TAKING CONTROL
The Many Faces of Addiction
Part I I

by

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Radio 08/20/09

Introduction

- John 6:37 – "All that the Father giveth me shall come to me; and him that cometh to me I will in no wise cast out.
- I Corinthians 3:16 - "…ye are the temple of God…"
- I Corinthians 3:23 – "… ye are Christ's…"
- I Corinthians 6:12 - "All things are lawful unto me, but all things are not expedient."
- I Corinthians 6:20 – "For ye are bought with a price…"
- I Corinthians 10:31 - Whether therefore ye eat, or drink, or whatsoever ye do, do all to the glory of God.

- Outline
  - the Bible and addictions
  - drugs of abuse – points of interest
  - drugs of abuse – street name
  - drugs of abuse – sites of action
  - symptoms of alcohol withdrawal
  - alcohol screening questionnaire
  - statistics on drugs of abuse
  - malfunction of reward circuits in addiction
  - methamphetamine
  - marijuana
  - opiate addiction
  - Xyrem (GHB) addiction
  - substance use disorder treatments tried – opioids, alcohol, cocaine, THC, nicotine
  - resources
- drugs of abuse—points of interest
  - most unlikely to quit – nicotine
  - most deadly – nicotine (15% of deaths)
  - most vehicle accidents – alcohol (50%)
  - most homicides – alcohol (50%)
  - most suicides – alcohol (25%)
  - drug craving for cocaine – lasts months
  - opioids (IV) associated with HIV and hepatitis C
  - testing deters use (military 1981 48% → 2000's 3%)
  - In 1512 Juan Ponce de Leon, after searching in vain for the fountain of youth, brought the tobacco plant to Portugal; this is ironic since each cigarette ages the user 15 minutes.

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        - most potent stimulant of natural origin – cocaine
        - annual tobacco use in USA
            - 1900 = 2.5 billion cigarettes
            - 1981 = 640 billion cigarettes
            - 2000 = 430 billion cigarettes
    - benzodiazepines
        - introduced 1960's
        - popular 1970's
        - backlash 1980's
        - upturn 2000's
    - polysubstance abuse common today: for example, 90% of alcoholics are heavy smokers
    - substance abuse is associated with leading causes of adolescent mortality (MVA, suicide, violence, sexual behavior)
    - most widely used illicit drug in USA – marijuana
    - marijuana decreases male and female hormones
    - dual diagnosis information:
        - 50% of those with a substance use disorder have at least one other psychiatric disorder.
        - 30% of those with a psychiatric disorder have a substance use disorder.
    - prevalence of drugs abuse in adolescents
        - 1980's = decreased
        - 1990's = increased
        - 2000's = leveled off
    - gateway drugs
        - 50% started by sixth grade
        - gateway drugs are tobacco, inhalants, alcohol
- Drugs of abuse—selected street names of drugs of abuse
    - ice – methamphetamine (smoke)
    - angel dust – PCP
    - ecstasy – MDMA
    - liquid ecstasy – GHD
    - window panes – LSD
    - pasta – cocaine (smoke)
    - crack – cocaine (smoke)
    - toot, snow, white lily – cocaine
    - speedballing – cocaine + heroin (IV)
    - liquid lady – cocaine + alcohol (PO)
    - hookah, shirka, boory, goza, nargile, arghile, hubble bubble – smoking tobacco through a pipe
    - crack – cocaine
    - crank (crystal or crystal ice) – methamphetamine
    - cheese – heroin + Tylenol PM
- Drugs of abuse—sites of action
    - alcohol = ↑GABA-A, ↓glutamate = ↑D

- barbiturates = ↑GABA-A
- benzodiazepines = ↑GABA-A
- cannabis (THC) = CB1 cannabinoid receptor (agonist)
- nicotine = ↑Ach (nicotinic) = ↑D
- opiates = ↑mu and delta
- PCP (phencyclidine) and ketamine (an analgesic) = antagonist NMDA
- cocaine = blocks reuptake of dopamine, NE, 5HT, also a neurotransmitter release stimulator
- amphetamine = ↑D → release stimulator, other D augmenting actions as well

