PHARMACOLOGIC MANAGEMENT OF SUBSTANCE USE DISORDERS

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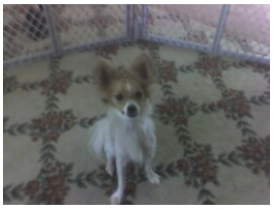
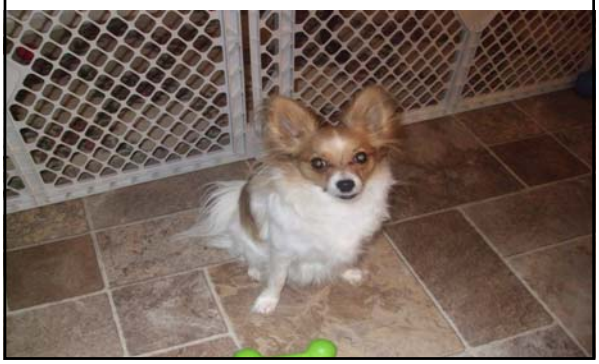
April 17, 2012

Logan – "The Alpha Male"

Luke – "The Million $ Dog"



Luke – "Today"



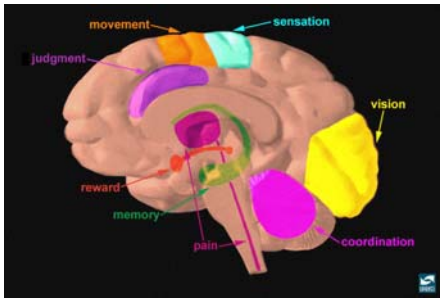
Learning Objectives

- 1. Discuss the pharmacologic therapies for detoxification for substance use disorders.
- 2. Discuss the pharmacologic therapies for relapse prevention for substance use disorders.

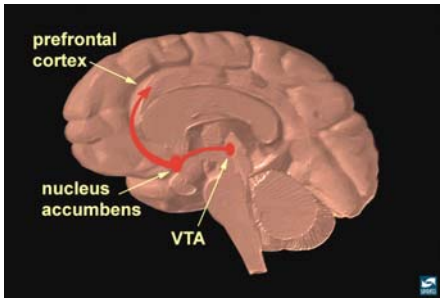
My Belief About Addiction

- A biopsychosocial & spiritual disease model
- A chronic disease, that is, one that is never cured but one that is managed and controlled
- Relapse prevention is a vital concept to understand, explore & embrace
- One does not elect to become addicted
- Every person has some type of addiction
- Addictions is a disease of the BRAIN

The Brain



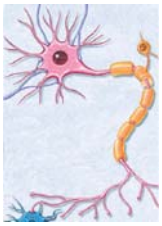
Addiction and the Brain



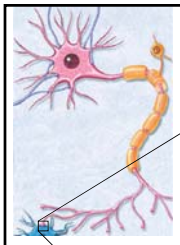
Four Primary Areas

- Ventral Tegmental Area (VTA)
- Nucleus Accumbens
- Amydala
- Prefrontal Cortex

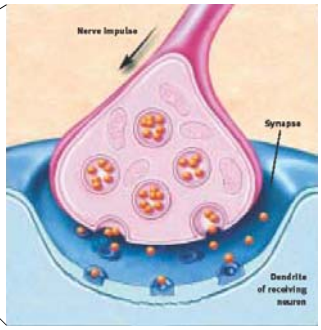
Neurons communicate by sending signals to each other at specialized connections.



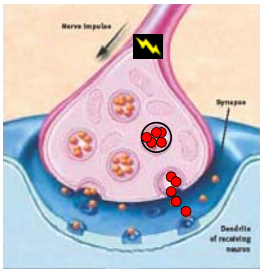
What is the connection between two neurons called?



S Y N A P S E !



