Bio-psycho-social Approaches to Addiction Medicine

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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, demonic possession

**Buddhist view:** Craving = suffering

**Cherokee view:** Scarcity mind

**Social:** Bad family

**Medical:** Bad blood

**Early Neurological:** Brain weakness

**Early Psychiatric:** Nervous disorder
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
CADUMS 2011

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

None
Moderate
Severe
Chronic

1º Prevention
2º Prevention
Rehabilitation
Disease Management

Modality

1º Prevention
2º Prevention
Rehabilitation
Disease Management

Courtesy of Mark L Willenbring, MD.
Primary Prevention

Secondary Prevention

“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 period
- 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

Vaillant

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
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
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
Movement

Motivation

Dopamine

Addiction

Reward & well-being
Natural Rewards Elevate Dopamine Levels

Food

NAc shell

% of Basal DA Output

0 50 100 150 200

0 60 120 180

Time (min)

Empty Box Feeding

Sex

DA Concentration (% Baseline)

0 50 100 150 200

Sample Number

1 2 3 4 5 6 7 8

Female Present

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

Drug Abuser

Non-Drug Abuser

Fundamentals: Bio-Psycho-Social Approaches to Addiction Medicine
Individual Differences in Response to Drugs: DA Receptors influence drug liking

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

Striatum

Substantia nigra

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

Serotonin Pathways

Nucleus accumbens

VTA

Hippocampus

Raphe nucleus

Functions
- Mood
- Memory processing
- Sleep
- Cognition

NIDA
Visual Cue & PET scan: Craving Alarm

Amygdala not lit up

Amygdala activated

Nature Video  Cocaine Video
Alcohol

- GABA → CNS Inhibition
- Glutamate → CNS Excitation
- Opioid → Euphoria
- Dopamine → Addiction
- Serotonin → Impulsivity
- Cannabinoid → Pleasant Feeling
Conceptual Framework for Neurobiological Bases of the Transition to Excessive Drinking - Koob

Fundamentals: Bio-Psycho-Social Approaches to Addiction Medicine

Neurocircuits ↔ Synaptic Systems ↔ Molecules
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 – reverses transporter

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

- Withdrawal: Depressed, hypersomnolent, hyperphagic, cravings, restlessness, agitation
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
Designer Drugs

MDMA “Ecstasy” - hallucinogen & stimulant
- Empathogen, entheogen, synthesthesias
- Intox = bruxism & dry mouth (soother sign), ↑HR, hyperthermia (dancing), rhabdomyolysis, renal failure and occasionally death
- Or water intox, hyponatremia, N+V, brain swelling (can lead to brain damage and rare death)
- Monitor for elevated CK, may need hemodialysis
- bring down fever aggressively, correct hyponatremia
- w/d = like cocaine + muscle aches – supportive care
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
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
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 dehydrogenase (ALDH)

acetaldehyde

flushing reaction
tachycardia
hypertension
nausea
vomiting

prostaglandins
catecholamines
histamine

acetate
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

Graph: Reinforcers (per session) vs. Cocaine (mg/kg/injection)
- Subordinate
- Dominant

Adolescent Marijuana Use

[Graph showing trends in availability, risk, and use of marijuana from 1975 to 2011.]

USE: % using once or more in past 30 days (on left-hand scale)
RISK: % saying great risk of harm in regular use (on right-hand scale)
AVAILABILITY: % saying fairly easy or very easy to get (on right-hand scale)

MonitoringTheFuture.org.
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.
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

Levouinis and Herron

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+ days
  - 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)
Recovery

- The patient must eventually take responsibility
- Correct negative cognitive distortions
- Identify and practice recovery/happiness skills: aerobic exercise, balance, altruism, social interactions/accountability, spiritual growth, meditation, nutrition, and fun

- Recovery takes time – in adults average 8 years from identification to sustained sobriety
Extended Abstinence is Predictive of Sustained Recovery

<table>
<thead>
<tr>
<th>Duration of Abstinence at Year 7</th>
<th>% Sustaining Abstinence through Year 8</th>
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<tbody>
<tr>
<td>1 to 12 months (n=157; OR=1.0)</td>
<td>36%</td>
</tr>
<tr>
<td>1 to 3 years (n=138; OR=3.4)</td>
<td>66%</td>
</tr>
<tr>
<td>3 to 5 years (n=59; OR=11.2)</td>
<td>86%</td>
</tr>
<tr>
<td>5+ years (n=96; OR=11.2)</td>
<td>86%</td>
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</tbody>
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Dennis et al, Eval Rev, 2007
Relapse

- Stress
- Pain
- Drug re-exposure

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

McLellan et al., JAMA, 2000.
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

NIDA