- Drugs of abuse—symptoms of alcohol withdrawal
  - elevated or fluctuating pulse, blood pressure, and temperature
  - hallucinations
  - seizures
  - anxiety
  - agitation
  - diaphoresis (↑ perspiration)
  - tremors
- Drugs of abuse—TWEAK test—do you have an alcohol problem?
  - T - tolerance
  - W - worry of friend
  - E - eye opener to get going
  - A - amnesia
  - K - tried to cut down
- Drugs of abuse data—individual studies
  lifetime prevalence
  - alcohol—13.5%
    - alcohol comorbid psychiatric—37%
    - alcohol w/MDD—9.6%
  - drug—6.1%
    - drug comorbid psychiatric—53%
  - any psychiatric diagnosis—29% had a substance use disorder
  - MDD—21% had alcohol use disorder
  - bipolar I disorder—61% had a substance use disorder
  - bipolar I and II—45% had an alcohol use disorder
  - substance use disorder—20% had ADHD
  - PTSD
    - 75% had alcohol use disorder
    - another study—33% had substance use disorder
  - schizophrenia—30% had alcohol and drug use disorder
- ***reward circuits in health and addictions***
  In the normal reward circuit from sex in marriage to exercise to feelings of accomplishment the neurotransmitter dopamine is released which encourages repetition of the behavior. Brain centers important in reward include the limbic brain (amygdale, hippocampus, and nucleus accumbens) and the cerebrum (prefrontal cortex, DLPC, VLPC, OFC, and ACC). Chemicals include dopamine

(D) and glutamate (Glu). Dopamine (D) is released not only during the healthy activity but also from the memory (anticipation) of the event. Addictive drugs or behavior subvert the reward system. With addiction a dopamine rush is delivered to the nucleus accumbens. Through repetition the dopamine becomes depleted and a feedback system to the various parts of the brain is shut off. Desire for the drug or inappropriate behavior trumps other desires. The drug or inappropriate behavior no longer provides the desired pleasure or reward but everything else (pleasure from faith, family, and friends) provides even less. However, the brain continues to receive some dopamine by the repetition of the drug or inappropriate behavior.

Relapse can come after months of recovery because of memories that can be triggered by various cues that give a rush of dopamine that create a craving again for the drug or inappropriate behavior.

In addictions the neurons eventually change; transcription factor delta FosB (an RNA protein) in the nucleus accumbens cause new dendrite connections that respond to memory cues that increase the risk of relapse for months and even years. Glutamate (Glu) is an important neurotransmitter in learning and memory; addictive behaviors or drugs alter the responsiveness of neurons to glutamate. Long term memories are formed by FosB; FosB turn on genes that manufacture proteins that strengthen neural connections; thus, the craving will not go away. The addict becomes a slave for the memories.

In summary the chemical addiction cycle is as follows:

- After a potentially addicting drug or behavior a dopamine rush is delievered to the nucleus accumbens of the emotional limbic brain and intense pleasure is felt.
- Repetition of the inappropriate behavior or drug use occurs in order to again experience the pleasure.
- Eventually deplete dopamine occurs.
- The feedback system of the cerebrum and other parts of the limbic brain malfunctions.
- Decreased pleasure occurs with the addictive drug or behavior.
- Increased desire for a more intense experiencing of the drug or behavior occurs. A higher level of addictions in behavior occurs.
- Desire for the drug or inappropriate behavior trumps other healthy desires (faith, family, and friends). Faith, family, and friends are neglected.
- Perhaps abstinence occurs.
- However, memory cues with environmental encouragement, release dopamine that can cause release.
- Neuronal damage continues. Transcription factor delta FosB (an RNA protein) in the nucleus accumbens causes more dendrite connections; glutamate has increased with increased memories of the

addictive experience; the addiction continues. Also, when inappropriate highs are sought, axonal degeneration occurs resulting in ↓ dopamine.

