



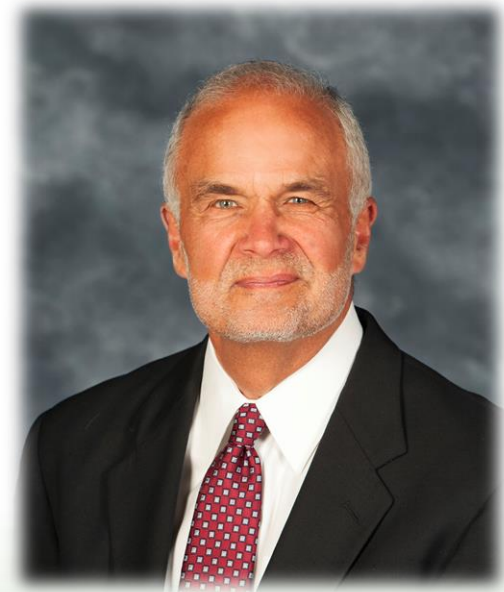
# Advanced Treatment for Opioid & Alcohol Dependence

John Larson, M.D.  
Corporate Medical Director  
Gateway Foundation



# Background

- 41 years practicing psychiatry
- Last 15 in addiction medicine
- I've watched a number of failed attempts to find a “magic pill”
- Hopeful skeptic



# Overview

- Historical background, treatment philosophy
- Brief review of common neurotransmitters and receptors
- Drugs of abuse and how we think they work
- The nature of cravings
- Medications used in addiction medicine and how we think they work
- Problems and controversies
- Q and (hopefully) A

# Audience Poll

In my opinion, medication assisted treatment:

- A. Is effective
- B. Is not effective
- C. May be effective but is a problem ethically
- D. I have no experience with it

# Historical Background

- Freud proposed the idea that drug use/abuse was an attempt to self-medicate
- Subsequent failure to view addiction as a problem of its own
  - Psychoanalysis could cure addiction by treating the underlying problem
  - Discovery of antidepressants and anxiolytics
- Social model



# Treatment Philosophy

- Polar extremes
  - Abstinence from all “mind-altering” substances
  - Penn and Teller model
- Sobriety vs. Harm-reduction
  - Thinking
  - Interpersonal relationships
  - Meaning

# Audience Poll

Heroin withdrawal symptoms can last up to:

- A. 24 hours
- B. 48 hours
- C. 72 hours
- D. 1 Week



# Potential Roles for Medication

- Withdrawal/detox
- Ease craving during early phases of treatment
- Long-term craving management
- Substitution
  - months to years
  - lifelong



