the cell determine length of biosynthetic pathway
- Norepinephrine and dopamine are synthesized in axonal terminals
- Epinephrine is released by the adrenal medulla
Neurotransmitters: Amino Acids

- Include:
  - GABA – Gamma (γ)-aminobutyric acid
  - Glycine
  - Aspartate
  - Glutamate
- Found only in the CNS
Neurotransmitters: Peptides

- Include:
  - Substance P – mediator of pain signals
  - Beta endorphin, dynorphin, and enkephalins
- Act as natural opiates; reduce pain perception
- Bind to the same receptors as opiates and morphine
- Gut-brain peptides – somatostatin, and cholecystokinin
Neurotransmitters: Novel Messengers

- ATP
  - Is found in both the CNS and PNS
  - Produces excitatory or inhibitory responses depending on receptor type
  - Induces Ca\(^{2+}\) wave propagation in astrocytes
  - Provokes pain sensation
Neurotransmitters: Novel Messengers

- Nitric oxide (NO)
  - Activates the intracellular receptor guanylyl cyclase
  - Is involved in learning and memory
- Carbon monoxide (CO) is a main regulator of cGMP in the brain
Functional Classification of Neurotransmitters

- Two classifications: excitatory and inhibitory
  - Excitatory neurotransmitters cause depolarizations (e.g., glutamate)
  - Inhibitory neurotransmitters cause hyperpolarizations (e.g., GABA and glycine)
Functional Classification of Neurotransmitters

- Some neurotransmitters have both excitatory and inhibitory effects
  - Determined by the receptor type of the postsynaptic neuron
  - Example: acetylcholine
    - Excitatory at neuromuscular junctions with skeletal muscle
    - Inhibitory in cardiac muscle
Neurotransmitter Receptor Mechanisms

- Direct: neurotransmitters that open ion channels
  - Promote rapid responses
  - Examples: ACh and amino acids

- Indirect: neurotransmitters that act through second messengers
  - Promote long-lasting effects
  - Examples: biogenic amines, peptides, and dissolved gases
Brain Video

- Neurotransmitters – Noradrenalin, serotonin, dopamine and endorphins
Blood Flow to the Brain

- Brain requires more blood flow and oxygen
- Receives 15 – 20% of body’s blood flow
- Uses 15 – 20% of body’s oxygen
Arteries of the Head and Neck

- Superficial temporal artery
- Basilar artery
- Occipital artery
- Vertebral artery
- Internal carotid artery
- External carotid artery
- Common carotid artery
- Thyrocervical trunk
- Costocervical trunk
- Subclavian artery
- Axillary artery
- Ophthalmic artery
- Maxillary artery
- Facial artery
- Lingual artery
- Superior thyroid artery
- Larynx
- Thyroid gland (overlying trachea)
- Clavicle (cut)
- Brachiocephalic trunk
- Internal thoracic artery

(b)
Arteries of the Head

- Frontal lobe
- Optic chiasma
- Middle cerebral artery
- Internal carotid artery
- Pituitary gland
- Temporal lobe
- Pons
- Occipital lobe

Circle of Willis
- Anterior communicating artery
- Anterior cerebral artery
- Posterior communicating artery
- Posterior cerebral artery

Basilar artery
Vertebral artery
Cerebellum
Section 2:

- Blood Flow to the Brain
- Ischemia vs. Hypoxia
- Syncope
- TIA – transient ischemic attack
- CVA - cerebrovascular accident
Ischemia vs. Hypoxia

- **Ischemia** – local decrease in blood supply to any tissue (Blood has oxygen, just can’t get enough blood.)

- **Hypoxia** – Any condition in which inadequate oxygen is available to tissues.

- **Ischemic hypoxia** – inadequate oxygen delivery to tissues due to blockage or impairment
Blood Flow: Brain

- Blood flow to the brain is constant, as neurons are intolerant of ischemia.

- Metabolic controls—brain tissue is extremely sensitive to declines in pH, and increased carbon dioxide causes marked vasodilation.

