

Addiction, the Brain and Recovery

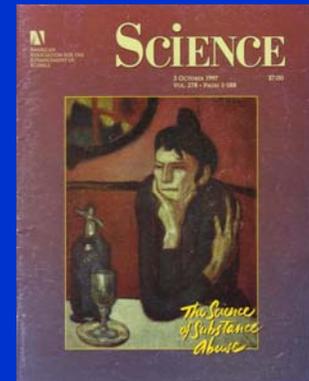
Opioid Substitution Therapy Conference
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The Neuroscience of Addiction



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Objectives

- Increased appreciation for the hallmarks of addiction as illustrated by neuroscience research
 - compulsive out-of-control use
 - continued use despite negative consequences
 - cravings
 - relapse
- Overview of long-term effects of drug abuse on the brain
- Implications of neuroscience findings for treatment systems

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Views of Addiction

- **Old View:** a character flaw, a failure of the will, poor self-control, self-inflicted, personal choices
 - Will & choice not irrelevant but not the whole story
 - if someone is in a Major Depressive Episode, MH professionals do not think that if the person would only think positive thoughts their depression would no longer be a problem
 - clinical depression is not that simple and neither is addiction
- **Current Neuroscience View:** A chronic, relapsing, brain based condition associated with compulsive and continued use despite known negative consequences

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Outline

- Views of Addiction
- Definitions of Addiction
- Major Brain Structures involved in Addiction
- Early Addiction Research & Trt Implications
- Recent Brain Research
 - effects of chronic use on brain structure & function
- Developing treatment systems to address the chronic nature of addiction

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Early Use

- Fact that addiction associated with brain based changes doesn't mean individual plays no part in its onset or recovery
- Addiction starts as a voluntary act of using drugs
 - often influenced by:
 - peer pressure, distress relief, thrill seeking and
 - occasional coercion
- People do not start using to become addicted
 - most think they will be able to control their use *

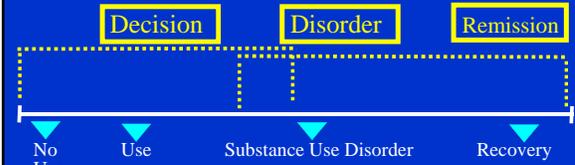
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Development of Addiction

- Over time drugs alter brain function leading to:
 - cravings
 - compulsive drug seeking and use
 - loss of pleasure from normal activities
 - depression or anxiety when not using
 - decreased thinking ability & judgement
- These brain based changes make it difficult to stop using despite sincere attempts
- This is why treatment (self-help/professional) is important

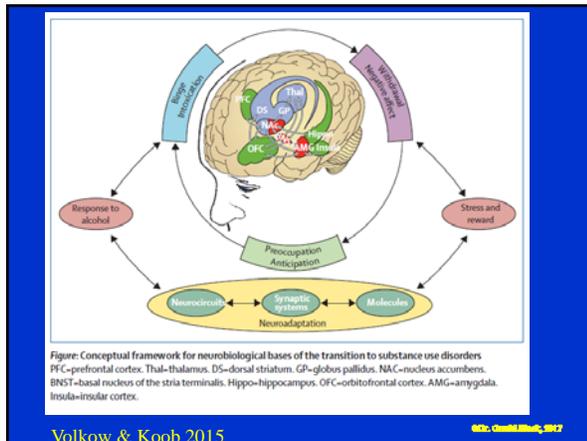
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From Decision to Disorder to Recovery



Adapted From Davis 2003, SAMHSA

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Volkow & Koob 2015

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When you think about addiction do you think about the influence of brain based changes?