In the healthy and normal reward circuits (sex in marriage, accomplishments, exercise, etc.) dopamine is also released in the nucleus accumbens of the limbic brain producing pleasure. The feedback system in the cerebrum and other parts of the limbic brain is intact and the person is satisfied with the pleasure experienced; no excessive sprouting of the dendrites has occurred, no neuronal damage has occurred, and undue craving does not occur.

The diagnostic criteria for substance dependence may create tolerance and withdrawal problems. People who are dependent on chemical substances may use larger amounts of chemicals or for longer periods than intended. They may have a desire to stop, but they have unsuccessful attempts to stop. Much time is spent obtaining the substances. Abusers may give up social, occupational, and recreation activities. Substances use continues despite the knowledge of the problem. In summary, symptoms of substance dependency may include:

- using more drug for longer periods
- desire to stop
- unsuccessful attempts to stop
- much time spent obtaining the drug
- giving up social, occupational, recreational activities
- continued use despite knowledge of the problem

- ***methamphetamine***

  Methamphetamine is the most widely used illegal drug in the world after cannabis. It works through the dopamine system. It can cause irreversible neuronal damage. It can induce paranoia, hallucinations, and numerous cardiovascular side effects. Street names include speed, crank, crystal, ice, and tina. It's half-life is 8-12 hours.

- ***marijuana***

  Marijuana is a drug of abuse. Intoxication symptoms can include euphoria, altered perceptions, rapid heartbeat, anxiety, paranoia, red conjunctiva, and incoordination. Smoked marijuana may be carcinogenic. It has been experimented with for medical reasons—pain, nausea, weight loss. THC (tetrahydrocannabinol) is the main ingredient in marijuana. THC use might be decreased with BuSpar (buspirone) or Prozac (fluoxetine).

  Lifetime marijuana dependency is associated with a two-to-sevenfold increase in the risk of MDD (major depressive disorder).

- ***marijuana addiction: neurotransmitters and treatments tried***
  - The active ingredient of marijuana is THC (delta 9-tetrahydrocannibol); it acts at CB1 presynaptic cannabinoid receptors that triggers dopamine release in the nucleus accumbens of the limbic brain. Other brain areas involved include the VTA and the amygdale.
  - CB1 receptors play a role in not only marijuana addiction but also in other addictions—alcohol and food (sugars and fats).

- Rimonabant is a CB1 antagonist that has been tried in the treatments of various addictions—marijuana, alcohol, and food.
- Buspirone (Buspar) has been tried in treatment.
- Nefazodone (Serzone) has been tried in treatment.

- ***opiate addiction: neurotransmitters and treatments tried***
  - Opiates are neurotransmitters from the arcuate nucleus to the VTA in the midbrain to the nucleus accumbens in the limbic brain. There are three types of opiate receptors—mu, delta, and kappa; pain relievers use mu the most. Endogenesis opiates include endorphins and enkephalins. Opiates in ascending doses produce pain relief, euphoria, calmness, sedation, mood changes, respiratory depression and coma. They can in some people produce addiction and tolerance if used too long.
  - Withdrawal signs include craving, sadness, anger, tremor, rapid heartbeat, automatic hyperactivity, sweating, and piloerection; clonidine is an alpha 2 agonist that has been used to treat the autonomic hyperactivity.
  - Treatments tried for opiate addiction include:
    - morphine
    - buprenorphine plus naloxone (suboxone) in sublingual form
    - LAAM (L-alpha-acetylmethadol acetate) with a long-acting opiate withdrawal effect; because of PT prolongation on EKG it has been withdrawn from the market
    - vaccine
    - some alcoholics respond better to naltrexone than others—those who have the 118 G genetic variant of the u- opioid receptor

- ***Xyrem***

  Xyrem (sodium oxybate) is used in narcolepsy. It is the sodium salt of the endogenous neurotransmitter gamma-hydroxybutyrate (GHB). It metabolizes to GABA. At low doses it increases glutamate (Glu) and dopamine (D); at high doses it decreases Glu and D and increases 5HT in mesolimbic system and striatum. Possible side effects of Xyrem include flu-like symptoms, confusion, sleepwalking, sedation, headaches, anxiety, seizures, increased blood pressure, and GI.