- Myogenic (vascular smooth muscle) controls protect the brain from damaging changes in blood pressure.
  - Decreases in MAP (mean arterial pressure) cause cerebral vessels to dilate to ensure adequate perfusion.
  - Increases in MAP cause cerebral vessels to constrict.
Blood Flow: Brain

- The brain can regulate its own blood flow in certain circumstances, such as ischemia caused by a tumor.
- The brain is vulnerable under extreme systemic pressure changes.
  - MAP below 60 mm Hg can cause syncope (fainting).
  - MAP above 160 can result in cerebral edema.
Cerebrovascular Accidents (Strokes)

- Ischemia/hypoxia severe enough to cause death of brain cells
- Are the 3rd leading cause of death in US
- 85% of strokes are the result of blockage of BF in an artery of the brain due to spontaneous formation of a clot. (thrombus or embolus)
- 15% are hemorrhagic. (e.g. rupture of an aneurysm) (Which way do you guess if you have to?)
- Signs & Symptoms are determined by the portion of the brain affected.
Cerebrovascular Accidents (Strokes)

- Tissue plasminogen activator (TPA) is the only approved treatment for stroke (Then only ischemic stroke – fatal for hemorrhagic stroke.)

- Administered within 4 hours – sooner the better.
Cerebrovascular Accidents (Strokes)

- Effects may be minor or major, temporary or permanent because brain has limited ability to form new synapses and “relearn” its way around the damaged area.
Cerebrovascular Accidents (Strokes)

- A recent discovery is that most of the damage of neurons occurs several hours after the initial blockage of blood flow and death of cells due to hypoxia.

- Dead cells release a flood of glutamate which causes nearby cells to release free radicals such as Nitric Oxide (NO) which then damages or destroys many more neurons nearby. Thus the value of clot busters such as TPA (Tissue Plasminogen Activator).
Cerebrovascular Accidents (Strokes)

- Other causes include compression of the brain by hemorrhage or edema, and atherosclerosis
- Transient ischemic attacks (TIAs) – temporary episodes of reversible cerebral ischemia
Cerebrovascular Accidents (Strokes)

- Recognizing Strokes:

  - S  *Ask the individual to SMILE.

  - T  *Ask the person to TALK and SPEAK A SIMPLE SENTENCE (Coherently) (i.e. It is sunny out today.)

  - R  *Ask him or her to RAISE BOTH ARMS.

  - Stick out tongue (It should be straight)
Video on Strokes & Recovery

- (Show Video)
- Shows effects of stroke and repair
- Formation of new synapses
Other issues with blood flow to the brain

- **SYNCOPE** a.k.a. “fainting”
- Temporary loss of consciousness due to cerebral ischemia and/or hypoxia to the whole brain.
- Most often due to a sudden drop in blood pressure
  - blood loss via hemorrhage
  - emotional response to really good or really bad news
Transient Ischemic Attack

- Insufficient blood flow to a local portion of the brain for a brief period of time. (5-50 minutes)

- A portion of the brain is temporarily hypoxic but not permanently damaged.

- Signs & Symptoms may include impaired vision, speech, hearing, paralysis, numbness, or even LOC depending upon which part of the brain is hypoxic.
Physiology of Depression

- What is depression?
- It is not the occasional blues and sadness… these are normal, appropriate responses to events in our lives. 1-4 weeks.
Depression vs. Homeostasis

- Persons with confident “can do” attitudes and good self-esteem tend to have higher levels of NE and Serotonin.

- Depression: imbalance in NE & Serotonin cause unhealthy feelings of sadness, dejection, or melancholy... a pervading lack of enjoyment of life. Includes strong feelings of insecurity and inability to cope with everyday life... possibly suicidal.

- Persists for an extended period of time
Depression vs. Homeostasis

- May be temporary (due to traumatic events) or may be a life long battle (due to genetic predisposition)

- Observation: Depression often associated with person turning inward & focus on self (cause or effect?)
Depression – Drug options

- **MAO inhibitors** to inhibit the destruction of NE and Serotonin

- MAO normally destroys NE at both the synapses in the brain and at the liver because some NE diffuses away from the cleft into blood stream. Not widely prescribed any longer due to numerous complications. e.g. Nardil & Parmate

- **Tricyclic antidepressants** like Elavil ( & many others) inhibit the reuptake of NE and Serotonin so they stay in the cleft longer.
Depression – Drug options

- **SSRIs** Serotonin Specific Reuptake Inhibitors work the same way but on serotonin only (Prozac, Paxil, Effexor, Zoloft, others)

- Wellbutrin is not an SSRI. Wellbutrin is thought to work by altering levels of the brain chemicals norepinephrine and dopamine.

- Antianxiety Agents: Valium (diazepam), Ativan, Xanax

- Valium has its calming primarily through inhibition of the limbic system.