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Recovery

- Recovery also starts as the result of a decision to:
 - stopping or reducing use
 - sincerely evaluate the negative impact of use
 - seek help with craving management
 - seek help maintaining abstinence so brain can heal
 - get legitimate needs for distress reduction, excitement and acceptance met using health methods
 - develop understanding of individual relapse risks
 - use relapse intervention strategies (e.g., REAL)
 - Real R - Refuse by verbalizing a simple "no"
 - E - Explain reasons for refusing
 - A - Avoid situations that involve alcohol & drugs
 - L - Leave situation once substance use enters scene
- (Hecht in press, NIDA Notes 18(3))

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Neuroscience View of Addiction

- A behavioural and brain based condition associated with:
 - compulsive use
 - continued use despite known negative consequences
 - sustained vulnerability to relapse
 - sustained recovery (remission) happens & can be life long
 - With internal or external motivation, knowledge, and recovery strategies
 - Recovery is everywhere www.recoverywhom.com

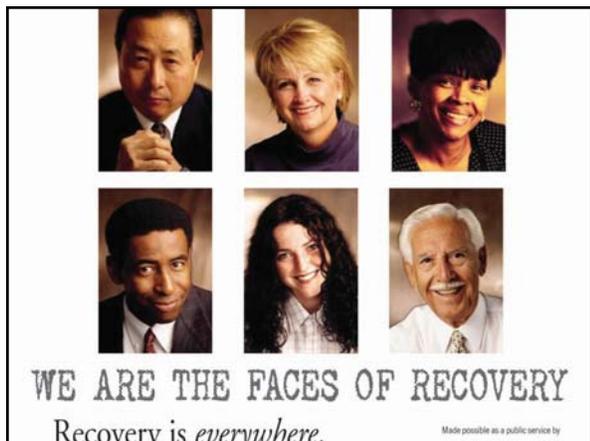
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Substance Use & Related Disorders (DSM-V)

- A cluster of cognitive, behavioral, and physiological symptoms associated with the continued use of substances despite significant related problems
- Ten Classes of drugs & Substance Use Disorders
 - Alcohol, Caffeine, Cannabis, Hallucinogens, Inhalants, Opioids, Sedative/Hypnotic/Anxiolytic, Stimulants, Tobacco, Other
- Drugs taken in excess involve direct activation of the brain reward system which is involved in the reinforcement of behavior and production of memories
- Individuals with lower levels of self control, predisposed to dev SUD
- Substance Induced Disorder
 - Intoxication, withdrawal, disorders (psychosis, bipolar, depressive, anxiety, obsessive-compulsive, sleep, sexual, delirium, and neurocognitive impairment)

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Substance Use Disorder (DSM-V)

Four Major Components (2 for 12)

- 1) **Impaired Control** - compulsive or "out of control" use
 - use of larger quantities or for longer period than intended
 - unsuccessful attempts to quit, despite sincere intention
 - much time spend using, obtaining & recovering from use
 - cravings or a strong desire or urge to use
- 2) **Social Impairment** - persistent use despite negative consequences
 - role impairment (school, work, home)
 - Social or interpersonal problems caused or exacerbated by use
 - NB social, occupational or recreational activities given up or reduced
- 3) **Risky Use**
 - physically hazardous use
 - physical (e.g., ulcer) / psychological (e.g., depression)
- 4) **Physiological**
 - Tolerance, withdrawal, use to relieve or avoid withdrawal.

Treatment: help person move towards abstinence ASAP

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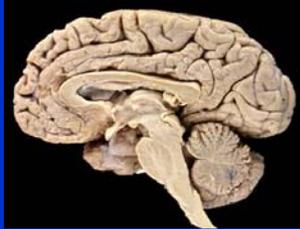
Contributing Factors

- Personal History
 - non-supportive family during childhood
- Mental Health or Medical Condition
 - (eg., ADHD, CD, Dep., PTSD, Schiz., Brain Injury, FASD)
- Environment - drug availability
 - active drug use by parents, friends, spouse, co-workers
- Genetics
 - family history of addiction (50% genetic, 50% environment)
- Personality
 - no such things as an "addictive personality"
 - high novelty seeking (Bardo, 1996)
- Sustained Use Alters Brain Function
 - (chemistry & structure)

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Major Brain Systems in Addiction

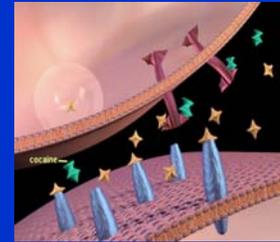
- Cortical
- Subcortical
- Neurotransmitters
 - dopamine
 - serotonin
 - opioids
 - GABA
 - glutamate
 - cannabinoids



