Bio-psycho-social-spiritual Approaches to Addiction Medicine

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Faculty/Presenter Disclosure

- **Faculty**: Dr. Launette Rieb
- **Relationship with commercial Interest:**
  - Grants/Research Support: No commercial support, just UBC
  - Speakers Bureau/Honoraria: No commercial support, invited conference lectures only
  - Consulting Fees: No commercial support
  - Other: Paid for clinical work at OrionHealth (Vancouver Pain Clinic), The Orchard Recovery Centre, and St. Paul’s Hosp.
Disclosure of Commercial Support

- This program/talk has NOT received financial nor in kind support from any organization

- Potential for Conflicts of Interest:
  - Dr. Rieb has NOT received payment/funding from any organization discussed in this talk
Mitigating Potential Bias

- None of my workplaces will be mentioned in my talk
Objectives

- Understand addiction as a brain disease in a bio-psycho-social-spiritual context

- Reflect on the role agent, host, and environment play in addiction risk and protective factors
Part of Human History

- The desire to take mood altering substances spans human history
- It is **normalized or ritualized**
  - Christian: Wine = The blood of Christ
    - Digestive, food pairing, social lubricant, relaxation
  - Huichol: Payote = Visionary sacrament
  - Rastafarians: Marijuana = God’s gift to experience him
  - World culture: Coffee and tea = daily stimulants
Historic Views of Addiction

- Judeo-Christian: Temptation, lack of will, spirit/demonic possession
- Buddhist view: Craving = suffering
- Social: Bad family
- Medical: Bad blood
- Early Psychiatric/neurological: Nervous disorder, brain weakness
Costs of Substance Abuse in Canada, 2002 (CCSA released 2006)

- Substance abuse costs ≈ $40 billion per year
- Almost $1,300 for every Canadian
- Tobacco ≈ $17 billion (43%)
- Alcohol ≈ $15 billion (37%)
- Illegal drugs all together ≈ $8 billion (20%)
- Every dollar invested in treatment the overall savings is 4-7 dollars to society
Prevalence of substance USE in last year

- **Alcohol** – 78% (14% > low risk guidelines)
  - youth age 15-24 – 71% consumed alcohol
  - Past year HARMS 8% males, 5% females
  - Lifetime HARMS - males 21%, females 11%
- **Marijuana** – 9% used
  - 22% of youth vs 7% adults over 25
- **Drugs** – 5% for youth vs 1% adults
Epidemiology – USA, cont.

- **NESARC 2001-2002**
- **Substance Use Disorder Prevalence**
  - 18 yr+, n = 43,000, response rate = 81%
- **Alcohol**: past yr – 8.5%, **lifetime** – 30%
- **Drugs**: past yr – 2%, lifetime – 10%
- **Marijuana**: past yr – 1.5%, lifetime – 8.5%
- **Cocaine**: past yr – 0.3%, lifetime – 2.8%
- **Opioids**: past yr – 0.4%, lifetime – 1.4%
Substance consumption definitions

- **Abstinence** – no consumption
  - Some studies incl. very low use ≤ 1 drink/month

- **Use**
  - Low level use without harm or consequence
  - Never met criteria for dependence
  - Eg. Drinking within low risk drinking guidelines

- **Hazardous (or “at risk”) use**
  - Above low risk limits but no consequences
Public Health and the DSM-V

Use & Problems

Modality

None

Moderate

Severe

Chronic

1º Prevention

2º Prevention

Rehabilitation

Disease Management

Courtesy of Mark L Willenbring, MD.
Primary Prevention

Secondary Prevention

Addiction Definition – ASAM + CSAM

“Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors…”
The “4 C”s of Addiction

- CRAVING
- Loss of CONTROL
- Use despite CONSEQUENCES
- COMPULSIVITY
DSM-V Substance Use Disorders

- Larger amounts or over a longer
- Cut down or control
- Time is spent
- Craving or urge
- Failure to fulfill major role obligations
- Social or interpersonal problems
- Activities are given up
- Hazardous conditions
- Continued use despite knowledge of problem
- Tolerance
- Withdrawal
DSM-V SUD - Qualifiers

- **Severity**
  - Mild: 2-3 symptoms
  - Moderate: 4-5 symptoms
  - Severe: 6 or more symptoms

- **Remission**
  - Early – 3-12 mo. -only criteria left may be craving
  - Sustained – 12 mo. or longer, craving may remain
  - In a controlled environment (access restricted)