The Synapse: Sending and Receiving

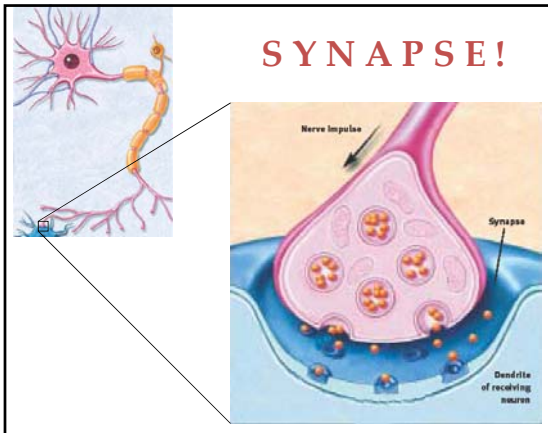


The terminals of the sending neuron has **vesicles** packed with **neurotransmitters**

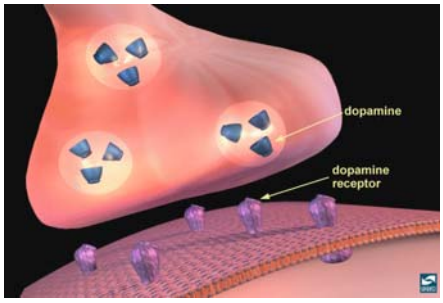
Neurotransmitters are released when the sending neuron fires

Neurotransmitters send the signal by binding to specific **receptors** on dendrites of the receiving neuron

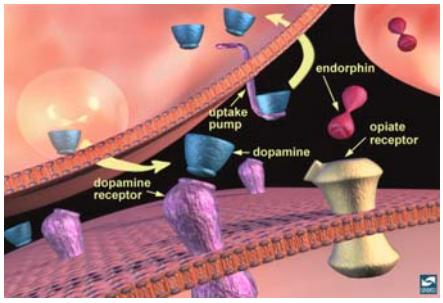
SYNAPSE!



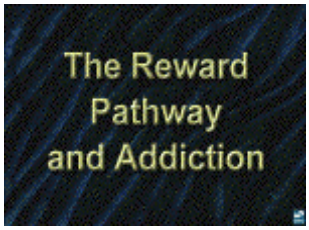
Receptors



Dopamine and Opiate Receptors

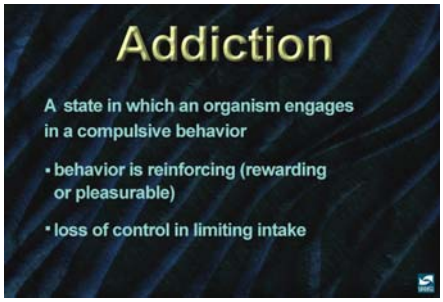


Pathway to Addiction

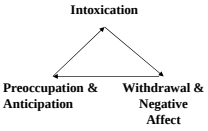


Natural Rewards

Addiction



Cycle of Addiction



Morphine is a powerful pain killer used in hospitals

What street drug of abuse is related to morphine?

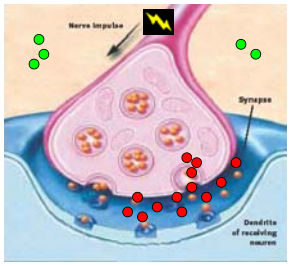
Heroin (also opium & methadone)

What's happening outside?

Behavioral effects of heroin use include:

- "rush" = euphoria, reduced anxiety, nausea, drowsiness
- "withdrawal" = intense muscle aches & pain, piloerection, fever, diarrhea, irritability, increased lacrimation (rhinorrhea, tearing of eyes)
- Primarily snorted or used intravenously
- DEATH by respiratory arrest

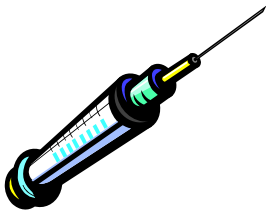
What's happening inside?