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Cocaine Intoxication

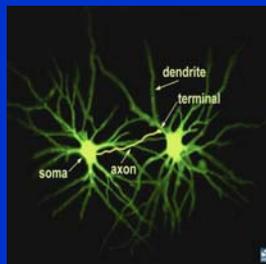
- ↓ Activation Dopamine Receptors by Blocking Re-absorption
- Produces Euphoria
- Intensity of “high” directly related to degree of dopamine re-absorption blockage (Volkow, 1997)



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Neurons

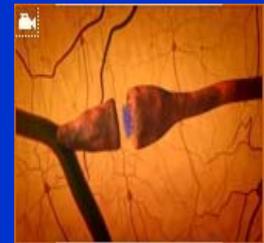
- The brain is comprised of billions of cells
 - a complex communication network
- Each neuron has branches
 - send and receive information using neurotransmitters



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Drugs and Neurotransmitters

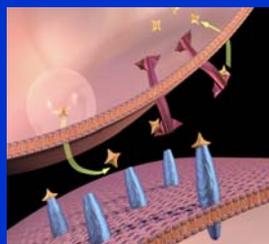
- **Dopamine**
 - pleasure & reward
- **Serotonin**
 - mood, appetite, senses, sex, pain sensitivity, inhibition
- **Cannabinoids**
 - appetite, senses, pain
- **Opioids**
 - pain suppression
- **GABA**
 - primary inhibitory neurotransmitter
- **Glutamate**
 - primary excitatory neurotransmitter



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Neurotransmission

- Cell Communication
 - release
 - receptor activation
 - re-absorption
- Drugs Alter Cell Communication
 - ↓ or ↑ receptor activation
 - ↓ release
 - ↓ re-absorption



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Drugs and Neurotransmitters

- Cocaine (crack, rock)
 - ↓ dopamine re-absorption
 - “high” 20 minutes
- Methylphenidate (Ritalin)
 - ↓ dopamine re-absorption
 - ↓ dopamine release
 - “high” 2-3 hours
- Methamphetamine (speed, crystal, ice)
 - ↓ dopamine re-absorption, ↓ dopamine release
 - serotonin re-absorption
 - “high” 8-12 hours

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Drugs and Neurotransmitters

- Opiates (Codeine, Morphine, OxyCofin, Talwin, Methadone, Fentanyl, Heroin)
 - ↓ natural opioids (endorphins, enkephalins)
 - ↓ dopamine re-absorption, ↓ dopamine release
- Hallucinogens (Acid/LSD, Mushrooms/Psilocybin, Mescaline, Ketamine, PCP)
 - ↑↑ serotonin release
 - ↓ NMDA Glutamate (excitatory neurotransmitter)
- Sedative/Benzodiazepines (Valium, Ativan)
 - ↓ GABA (inhibitory neurotransmitter)

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Why would animals die for drugs?

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Drugs and Neurotransmitters

- Cannabis (marijuana, hashish)
 - ↓ cannabinoids (CB1 and CB2 receptors)
 - ↓ dopamine
- Alcohol
 - ↓ dopamine release
 - ↓ norepinephrine (inhibitory neurotransmitter)
 - ↓ GABA (inhibitory neurotransmitter)
 - ↓ glutamate (excitatory neurotransmitter)
 - ↓ serotonin release
 - ↓ opioid release

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Why would animals die for drugs?

- Pleasurable activities, such as food & sex increase dopamine level by 50 to 100%.
 - Drugs of abuse ↑ dopamine by 300 to 900%.
- Wise 2003

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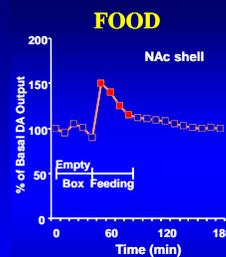
Early Brain & Addiction Research

- Animals consistently choose this stimulation over food, water and an available sexual partner (Olds & Milner, 1954)
- Addicted animals will self-administer drugs until death (Wise, 1985)