- **On maintenance therapy**
  - Agonist, agonist/antagonist, full antagonist
Risk (and Protective) Factors

❖ **Agent**
  - Availability, cost, rapidity to reach brain, efficacy as a tranquilizer (to relieve withdrawal)

❖ **Host**
  - Genetic predisposition, multi-problem family, co-morbid psych/med disorders (age, gender)

❖ **Environment**
  - Occupation, peer group, culture, instability
  - Sanctioned use, prohibition, restrictions
AGENT
Neurochemical - Reinforcement

- 13 million substances on the planet
- About 120 are addictive

**DOPAMINE**

*is the key*

- The mesolimbic system is involved with behavioral reinforcement – primal drive
Natural Rewards Elevate Dopamine Levels

Effects of Drugs on Dopamine Release

Amphetamine

Cocaine

Nicotine

Morphine

Di Chiara and Imperato, PNAS, 1988
Dopamine D2 Receptors are Lower in Addiction

- Cocaine
- Alcohol
- Heroin

Control
Addicted

Reward Circuits
Non-Drug Abuser

Reward Circuits
Drug Abuser
Individual Differences in Response to Drugs: DA Receptors influence drug liking

High DA receptor

Low DA receptor

As a group, subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant

Adapted from Volkow et al., Am. J. Psychiatry, 1999.
But Dopamine is only Part of the Story

- Scientific research has shown that other neurotransmitter systems are also affected:
  - Serotonin
    - Regulates mood, sleep, etc.
  - Glutamate
    - Regulates learning and memory, etc.
- Involved with craving and relapse
Serotonin Present in Cerebral Cortex Neurons

Normal

2 weeks after Ecstasy

7 years after Ecstasy
Dopamine Pathways

- Frontal cortex

Functions
- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine-tuning)
- Compulsion
- Perseveration

Serotonin Pathways

- Striatum
- Substantia nigra

Functions
- Mood
- Memory processing
- Sleep
- Cognition

VTA
- Nucleus accumbens
- Hippocampus
- Raphe nucleus
Visual Cue & PET scan: Craving Alarm

Nature Video

Cocaine Video

Amygdala not lit up

Amygdala activated
Alcohol

- GABA → CNS Inhibition
- Glutamate → CNS Excitation
- Opioid → Euphoria
- Dopamine → Addiction
- Serotonin → Impulsivity
- Cannabinoid → Pleasant Feeling
Alcohol to vinegar = pickled

alcohol dehydrogenase (ADH) → acetaldehyde dehydrogenase (ALDH)

acetaldehyde → acetaldehyde dehydrogenase → acetate

flushing reaction
- prostaglandins
- catecholamines
- histamine
- tachycardia
- hypertension
- nausea
- vomiting
- vomiting

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Conceptual Framework for Neurobiological Bases of the Transition to Excessive Drinking - Koob
Drugs can be “Imposters” of Brain Messages

Brain's Chemical

Anandamide

Drug

THC
Cocaine and other Stimulants

- ↑ DA, ↑ 5HT, and ↑ NOR
  - Cocaine = reuptake inhibitor
  - (Meth)amphetamines = ↑ release

Use:
- Alert, powerful, drive, anorexic
- Paranoid, psychotic, arrhythmias, stroke, MI, altered impulse control, violent

Withdrawal: Depressed, hypersomnolent, hyperphagic, cravings, restlessness, agitation
- Release DA from vesicles and reverse transporter

Methamphetamine

Miner, 2005.
Stimulants - treatment

- Use can be life threatening, withdrawal is not
- Treatment is largely **environmental support**
  - Change of scene, rest, eat, calm, no triggers
- If agitated an atypical antipsychotic can be used as long as no access to stimulants
  - eg quetiapine 25 mg tid-qid, titrated up to effect
- Avoid benzos (dysinhibiting, ↑ relapse)
- Generally avoid stimulant substitution
Partial Recovery of Brain Dopamine Transporters in Methamphetamine (METH) Abuser After Protracted Abstinence

Normal Control

METH Abuser (1 month abstinent)

METH Abuser (24 months abstinent)