Activation of opiate receptors = increased transmission = "rush"

Narcotics/Opioids

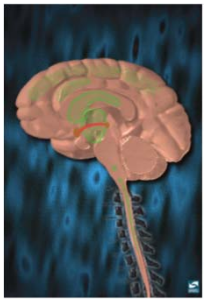
- Derived from the opium poppy
- Used medically as pain killers with the exception of heroin
- Blocks pain, produces euphoria
- Highly addictive
- Found in snortable, smokable, injectable forms
- ER visits have increased by 50% over the past 2 years



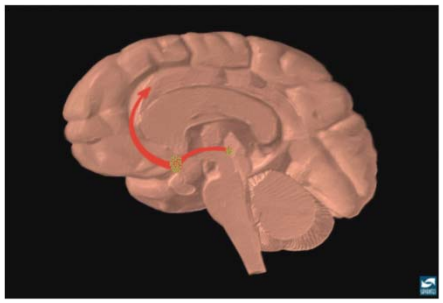
Opioid Addiction

- Morphine
- Heroin
- Codeine
- Oxycodone
- Meperidine
- Fentanyl

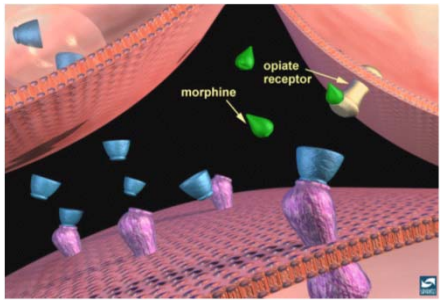
Action of Heroin



Action of Morphine



Morphine and Opiate Binding Sites



Opioids

- If dependence develops, drug procurement often dominates the individual's life and often leads to criminal behavior.

Opioids

- Heroin (diacetylmorphine) is more lipid soluble than Morphine and therefore crosses the blood brain barrier more easily
- Causes more intense euphoria and sedation
- Quickly metabolized
- Excreted in the urine as free or conjugated morphine
- Euphoria, sedation, and analgesia are the desired effects

Heroin

- Overdoses may cause respiratory depression, bradycardia, hypothermia, and death.

Method of Use

- Intravenous
- Nasal Insufflation (snorting)

Complications

- Overdoses may result from variability in the potency of the heroin purchased on the street, rapid loss of tolerance after abstinence, and concurrent use of other central nervous system depressants.
- Other physical complications

Withdrawal

- Symptoms start within 2 to 48 hours of last use
- Abrupt withdrawal of heroin, which has a short half-life, causes prompt and severe withdrawal symptoms

Withdrawal Symptoms

- Restlessness
- Lacrimation
- Rhinorrhea
- Nausea
- Mydriasis
- Muscle Aches
- Diarrhea

Withdrawal Symptoms

- Piloerection
- Tachycardia
- Hypertension

Management

- Clonidine
- Phenobarbital
- Librium
- Suboxone or Subutex
- Symptomatic, for example, Tigan for nausea and vomiting
- Levsin & Robaxin, Flexeril
- Counseling/Psychotherapy/Alternative Therapies

Relapse Prevention

- Naltrexone in dosages previously described
- Note – Can NOT begin Naltrexone Rx. until the patient is opioid naïve for 10 days
- Suboxone
- Subutex
- Methadone

Suboxone

- Buprenorphine, a partial opioid receptor agonist/antagonist
- Drug Addiction Treatment Act of 2000 allows qualified physicians to treat opioid-dependent patients with sublingual Suboxone in their practices
- Suboxone provides a new management option for opioid dependent clients

Suboxone

- Physicians must complete an approved 8 hour course on Suboxone treatment
- Physicians can only have a maximum of 30 (recently changed to 100) clients in their practice at one time
- If more than one physician is in the practice, then an additional clients can be added per physician as long as above requirements are met
- DEA monitors physicians prescribing Suboxone
- ***Advanced Practice Nurses can not prescribe Suboxone***

Suboxone

- Occupies opioid receptor sites
- Blocks effects of opioid agonists
- Not easily displaced by other opioids
- Lower potential for abuse
- Less physical dependence
- Reduced cravings
- Greater safety in accidental overdose