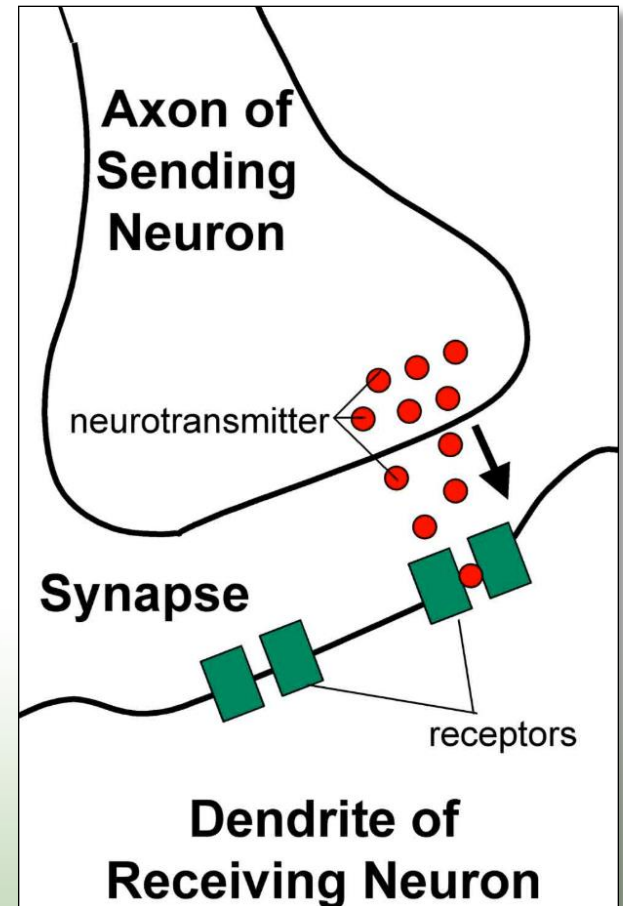


# Withdrawal/Detox

- Generally uncontroversial
  - Risk if not treated
    - Physical risk
    - Pre-mature termination of treatment
  - Course of treatment is relatively brief
- Alcohol and sedatives
  - benzos
- Opiates
  - Subutex<sup>®</sup> or Suboxone<sup>®</sup>
- Stimulants
- Psychedelics

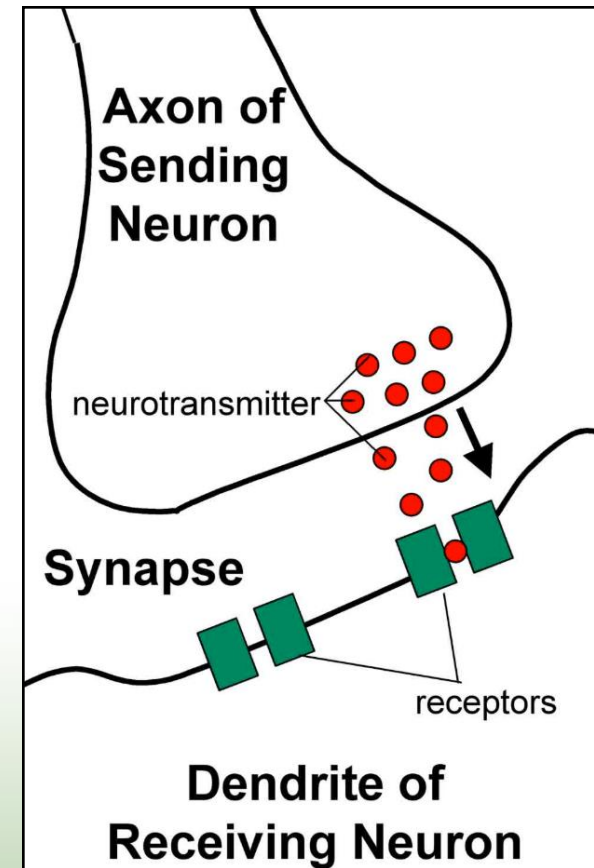
# Intro to Neurochemistry

- Important neurotransmitters
  - Dopamine, GABA, endorphins, serotonin, glutamate, endogenous cannabinoids
- Important neuroreceptors
  - Dopamine, GABA, serotonin, opioid, nicotinic, MDMA, glutamate, cannabinoid
- Agonists, antagonists, and partial agonists

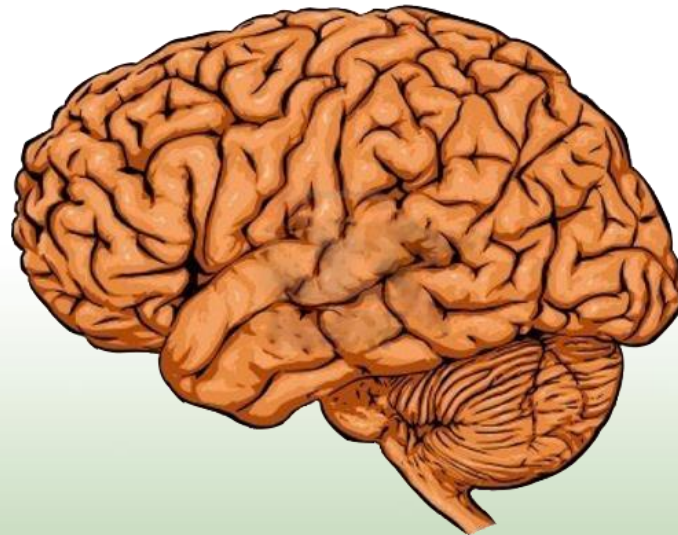


# Possible Ways to Alter Neurochemistry

- Directly stimulate receptor (agonist, partial agonist)
- Stimulate release
- Inhibit re-uptake
- Increase synthesis
- Enhance endogenous neurotransmitter action
- Block receptor (antagonist)
- Down- or up-regulation