Designer Drugs

- MDMA “Ecstasy”- hallucinogen & stimulant
  - Empathogen, entheogen, synthesthesias
  - Intox = bruxism & dry mouth (soother sign), ↑HR, hyperthermia (dancing), rhabdomyolysis
  - w/d = like cocaine + muscle aches
  - Supportive care like with cocaine
  - Monitor for elevated CK, may need hemodialysis
  - bring down fever aggressively
Designer Drugs

- **GHB** - sedative/hypnotic
  - action like a benzodiazepine
  - w/d similar to benzo and lasts 3-15d
  - There is a seizure risk so treat with…
  - diazepam or phenobarbital (monitor)
Other Club Drug and Inhalants

- **Ketamine (special K, Kit-Kat)**
  - NMDAr antagonist like phencyclidine (PCP) and dexamethorphan (DM)
  - Dissociative anesthetic, K-hole
  - Out of body - near death experience

- **Inhalants**
  - Use dangerous: Dissolves neural membrane, disorientation, psychosis
  - w/d mild, rare seizure, supportive (phenobarb?)
Other Club Drugs

- “Bath Salts”
  - Synthetic canthinones
  - Modeled after the chemicals in the herb khat grown in Yemen, Somalia and other East African countries
  - Properties like mixed methamphetamine, MDMA, and PCP (phencyclidine)
  - Lethal OD, extreme psychosis, hard to restrain
  - Tx: Bring down fever, sedate
Addiction Liability

Risk of becoming dependent if tried:
- Tobacco = 32% = 1 in 3
- Heroin = 23% = 1 in 4
- Cocaine = 17% = 1 in 6
- Alcohol = 15% = 1 in 7
- Cannabis = 9% = 1 in 11

- Time from initiation to dependence varies
Dopamine System in Mammalian Brain - Schematic

- Amphetamine
- Cocaine
- Opiates
- Cannabinoids
- Phencyclidine
- Ketamine
- Opiates
- Ethanol
- Barbiturates
- Benzodiazepines
- Nicotine
- Cannabinoids

Key:
- Acc: Accumbens
- VTA: Ventral Tegmental Area
- FCX: Frontal Cortex
- AMYG: Amygdala
- VP: Ventral Pons
- GABA: Gamma-Aminobutyric Acid
- ENK: Enkephalin
- OFT: Orbitofrontal Cortex
- ICSS: Intracranial Self-Stimulation
- BNST: Bed核
- CRF: Corticotropin Releasing Factor
- HYPOTHAL: Hypothalamus
- LAT-TEG: Lateral Tegmental Area
- PAG: Periaqueductal Gray
- END: Edinger-Westphal nucleus
- RETIC: Reticular Formation
- Raphé: Raphé nucleus
- HIPP: Hippocampus
- GLU: Glutamate
- OPIOID: Opioid
- 5HT: Serotonin
- NE: Norepinephrine
- DA: Dopamine
- To dorsal horn

The diagram illustrates the complex network of neurons and neurotransmitters involved in the dopamine system, highlighting key brain regions and neurotransmitters that are affected by various drugs of abuse.
Chronic Alcohol or Drug Use = Different Nervous System

- **Long term brain changes:**
  - Metabolic activity
  - Neurotransmitter release
  - Gene expression
  - Receptor sensitivity & availability
  - Cue responsiveness
  - Neurons that fire together, wire together
HOST
Genetics and Alcohol

- The greatest genetic risk factors for developing an Alcohol Use Disorder:
  - Male
  - Positive family history of alcohol dependence
    - 4x increased risk if biologic parent has AUD
  - Low response - little intoxication
  - Novelty seeking (DRD4 polymorphism)
  - Little acetaldehyde build-up (ADH1B1/1 and ALDH2*1/2)
Alcohol to vinegar = pickled

alcohol dehydrogenase (ADH) → acetaldehyde (ALDH)

flushing reaction
- tachycardia
- hypertension
- nausea
- vomiting

prostaglandins
catecholamines
histamine

acetate

H₃C\text{COO}⁻
Psychiatric – Co-Occurring Disorders

- People with SUD increased past year prevalence of mental disorders (ECA ’90)
  - AUD – 37% had mental disorder
  - DUD – 53%, and 23% had 6+ mental disorders
- ↑Mood disorders, anxiety disorders, PTSD
- ↑Antisocial males, borderline females
- Suicide attempts:
  - ETOH = 4.5% (=7xRR), cocaine = 62xRR
Psychiatric – Co-Occurring Disorders

- Those with a mental health disorder have
  - 29% increased lifetime prevalence of a SUD
  - 22% for AUD
  - 15% for DUD
Mental Health Risk for SUD

Q: Patients with which mental health disorder have the highest prevalence of substance use disorders?

