

Psychopharmacology

Part 2

Presented by Demetra Antimisiaris, PharmD, CGP, FASCP
Associate Professor
Department of Family Medicine and Geriatrics
Associate, II of I, Department of Neurology

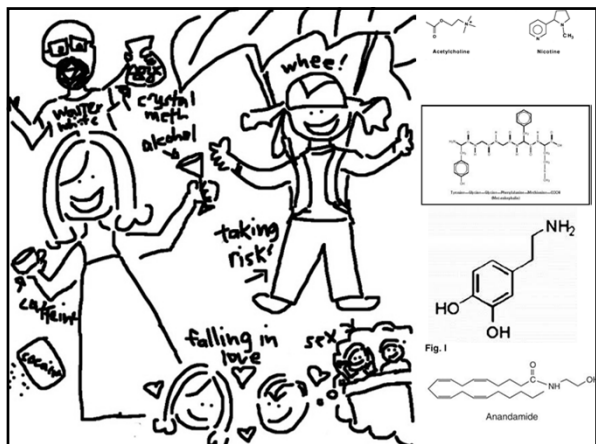
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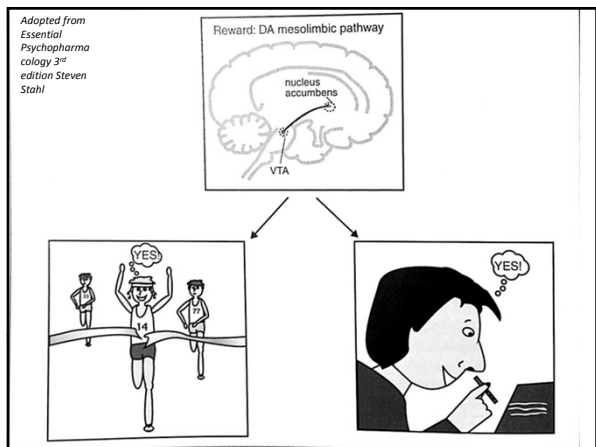
PART 2

- Mesolimbic Reward Circuits
- Substance Abuse Disorders
- Depressants
- Stimulants

MESOLIMBIC DOPAMINE CIRCUIT

- Final common pathway of reward
- “pleasure center of the brain”
- Dopamine is the “pleasure neurotransmitter”

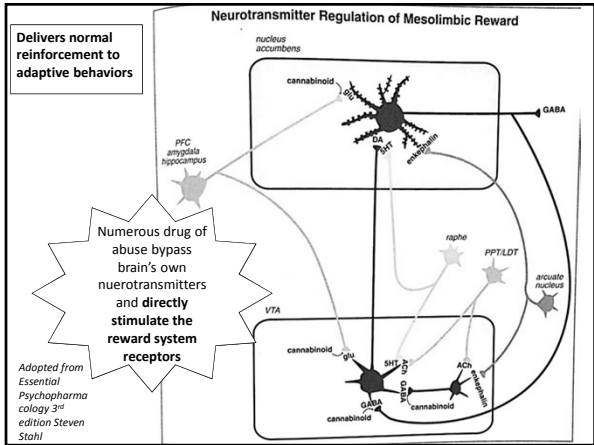


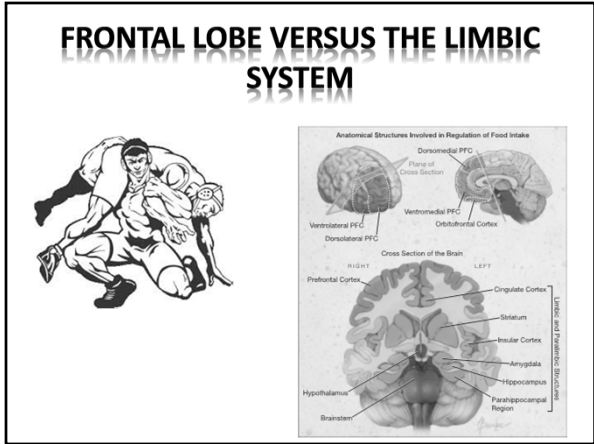


Natural Ways to Trigger Mesolimbic DA

- Intellectual accomplishments
- Athletic accomplishments
- Enjoying a concert
- "Natural Highs"
- Brain's OWN
 - Morphine/Herion (endorphins)
 - Marijauna (anandamide)
 - Nicotine (acetylcholine)
 - Cocaine or Amphetamine (Dopamine)