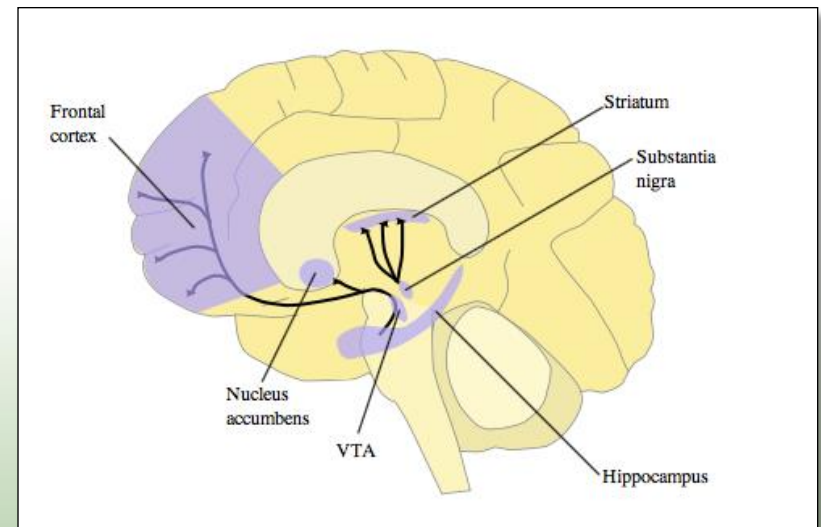


# The brain works hard to maintain homeostasis



# Dopamine

- Major role in motivation/reward
  - Food (sugar, fat, salt, chocolate), sex, nurturing
  - Final common pathway for most drugs of abuse
- Movement
  - Parkinson's Disease
  - Restless leg syndrome



# Primary (Known) Action of Addictive Substances

- Alcohol and sedatives
  - GABA and dopamine indirectly
- Opiates
  - Dopamine indirectly
- Stimulants
  - Dopamine
- Food
  - Dopamine
- Nicotine
  - Dopamine indirectly
- Caffeine
  - Multiple sites of action