Suboxone

- Initiation of therapy can vary
- Administered sublingually as a tablet
- Now available as melt away strip
- Once daily dosing
- Milder withdrawal profile
- Can be dispensed for take home use
- Maintains clients in outpatient treatment
- Best results are when pharmacology is combined with psychosocial treatment and counseling

Butrans

- Buprenorphine Transdermal System for chronic pain

Methadone

- Most frequently used medication for opioid addiction treatment
- Allows patients to socialize and function normally
- Prevents physical withdrawal symptoms
- Relieves the craving of opioids

Benefits of Methadone

- Administered orally
- Once daily dosing
- Minimal side effect profile
- Safe and effective when dosed correctly

Pharmacology of Methadone

- Long-acting full opioid receptor agonist
- Functions at mu receptor sites
- Mu receptor sites exist on the surfaces of brain cells
- Belief is that the activation of the mu receptors are responsible for the analgesic and euphoric effects of opioids

Methadone Kinetics

- 80% bioabsorption
- Blood levels peak within 2 – 4 hours
- Pain relief within 4 – 6 hours
- Half life is 24 – 36 hours
- Steady state reached within 5 – 7.5 days
- *Note: Blood levels are influenced by absorption, metabolism, protein binding, urinary pH, other medications, diet, age, physical activity level, pregnancy & vitamins*

Methadone Induction

- Induction is the most risky phase of methadone maintenance treatment.
- START LOW & GO SLOW!!!
- Treatment must be individualized
- Optimal doses for patients will vary
- Understand the cumulative property of methadone
- Communicate with patients

Initial Dose

- Use COWS (Clinical Opiate Withdrawal Scale)
- Score Maximum Initial Dose
- 0 – 5 (no wd) 0 mg.
- 5 – 12 (mild wd) up to 15 mg.
- 13 – 24 (Moderate wd) up to 20 mg.
- 25 – 36 (Mod.Sev.wd) up to 25 mg.
- > 36 (Severe wd) up to 30 mg.
- *Note: If withdrawal does not follow, methadone treatment cannot be initiated.*

Goals of Methadone Therapy

- Ensure individualized and "adequate dose."
- Titrate dose to achieve a steady-state with methadone levels (clinically determined) in the "comfort zone" throughout and beyond the dosing interval.
- Allow time to react to the initial dose
- Allow time to react to a dose increase (3-5 days).
- Avoid overly aggressive (toxicity, overdose) and ultra-slow titration of dosing (continued illicit drug use).
- Continued assessment and monitoring of the patient is essential.

Methadone's Cumulative Effect

- Dose A is 30 mgs. daily with no increase for 6 days. Cumulative effect by day 6 is equivalent to 59.0625 mgs. of the drug.
- Dose B has an initial dose of 30 mgs. On day 1 and then the dose is increased daily by 10 mgs. for another 5 days, i.e. day 2 the dose is 40 mgs., 50 mgs., 60 mgs., 70 mgs., 80 mgs. Thus by day 6 the cumulative effect of dosing is 139.6875 mgs.

Keys to Methadone Therapy

- ANY SIGN OR SYMPTOM OF OVER-MEDICATION DURING THE EARLY INDUCTION PHASE REQUIRES A DOSE REDUCTION!!!
- Beware of the subtle signs/symptoms of overmedication; i.e. feeling good, extra energy, staying awake at work, etc.
- Patients may need more TIME, not more MEDICATION!!!

Adverse Reactions

- Constipation
- Excessive sweating
- Paresthesias in hands and feet
- Weight gain
- < libido/sexual dysfunction
- Rash

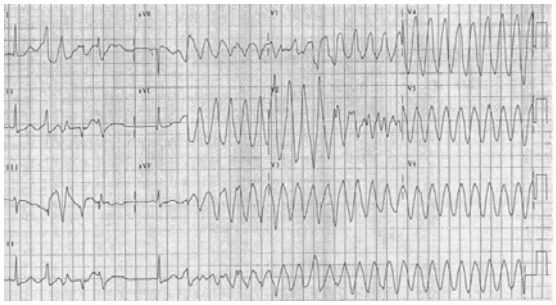
Health Conditions That May Affect Dose

- Age
- Hepatitis C
- HIV/AIDS
- Cardiac Risk
- Pain
- Pregnancy
- Lactation

Cardiac Adverse Effects

- **FDA Black Box Warning**
- Prolonged QT syndrome in doses greater than 200 mgs. or with IV administration
- QT prolongation may lead to Torsades de Pointes
- Need to assess individual risks
- EKG pre administration???