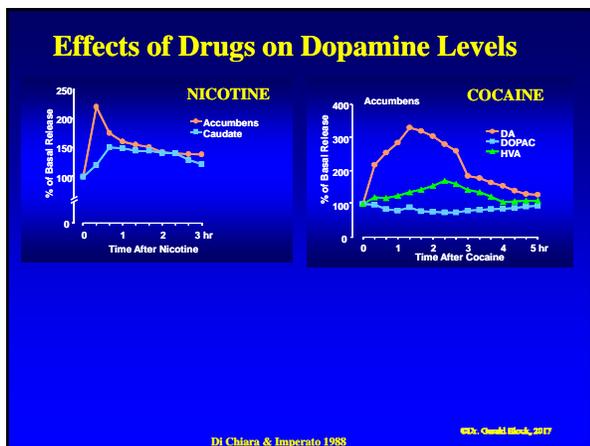
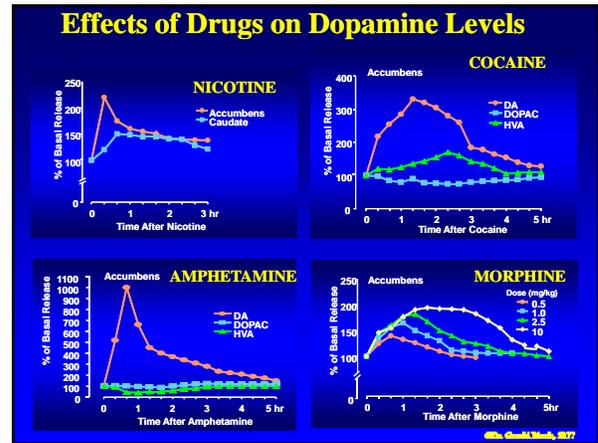
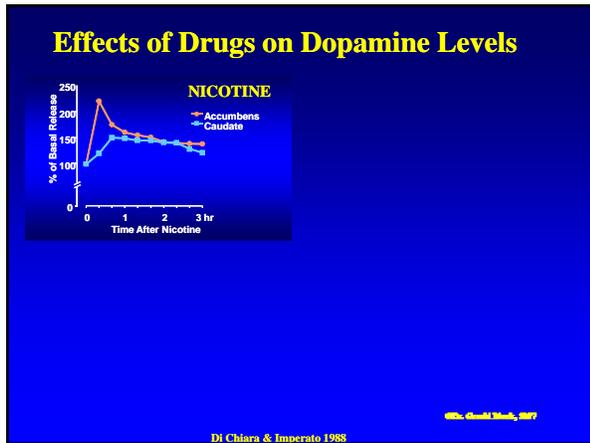
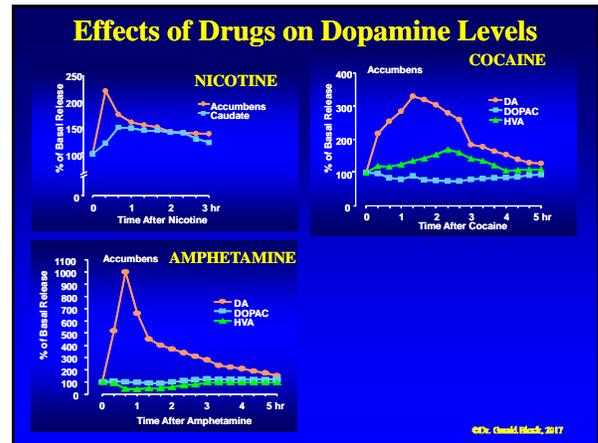
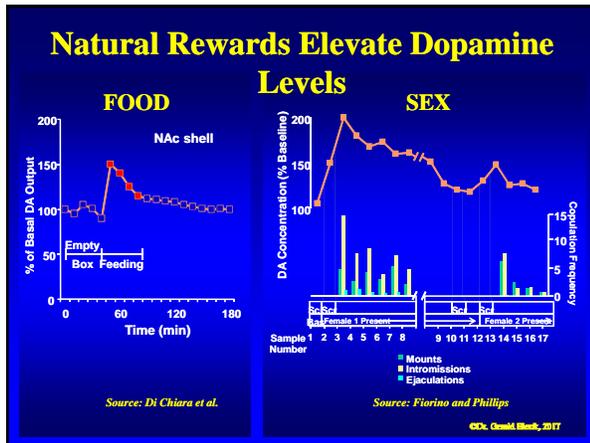
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Natural Rewards Elevate Dopamine Levels



Source: Di Chiara et al.