# Other Abused Substances

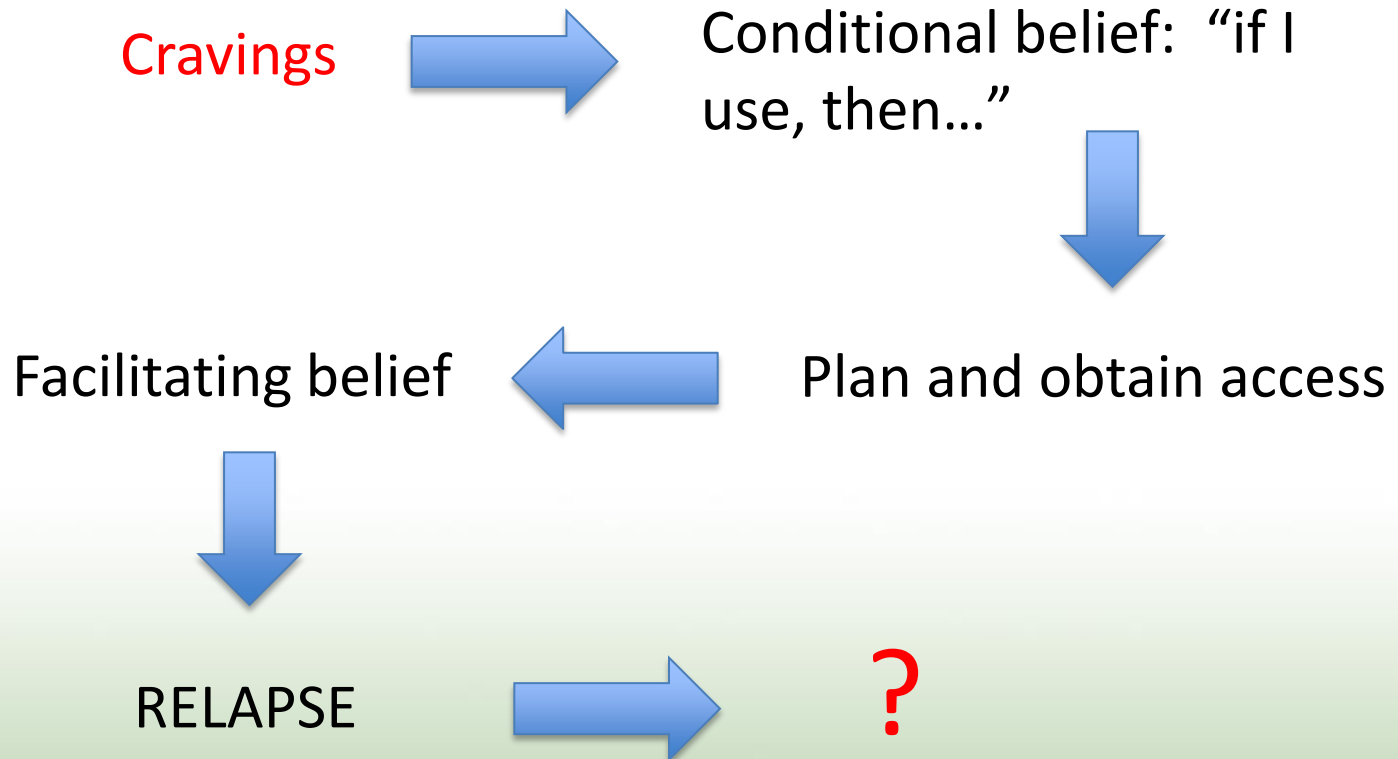
- Marijuana
- K2
- Bath salts and other Khat drugs
- Club drugs
- Inhalants
- Hallucinogens
  - LSD
  - Psilocybin
  - Mescaline
  - Dextromethorphan
- Carbonated drinks



# Cravings

- Urge to use
  - Post-acute withdrawal
  - Sensory cues produce a neurochemical reaction
  - Relapse
- Urge to continue using once started: “The salted peanut effect”

# Cognitive Model of Relapse



# MAT General Considerations

- FDA approved use
- “Off-label” use
- Reduce cravings
  - Urge to use
  - Urge to continue using
- Modestly effective

# Specific Drugs

- Disulfiram<sup>®</sup> (Antabuse<sup>®</sup> )\*
- Acamprosate<sup>®</sup> (Campral<sup>®</sup>)\*
- Naltrexone<sup>®</sup> (Revia<sup>®</sup>, Vivitrol<sup>®</sup>)\*
- Buprenorphine<sup>®</sup> (Suboxone<sup>®</sup>, Subutex<sup>®</sup>)\*
- Vareniclyline<sup>®</sup> (Chantix<sup>®</sup>)\*
- Bupropion<sup>®</sup> (Wellbutrin<sup>®</sup>, Zyban<sup>®</sup>)\*
- Baclofen<sup>®</sup>
- Topiramate<sup>®</sup> (Topamax<sup>®</sup>)
- Ramonabant<sup>®</sup> (Bethin<sup>®</sup>)
- Provigil<sup>®</sup>
- Odansetron<sup>®</sup> (Zofran<sup>®</sup>)
- Cocaine vaccine

# Disulfiram<sup>®</sup> (Antabuse<sup>®</sup>)

- Around since 1951
- Blocks the metabolism of alcohol producing acetaldehyde (responsible for hangover)
- Results in headaches, nausea, even death
- May block dopamine metabolism
- Essentially no effect on physiological craving
- Side effects and precautions
- Indications
  - Alcoholism
  - Off-label for cocaine addiction



# Acomprosate<sup>®</sup> (Campral<sup>®</sup>)

- Approved in 2004
- GABA agonist, glutamate antagonist
- Does seem to have a modest effect on alcohol cravings, not so much on the urge to continue after the first drink
- Side effects and precautions
  - GI distress, dizziness, kidney disease, dosing issues
- Indications
  - Alcoholism with repeated relapse
  - Combination with naltrexone