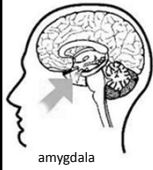




THE REACTIVE REWARD SYSTEM

Repeated Exposure to Drugs of Abuse Triggers Drug Seeking Behavior

RESULT: Instructs the spiny neurons to take action impulsively, right away, automatically, obligatorily and without thought. These changes in the reactive system hijack the entire reward circuitry when addiction develops.



The Amygdala is the site of emotional learning (fear, fear extinction). Proximity to another structure makes the Amygdala remember not just pleasure but environmental cues assoc. with pleasurable or non pleasurable in withdrawal) memory.

THE REFLECTIVE REWARD SYSTEM

Competitive with Reactive System From Prefrontal Cortex

RESULT: Maintained



The O PFC regulates impulses, analyze situations, keeps flexibility of choice, rationality to take action.

CNS DEPRESSANTS



ETHYL ALCOHOL, ETHANOL, ETOH

- Pharmacology:

- Pharmacokinetics:

ETHYL ALCOHOL, ETHANOL, ETOH

- Effects:

- Tolerance and Dependence:

- Toxicology:

ETHYL ALCOHOL, ETHANOL, ETOH

- Treatment for Dependence and Abuse:

INHALANTS

- Types:
 - Anesthetics, industrial or household solvents, office supply solvents, Commercial gases, household products, propellants and Aliphatic nitrites or organic solvents.
- Toxicity:
- Treatment:

BARBITURATES

- Pharmacology:

- Pharmacokinetics:

BARBITURATES

- Effects:

- Tolerance and Dependence:

- Toxicology:

GENERAL ANESTHETICS

- Thiopental (Pentothal)
- Methohexital (Brevital)
- Propofol (Diprivan)
- Etomidate (Amidate)

Propofol

- Designed to use as a hypnotic for induction and maintenance of general anaesthesia for **MECHANICALLY VENTILATED** patients.
- Euphoria and Amnesia properties lend it to be a drug of abuse.
- 30-60 minute half life, highly protein bound excreted by the kidney, half dose adj for frail
- MJ found to have been given 25mg w lidocaine plus lorazepam before death

BENZODIAZEPINES

- GABA receptor:

- Pharmacokinetics:

BENZODIAZEPINES

- Effects

- Toxicity

- Tolerance and Dependence:

SECOND GENERATION ANXIOLYTICS

- Zolpidem (Ambien)
 - Pharmacokinetics:

 - Pharmacodynamics:

 - Effects and Toxicity:

SEROTONINERGIC DRUGS AS ANXIOLYTICS

- Pharmacology:

- Special Class:

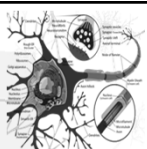
Ketamine

- NMDA receptor
 - NMDA receptor is excitatory for glutamate which is released with noxious peripheral stimuli causing neuropathic pain, reduced functionality of opioid receptors.
 - Activation of the NMDA receptor can result in lower opioid receptor sensitivity.
- NMDA receptor antagonism
 - might play a role in neurodegenerative and psychotic disorders, like Alzheimer's disease and schizophrenia
 - Indirectly disinhibits glutamatergic and cholinergic projections to the cerebral cortex
 - these compounds cause adverse behavioral (psychotomimetic) effects and can produce neurotoxicity characterized by **neuronal vacuolization, induction of heat-shock protein, neuronal/axonal degeneration and regional brain cell death**

