Physiology of additive drugs

Cocaine, methamphetamine, marijuana, and opiates influence the neurotransmitter dopamine.

Neurotransmitter: dopamine

Dopamine - a neurotransmitter associated with several functions, including muscle control and feelings of reward.

Schizophrenia, manic depression are associated with too much dopamine. Antipsychotic drugs block dopamine receptors.

Dopamine and reward

To signal the pleasure center here, neurons use dopamine.
Cocaine and methamphetamines prevent reuptake of dopamine.

Neurons using serotonin are associated with mood, sleep, & appetite. Antidepressants often enhance levels of serotonin (Zoloft, Prozac, Paxil).

Ecstasy temporarily increases serotonin, but the body makes less serotonin in response to ecstasy blocking reuptake of serotonin.

All are monoamines.
THC binds to cannabinoid (CB) receptors, mimicking endocannabinoids (from body) (anadaminde, arachidonate lipids)

CB receptors are in pleasure pathway (VTA), motor coordination (cerebellum) and memory (hippocampus) areas

Signaling bw neurons during learning is disrupted (GABA neurons w CB1 receptors)

Cannabis effects

What makes drugs addictive?

Drug tolerance – occurs because the body tries to maintain homeostasis in presence of high neurotransmitter levels

What makes drugs addictive?

Repeated drug use causes elevated dopamine

Body decreases # dopamine receptors, dopamine prod’n “Down regulation”

Dopamine receptors

Normal Abuser
Study showing down regulation

Repeated doses of morphine reduce # of dendrites in dopamine neurons

What makes drugs addictive?

Now a higher dose is necessary for ‘high’

Normal ‘happy’ increases in dopamine can’t stimulate pleasure bc the pleasure center is badly altered

Endocrine system

Hormones are transported by the blood, but only cause responses in target cells

Endocrine functions

Regulation of growth and development

Homeostasis - ex: salt/water balance, stress, metabolism

Reproduction
Types of hormones

- **Amines** use tyrosine (epinephrine and norepinephrine)
- **Peptides** (oxytocin, vasopressin, GH, insulin, TSH)
- Both types are water soluble

How do hormones signal cells?

Steroid and thyroid hormones activate genes
- Diffuse freely into and out of cells
- Receptor proteins are in cytoplasm. Hormone binds and moves inside nucleus

Types of hormones

- **Steroids** - from cholesterol (adrenal cortex, testis, ovary and placenta). Hydrophobic, transported by proteins

How do hormones signal cells?

Peptide hormones utilize a 2nd messenger mechanism
- Target cells have specific receptor for hormone on cell surface, which triggers 2nd messenger
Comparing the two systems

**Nervous system** - signals sent via specific “wiring”
- rapid, precise responses

**Endocrine system** - specificity is at the receiving end
- overall body responses, effect may take hours

Nervous system - divided into **central** and **peripheral** regions

- **Somatic** nerves innervate skeletal muscles
- **Autonomic** nerves innervate internal organs
**Neuroglia**

- Most CNS cells are glial cells
- They provide structure and maintain interneurons in the CNS
- Are capable of dividing, even in adulthood

**Astrocytes:**
- Hold neurons together
- Establish a blood-brain barrier with capillaries
- Repair brain injuries
- Breakdown some neurotransmitters
- Take up excess $K^+$ from the brain ECF

**Microglia** are the immune defense of the CNS

**Oligodendrocytes** form myelin sheaths around axons

**Ependymal cells** line the internal cavities of the CNS.

**MS involves oligodendrocytes**

Multiple sclerosis – immune system targets oligodendrocytes, causing degeneration of myelin in CNS.
Cranial meninges

- Dura mater
- Arachnoid mater
- Pia mater

Subarachnoid space of brain

Ventricles

- Right lateral ventricle
- Left lateral ventricle
- Third ventricle
- Fourth ventricle

Cerebral spinal fluid (CSF)

- Provides almost neutral balance for brain (it "floats")
- Cushions and nourishes brain
- Produced by tissue in ventricles

CSF produced in ventricles and resorbed in venus sinus
Hydrocephalus

Meningitis
- Meningitis: infection, inflammation of meninges - viral or bacterial.
- Bacterial infections are quite serious and can result in encephalitis, brain damage, death.

Why is it often difficult to deliver drugs to the brain?

Blood brain barrier
- Exists at capillaries that serve the brain
- Capillaries have tight junctions

Normal capillary
- Water-lined pore
- Lipid-soluble substances
- Astrocyte processes

BBB capillary
- Carrier-mediated transport
- Lipid-soluble substances
- Tight junction
Lipid soluble vs. water soluble

Brain infections are generally rare, but harder to fight when established (antibodies can’t pass)

What molecules pass through the blood brain barrier?

The BBB makes it difficult for drug treatments to enter brain
Not everything can be small, lipid soluble
Via nanotechnology, engineered molecules may carry treatments otherwise water soluble

How can drugs pass through the blood brain barrier?

via nanotechnology, engineered molecules may carry treatments otherwise water soluble
Cerebrum

- Cerebral cortex is highly convoluted, outer layer of gray matter. It covers an inner core of white matter.

- An inner core of basal nucleii are located deep within the white matter.
Primary motor cortex
Somatosensory cortex
Frontal lobe
Central sulcus
Parietal lobe

Sensory homunculus
Left hemisphere

Motor homunculus

Posterior parietal cortex – transforms visual information into movement commands
Associative areas:
Prefrontal (association) cortex - plans voluntary activity, decision-making, creativity, and personality traits.

Then the pre-motor cortex (w/ neighboring area) will orient the body, help plan and coordinate movements.

Areas that communicate to the 1st motor cortex to control voluntary movement

Language areas
- **Broca’s area** is responsible for speaking ability.
- **Wernicke’s area** functions for language comprehension.
Lateralization of hemispheres

Basic EEG (‘brainwaves’)

EEG records synchronous firing of pyramidal neurons in cortex (many combined dipoles). EEG measures combined activity of ~10 million neurons.
Basic EEG (‘brainwaves’)