# Naltrexone<sup>®</sup> (Revia<sup>®</sup>, Vivitrol<sup>®</sup>)

- Approved 1984 for opiate addiction, 1994 for alcoholism
- Used more in alcoholism
- Oral (Revia<sup>®</sup>) or injectable (Vivitrol<sup>®</sup>) or implant ?
- Opioid antagonist
- Reduces cravings, especially urge to continue after first drink, blocks opiate high
- Side effects and precautions
  - Liver issues, injection site soreness, expense, pain management
- Indications
  - Alcoholism
  - Opiate addiction
  - Combination with Acamprosate
  - Off-label use in self-mutilation
  - Comment about ultra rapid detox

# Buprenorphine<sup>®</sup>

## (Suboxone<sup>®</sup>, Subutex<sup>®</sup>)

- Approved 2002
- Opiate receptor partial agonist, “dog in the manger”
- Use in opiate detox (2 weeks or less) is uncontroversial
  - Subutex in pregnancy and nursing mothers
  - Suboxone contains Naloxone (Narcan) and is taken sublingually
  - Also available as a film
- Use in craving management and maintenance remains hotly debated
- Studies support efficacy in longer term withdrawal (months) and as a maintenance drug
- Side effects and precautions
  - Headache, constipation, sleep problems, depression?
  - Induction protocol, dosing issues
  - Diversion (weekday maintenance and weekend opiate use)
  - Difficulty getting clients from Suboxone to Naltrexone
- Indications
  - Opiate addiction
  - Prescription opiates and comorbid pain issues
  - Off label use in depression

# Vareniclycline<sup>®</sup> (Chantix<sup>®</sup>)

- Approved in 2006
- Partial nicotinic receptor agonist (another dog in the manger)
- Reduces cravings and blocks the pleasurable effect of nicotine
- Side effects and precautions
  - Nausea is common, depression and suicide, while rare, have prompted the FDA to require a “black box warning”
- Indications
  - Smoking cessation

# Bupropion<sup>®</sup> (Wellbutrin<sup>®</sup>, Zyban<sup>®</sup>)

- FDA approved as an antidepressant since 1985, as a smoking cessation aid since 1995
- Nicotinic receptor antagonist
- Blocks pleasurable effect of nicotine, reduces cravings
- Side effects and precautions
  - Seizures, black box warning regarding suicide risk common to all antidepressants
- Indications
  - Smoking cessation
  - Off-label use in methamphetamine addiction

# Miscellaneous

- Baclofen<sup>®</sup>, a muscle relaxant, demonstrated to be effective in reducing alcohol craving, small study, used in some VA harm-reduction studies, shows promise
- Topiramate<sup>®</sup> (Topomax<sup>®</sup>) an anticonvulsant and recently approved appetite suppressant with numerous off-label uses, used with mixed reviews as an anti-craving drug
- Ramonabant<sup>®</sup> (reverse marijuana, Bethin<sup>®</sup>) marketed as an appetite suppressant in Europe. Showed some promise as an alcohol craving suppressant but taken off the market due to deaths
- Cocaine vaccine reportedly under study at Cornell. Human trials scheduled to begin within a year.



# Other Considerations

- No matter how you explain it, the client often thinks it's a magic pill and a way to avoid the hard work of recovery
- The effect is modest at best
- Treating team member attitudes color the transaction
- Attitudes of family and outside support system
- Does MAT offer any promise re “food addiction”?

# MAT at Gateway Foundation

- Evidence-based use
- Used only in the context of a comprehensive recovery program
- Sobriety remains the primary goal
- One size does not fit all

# Summary

- Dopamine is the major neurotransmitter in our brain's reward system
- Dopamine is the common pathway for all addictive substances
- The brain tries desperately to maintain status quo
- MAT focuses on three aspects of recovery
  - Acute withdrawal
  - Urges to use
  - Urges to continue to use once started
- Gateway relies primarily on FDA approved medications
  - Antabuse, Campral, Revia or Vivitrol, Suboxone
  - Does not preclude an off-label use if supported by controlled studies and client needs

# Questions?