  Xyrem is often not used with other sedative hypnotic agents, alcohol, or CNS depressants.

  Xyrem can cause CNS depression, respiratory depression, confusion, depression, and neuropsychiatric side-effects.

  Xyrem (sodium oxybate or GHB) has been a drug of abuse. GHB abuse has been associated with respiratory depression, decrease in consciousness, seizures, coma, and death.
  Medical doctors must obtain a required prescription form.
  Xyrem increases daytime wakefulness, decreases cataplexy (up to 69% reduction), and improves sleep.

- ***nicotine addiction: neurotransmitters and treatments tried***

- Nicotine addiction is common—20% of the general population smoke; 70% of patients with schizophrenia, bipolar disorder, and ADHD smoke. Smoking accounts for 20% of deaths. Nicotine addiction is the hardest addiction to overcome. 66% of smokers want to quit; 33% try to quit, 3% succeed; varenicline triples placebo success rate (10% quit).
- Nicotine acts on AchN in the reward circuits. Nicotine receptors are of two types (alpha 4 beta 2 and alpha 7); activation of alpha 4 beta 2 AchN postsynaptic receptors on D neurons leads to D release in the NA (nucleus accumbens); activation of alpha 7 nicotine presynaptic glutamate neurons cause glutamate release which causes D release in the NA; nicotine also desensitizes alpha 4 beta 2 postsynaptic receptors by inhibiting GABA interneurons in the VTA causing D release in the NA by disinhibiting dopamine mesolimbic neurons.
- Treatments of nicotine dependency include:
    - nicotine—lozenges, gums, inhalers, nasal sprays, and transdermal patches; this produces steady nicotine levels that decrease cravings
    - varenicline (Chantix), a nicotine partial agonist, an alpha 4 beta 2 nicotine partial agonist in the VTA D neurons resulting in sustained small D release. Dosing is often as follows:
        - days 1-3 = 0.5 mg per day
        - days 4-7 = 0.5 mg bid
        - days 8-end of treatment (12 weeks) = 1 mg bid
    - cystisine, an NPA (nicotine partial agonist), a plant alholoid used in Europe
    - dianicline, an NPA, an alpha 4 beta 2 NPA
    - bupropian (Wellbutrin) an NDRI that decreases cravings by boosting dopamine; also an antagonist of alpha 4 beta 2 NPA; bupropion and nicotine alternatives are half a effective as varenicline is.
    - selegiline (Eldepryl), an MAO-B inhibitor that increases dopamine
    - moclobemide, an MAO-A inhibitor
    - naltrexone (Revia), an opioid antagonist
    - clonidine, an alpha 2 agonist
    - buspirone (Buspar), a 5HT1A partial agonist
    - TCAs
    - nicotine vaccine
    - rimonabant, a cannabinoid CBI receptor
    - D3 receptor partial agonist
    - B3 receptor antagonist

- ***nicotine dependency- treatments tried***

  Several drugs have been used in nicotine dependency. Nicotine replacement therapies have been used. Bupropion (Zyban or Wellbutrin) has been used. Varenicline (Chantix), a nicotinic agonist initially and then an antagonist has been used. Selegline (Eldepril), an MAOI, has been used (one component of tobacco smoke inhibits MAO-A and MAO-B); Eldepril increases dopamine. Finally, a nicotine vaccine (Xenova), that would block nicotine from entering the brain, is

being developed. The vaccine (the antibody) would combine with nicotine (the antigen) to prevent entrance into the brain and the rewarding effects of nicotine.