Drug	Anesthetic Dosing	Side Effects
Ketamine	IM: 2-4 mg/kg IV: 0.2-0.75 mg/kg Continuous IV infusion: 2-7 mcg/kg/min	CNS effects: hallucinations, confusion, dreamlike state, irrational behavior Other effects: Respiratory depression, increased CSF pressure, hypertension, tachycardia, tremor, nystagmus, myocardial depression
Metadone	Opioid-naïve: initial oral dose: 2.5-10 mg q6-12h (interval may range from 4-12 h as analgesic duration is short during initial therapy, although it increases with prolonged therapy) Opioid-tolerant: Oral morphine to oral metadone conversion is variable	CNS depression, respiratory depression, QTc prolongation, constipation, nausea and vomiting, dizziness, disorientation
Memantine	PO: 10-30 mg/day	Hypertension, dizziness, drowsiness, confusion, anxiety, hallucinations, cataract
Amantadine	IV: 200 mg infused over 3 h PO: 100-200 mg/day	Orthostatic hypotension, dry mouth, drowsiness, agitation, confusion, hallucinations, dyskinesia
Dextro-methorphan	PO: 45-400 mg/day	Light-headedness, drowsiness, confusion, nervousness, visual disturbances, serotonin syndrome

CNS: central nervous system; CSF: cerebrospinal fluid; IM: intramuscular; iv: intravenous; NMDA: N-methyl-D-aspartate.
Source: Reference 5, 7, 12.

US Pharmacist 2011;36(5): H54-H58



Dextromethorphan- DXM

DXM Plateaus

Abusers describe the DXM experience as occurring on four different plateaus. Abusers ingest increasing amounts of DXM (based on their weight) to reach each succeeding plateau. Abusers report the following effects occurring in each plateau:

First Plateau: Mild intoxication.

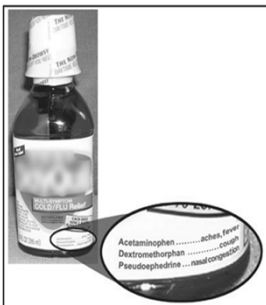
Second Plateau: An effect similar to alcohol intoxication and, occasionally, mild hallucinations. The abuser's speech can become slurred, and short-term memory may be temporarily impaired.

Third Plateau: An altered state of consciousness. The abuser's senses, particularly vision, can become impaired.

Fourth Plateau: Mind and body dissociation or an "out-of-body" experience. The abuser can lose some or all contact with his or her senses. The effects at this plateau are comparable to the effects caused by ketamine or PCP (phencyclidine).

Dextromethorphan- DXM

- Inexpensive
- Easy to obtain
- Combined w guaifenesin
- Internet: powdered form
- Tablets, capsules, liquids
- 140 cough and cold meds
- DEA could qualify CS act
- Texas and ND tried to prohibit sale to minors



STIMULANTS

- Cocaine

- Amphetamines
- Other behavioral Stimulants

COCAINE

- Background:

- Pharmacokinetics:

- Pharmacology:

COCAINE

- Effects short term:

- Toxic and psychotic effects, long term and high dose use:

COCAINE

- Treatment of dependency:

**AMPHETAMINES AND OTHER
BEHAVIORAL STIMULANTS**

Background:

Pharmacology:

AMPHETAMINES AND OTHER BEHAVIORAL STIMULANTS

- Dependence and Tolerance:

- ICE (Free based methamphetamine)
 - Pharmacokinetics
 - Effects
 - toxicity

AMPHETAMINES AND OTHER BEHAVIORAL STIMULANTS

- Non Amphetamine Behavioral Stimulants:
 - Methyphenidate(Concerta, Ritalin)
 - Pemoline (Cylert)
 - Subutramine (Meridia- off market)
 - Modafinil
 - Racemic Amphetamine (Addrall)

