Advanced Treatment for Opioid & Alcohol Dependence

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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® or Suboxone®
• Stimulants
• Psychedelics
Intro to Neurochemistry

• Important neurotransmitters
  – Dopamine, GABA, endorphins, serotonin, glutamate, endogenous canabanoids
• Important neuroreceptors
  – Dopamine, GABA, serotonin, opioid, nicotinic, NDMA, glutamate, canabanoid
• 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

Cravings \[\rightarrow\] Conditional belief: "if I use, then..."

Facilitating belief \[\leftarrow\] Plan and obtain access

RELAPSE \[\rightarrow\] ?
MAT General Considerations

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

- Disulfiram® (Antabuse®)*
- Acamprosate® (Campral®)*
- Naltrexone® (Revia®, Vivitrol®)*
- Buprenorphine ® (Suboxone®, Subutex®)*
- Vareniclycline ® (Chantix®)*
- Buproprion® (Wellbutrin®, Zyban®)*
- Baclofen®
- Topiramate® (Topamax®)
- Ramonabant® (Bethin®)
- Provigil®
- Odansetron® (Zofran®)
- Cocaine vaccine
Disulfiram® (Antabuse®)

• 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® (Campral®)

• 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® (Revia®, Vivitrol®)

- Approved 1984 for opiate addiction, 1994 for alcoholism
- Used more in alcoholism
- Oral (Revia®) or injectable (Vivitrol®) 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®
(Suboxone®, Subutex®)

• 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® (Chantix®)

• 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
Buproprion®
(Wellbutrin®, Zyban®)

• FDA approved as an antidepressant since 1985, as a smoking cessation aide 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®, a muscle relaxant, demonstrated to be effective in reducing alcohol craving, small study, used in some VA harm-reduction studies, shows promise

• Topiramate® (Topomax®) an anticonvulsant and recently approved appetite suppressant with numerous off-label uses, used with mixed reviews as an anti-craving drug

• Ramonabant® (reverse marijuana, Bethin®) 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?