Torsades de Pointes



Drug Interactions

- Multiple drug interactions exists:
- Sedatives
- Antidepressants
- HIV Medications
- Antibiotics & Antifungals especially Cipro, Fluconazole and Rifampin
- Inducers and Inhibitors of the CYP 450 enzyme system

Relapse Prevention

- No relapse prevention medication can be effective without counseling and psychotherapy.
- The issues and triggers in a patient's life that contribute to dependence and addiction must be explored and addressed

Alcoholism

- 90% of US population uses alcohol
- Amount & frequency of use vary
- Approximately 10% of men meet DSM-IV criteria
- Approximately 3% to 5% meet DSM-IV criteria
- Elderly drink less frequently and lesser amounts of alcohol resulting in their disease being less identifiable according to the criteria established

Medical Complications of Alcoholism

- GI Tract
- Cardiovascular System
- Metabolic Changes
- Central Nervous System Changes
- Nutritional Deficiencies
- Hematopoietic System Changes

Major Diagnostic Tests

- CAGE Questionnaire
- Elevated Liver Enzymes, especially GGT (gamma glutamyl transpeptidase)
- Increased Mean Corpuscular Volume

CAGE

- CAGE
- Have you tried to CUT DOWN on your drinking?
- Are you ANNOYED by people telling you to stop drinking?
  Do you feel GUILTY about your drinking?
  Do you drink on first getting up in the morning (EYE OPENER)?
- Two or more yes responses = (+) test

Detoxification Treatment

- Thiamine 100 mg IM or PO either daily or BID for 3 days, then Thiamine 100 mg po daily for LOS
- Folate 1 mg po daily for LOS
- Tegretol 200 mg po BID for LOS (in select patients)
- Serum Tegretol level after 5 - 7 days
- Patients must be weaned off of Tegretol

Detoxification Treatment

- Librium 50 mg po every 6 hours
- Librium 25 mg po every 6 hours prn for increased s/s of withdrawal
- Decrease dosing daily according to patient response until completely weaned off of medication
- Clonidine 0.1 mg po every 6 hours with holding parameters of systolic BP< 100 or heart rate < 50 - decrease dose on daily basis until weaned off of medication
- Assess patient with CIWA scale prior to administration of Librium

Detoxification Treatment

- Ativan instead of Librium
- Serax effective when liver impairment is present
- Counseling/psychotherapy
- AA
- 12 Step Program
- ALANON

Relapse Prevention

- Campral 666 mgs. TID
- Naltrexone (Revia) 25 mgs. daily at bedtime x 3 nights then increase Naltrexone to 50 mgs. daily at bedtime daily thereafter
- Naltrexone oral challenge
- Vivitrol 380 mgs. once monthly
- Combination of Vivitrol and Campral therapy
- Disulfiram (Antabuse)

Counseling and Psychotherapy

- No relapse prevention medication can be effective without counseling and psychotherapy.
- The issues and triggers in a patient's life that contribute to dependence and addiction must be explored and addressed.

References

- Adams. P.M. & Koch, R.W. (2010). Pharmacology: Connections to nursing practice. Upper Saddle River, NJ: Pearson Education, Inc.
- Edmunds, M.W. & Mayhew, M.S. (2009). *Pharmacology for the primary care provider. 3rd Edition.* St. Louis, MO: Mosby, Inc.

WEB Sites

- http://www.nih.gov/
  (National Institutes of Health)
- http://www.samhsa.gov/about/csat.aspx
  (Centers for Substance Abuse Treatment)
- http://www.samhsa.gov/
  (Substance Abuse and Mental Health Services Administration)

Questions

- That's All Folks!!!

Contact Information

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