Caffeine

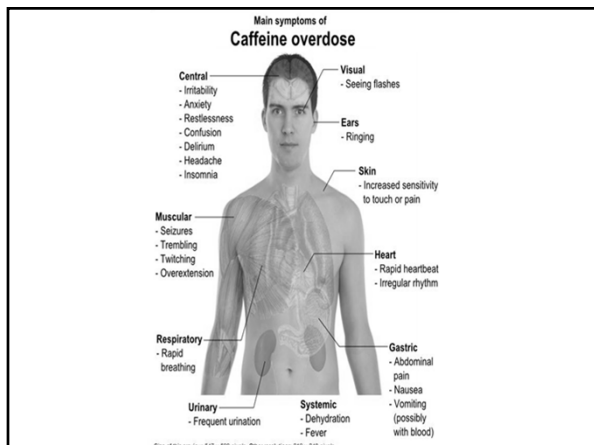
- Easy to get
- World's most popular psychoactive drug
- In plant species, caffeine acts as a pesticide
 - Caffeine paralyzes and kills some insects feeding upon the plant
 - Soil around coffee plants: insecticide and inhibits seed germination of other near plants

Energy drink	Size*	Caffeine**
5-Hour Energy	2 oz. (60 mL)	207 mg
AMP regular or sugar-free	8 oz. (240 mL)	72-74 mg
Cran-Energy	8 oz. (240 mL)	70 mg
Full Throttle	8 oz. (240 mL)	70-72 mg
Monster	8 oz. (240 mL)	80 mg
Red Bull	8.4 oz. (250 mL)	75-80 mg
Rocketstar regular or sugar-free	8 oz. (240 mL)	79-80 mg
Vault, regular or sugar-free	8 oz. (240 mL)	47 mg

Adapted from Journal of Food Science, 2010; American Academy of Pediatrics, 2011; USDA National Nutrient Database for Standard Reference, Release 23, 2010; Consumer Reports, 2011; Mayo Clinic Proceedings, 2010
 *Sizes are listed in fluid ounces (oz.) and milliliters (mL).
 **Caffeine is listed in milligrams (mg).

Caffeine

- Hidden sources
 - Yerba mate
 - Guarana
 - Ilex guayusa
 - Headache tablets
- Pharmacology-Toxicology
 - Stimulant, tolerance, addictiveness, mental clarity
 - Both water and lipid soluble
 - LD=80 cups of coffee, typically V Fib
 - 2 Grams OD hospitalization

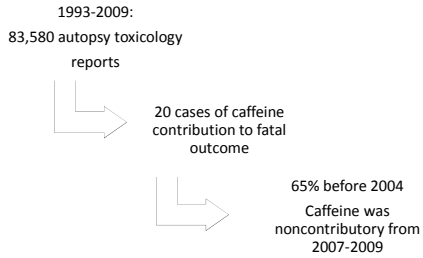


Caffeine

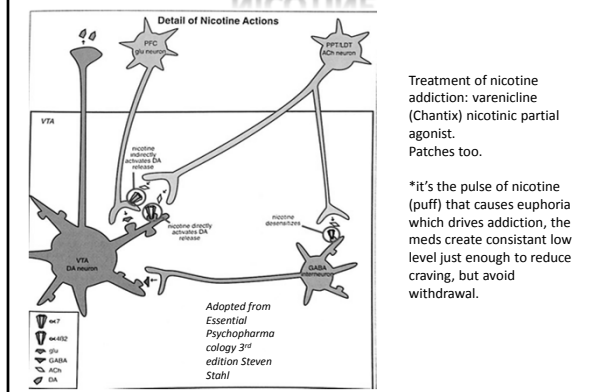
- Metabolism and Elimination
 - Varies widely amongst individuals
 - Liver function
 - Concurrent medications
 - Oral contraceptives can double half life
 - Fluvoxamine (Luvox®) can reduce clearance by 90% and extend half life by 10 fold
 - Fluoroquinolone antibiotics reduce clearance
 - European research looked at 47K subjects for genetic variants of metabolism: faster metabolizers consume more

Caffeine Restriction in Sweden

Decrease in the number of intentional caffeine related intoxications after OTC single purchase restriction from 250 to 30mg in 2004



NICOTINE



Treatment of nicotine addiction: varenicline (Chantix) nicotinic partial agonist. Patches too.

*it's the pulse of nicotine (puff) that causes euphoria which drives addiction, the meds create consistent low level just enough to reduce craving, but avoid withdrawal.

THE END PART 2

- Questions?
- Comments?
- Share Ideas?