- ***smoking cessation: pharmacological treatments tried***

  Twenty-three percent of adults in the USA smoke (50 million people); 70% want to stop; 41% tried to stop the previous year.

  Pharmacological treatments include:

  - nicotine patch (Nicoderm CQ generic patches)
    - 21 mg daily for 2 months (less if less than 10 cigarettes a day) then
    - 14 mg daily for 1 month
  - nicotine gum or lozenge (Nicorette)
    - greater than 25 cigarettes per day = 4 mg each at 24 pieces per day in response to craving but in decreasing doses for 2 to 3 months
    - less than 25 cigarettes per day = 2 mg each at less than 24 pieces per day in response to craving but in decreasing dose for 2 to 3 months
  - nicotine inhaler (Nicotrol Inhaler)
    - up to 80 inhalations per day which is 4 mg, decreasing dose over 3 to 6 months
  - nicotine nasal spray (Nicotrol NS)
    - up to 5 sprays per hour which is 1 to 2 of .5 mg per nostril per hour
  - nortriptyline (Pamalar)
    - 100 mg per day
  - bupropion SR (Zyban)
    - 150 mg each AM for 3 days then
    - 300 mg each AM for 2 to 3 months
  - clonidine (Catapress)
    - .1 mg bid up to .3 mg bid or
    - .1 mg to .2 mg per day transdermal
  - varenicline
    - .5 mg per day for 4 days then
    - .5 mg bid for 4 days then
    - 1 mg bid for 3 months

- substance use disorders – treatments tried
  - management of substance dependence

    acamprosate (Campral)
    bupropion (Zyban)
    clonidine (Catapres, Catapres-TTS patch .2 mg – 1 q week), an alpha 2 agonist that decreases opioid withdrawal
    disulfiram (Antabuse)
    methadone (Dolophine)
    naltrexone (ReVia)
    ondanseton (Zofran, Emeset, Ondemet)
    topiramate (Topamax)

varenicline (Chantix)

- other drugs that have been used in various aspects of substance use disorders
  - buprenorphine (Subutex, Buprenex), a sublingual form
  - buprenorphine plus naloxone (Suboxone)
  - carbamazepine (Tegretol)
  - chlordiazepoxide (Librium)
  - clonazepam (Klonopin)
  - diazepam (Valium)
  - L-acetylmethadol (LAAM)
  - lorazepam (Ativan)
  - methadone (Dolophine)
  - rimonabant, a cannabinoid CB1 receptor antagonist for THC
- alcoholism
  - disulfiram (Antabuse)
  - naltrexone (ReVia)
  - naltrexone IV (Vivatrol)
  - acamprosate (Campral), an amino acid from taurine
  - ondansetron (Zofran)
  - topiramate (Topamax)
  - Timonibant, a cannabinoid CB1 receptor antagonist
- cocaine
  - disulfiram (Antabuse)
  - naltrexone (ReVia)
  - desipramine (Norpramine)
  - cocaine vaccine
  - modafinil (Provigil)
  - aripiprazole (Abilify)
  - olanzapine (Zyprexa)
  - N-acetylcystein
- nicotine
  - varenicline (Chantix), alpha 4 beta 2 selective AchN partial agonist (NPA)
  - selegline (Eldepril)
  - bupropion (Zyban)
  - nicotine replacement therapies
  - nicotine vaccine (Xenova)
  - diancline, an alpha 4 beta 2 agonist
  - rimonibant, a cannabinoid CB1 receptor antagonist
- THC
  - entacapone (catechol O-methyltransferase inhibitory or COMT inhibitor)

- resources
  - Hope Line – 1-888-789-HOPE (4673)

- Minirth Clinic – 1-888-MINIRTH (646-4784) / www.minirthclinic.com
- Celebrate Recovery – local Churches
- AACC – American Association of Christian Counselors/ www.aacc.net
- www.2ndfiddleentertainment.com/margiespassage

Conclusion

I Corinthians 10:31
Proverbs 4:15