1. Anxiety disorders
2. Depression (affective disorders)
3. Schizophrenia
4. Bipolar Disorder (manic depression)
ENVIRONMENT
Adverse Childhood Experiences (ACE) – within first 18 years of life

- ≥ 4 ACE categories = 4-12x ↑ risk of SUD
- 1. Emotional abuse
  2. Physical abuse
  3. Sexual abuse
  4. Emotional neglect
  5. Physical neglect
  6. Mother treated violently
  7. Household substance abuse
  8. Household mental illness/suicide attempt
- 9. Parental separation or divorce
  10. Incarcerated household member
Social Stressor Affects Brain DA D2 Receptors and Drug Self-Administration

Individually Housed

Becomes Dominant
No longer stressed

Group Housed

Becomes Subordinate
Stress remains

Reinforcers (per session)

Adolescent Marijuana Use

MonitoringTheFuture.org.

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The Elderly and Environment

Addiction is grossly underdiagnosed due to:

- Reduction in everyday expectations resulting in decreased “transgressions”
- Societal stereotype of an addict as a young person
- Lack of peer group surveillance

Sedative and opioid drug-drug interactions are particularly prevalent
Medical Co-Morbidities

The Behavioral Addictions

Both impulsivity and compulsivity show inability to refrain from dysfunctional repetitive behaviors.

**Impulsivity** is driven by an effort to obtain arousal and gratification (norepinephrine and dopamine).

**Compulsivity** is driven by an effort to reduce anxiety (serotonin).
COMPULSIVE END – OCD

- Body Dysmorphic Disorder
- Anorexia Nervosa
- Depersonalization Disorder
- Hypochondriasis
- Tourette’s Syndrome
- Trichotillomania
- Autism
- Binge Eating
- Compulsive Buying
- Kleptomania
- Pathological Gambling
- Self-Injurious Behaviors
- Sexual Compulsions
- Borderline Personality Disorder

IMPULSIVE END – Antisocial PD
Treatment Options

Q: Which of the following is not considered “treatment” for alcohol dependence?

A) Medically supervised detoxification
B) Alcohol and drug counselors (1:1, group)
C) Residential recovery programs
D) Recovery houses, therapeutic communities
E) Self help groups (AA, Alateen, 16 step, RR)
Treatment Models for Recovery

- **Residential Treatment**
  - 28+d
  - Recovery houses – 3-6 months
  - Therapeutic communities- 6 months to 5+ years

- **Therapeutic Models for Residential & Outpatient**
  - 1 on 1: Cognitive behavioral therapy (CBT) and offshoots
  - 1 on 1: Motivational Interviewing (MI)
  - Education of patient/family – addiction is a brain disease
  - Relapse prevention training, life skills, social skills
  - Groups: Matrix model, Seeking Safety model, 12 step
  - Contingency management
Medication Therapy Highlights

- Patients with a SUD can be assisted with medications through a variety of mechanisms, for example...
  - Agonist therapy (methadone for opioids)
  - Aversion therapy (disulfiram for alcohol)
  - Antagonist therapy (naltrexone for opioids)
  - Withdrawal management (diazepam for alc.)
  - Reinforcement mitigation (naltrexone for alcohol)
Relapse

- Stress
- Pain
- Drug re-exposure

- Cues (people, places, things)
- Mood (depr/anx, distorted thinking)
- Fatigue, hunger, isolation
Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses

- Drug Addiction: 40 to 60%
- Type I Diabetes: 30 to 50%
- Hypertension: 50 to 70%
- Asthma: 50 to 70%

McLellan et al., JAMA, 2000.
Extended Abstinence is Predictive of Sustained Recovery

Dennis et al, Eval Rev, 2007
Recovery Highlights

- Recovery rates improve with medication management, along with psycho-social-spiritual support
- Identify and practice recovery/happiness skills:
  - aerobic exercise, nutrition
  - meditation
  - altruism
  - social interactions/accountability
  - spiritual growth… and fun!
Treating a Biobehavioral Disorder Must Go Beyond Just Fixing the Chemistry

We Need to Treat the Whole Person!

Pharmacological Treatments (Medications)  Behavioral Therapies

Medical Services  Social Services

In Social Context