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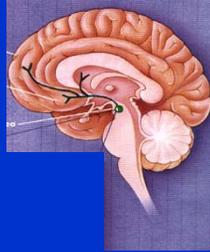
The Lethal Nature of Animal Addiction Indicates that:

- 1) Drugs of abuse so powerfully rewarding that they override typical decision making processes regarding negative consequences.
- 2) People are willing take risks to use drugs that they would not take for most other reasons.
 - This contributes to compulsive and continued use despite know negative consequence.

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Reward Circuit

- **Ventral Tegmentum**
 - dopamine producing neurons
- **Nucleus Accumbens and Amygdala**
 - reflexive emotional memories of powerful events
 - cravings
- **Prefrontal Cortex**
 - reasoning, decision making initiation and inhibition



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What Happens with Continued Cocaine Use?

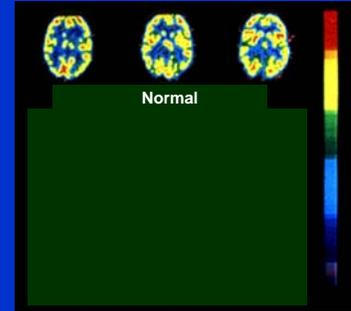
Cocaine Addiction & Glucose Metabolism

- efficiency of brain functioning

Normals n=10

Cocaine n=20

- no hx depression
- no hx brain injury



Volkow et al., 1992
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Recent Brain Research: Neuroimaging

Technology

- Positron Emission Tomography (PET)
- Magnetic Resonance Imaging (MRI)
- Functional MRI (fMRI)

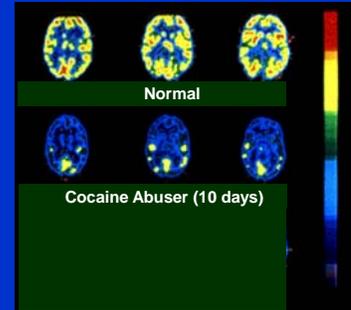


Questions:

- 1) What happens during intoxication & withdrawal?
- 2) Why is addiction a chronic relapsing condition?
- 3) What are the long-term effects of drug use regarding brain chemistry and structure?

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Brain Functioning After Short Abstinence



Volkow et al., 1992
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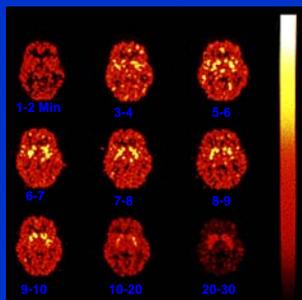
First Cocaine Use: Dopamine Transporter Blockage

PET

Normals n = 6

Brighter color indicates more transporter blockage

Synaptic dopamine levels and receptor activation ↑ with ↑ transporter blockage

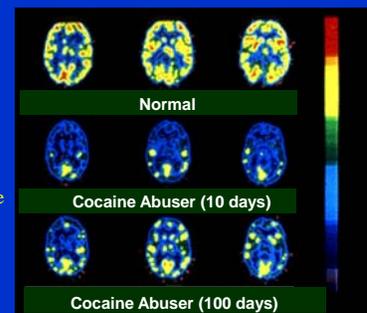


Fowler et al., 1989
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Brain Functioning After Sustained Abstinence

Sig ↓ frontal metabolism at both 10 days & 3 months

Degree of ↓ frontal metabolism related to intensity & duration use

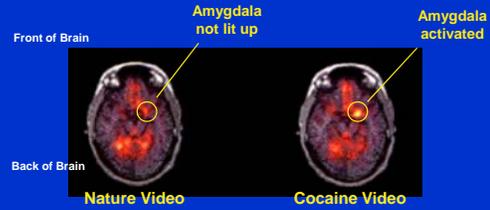


Volkow et al., 1992
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How can these neuroscience findings be used to support recovery?

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The Brain and Craving



Childress et al., 1999
Briener et al., 2000

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Why is Addiction a Chronic Relapsing Condition?

- Most people return to substance abuse within a year of first initiating abstinence (Grant, 1996)
- They often attribute relapse to “craving”
- Craving associated with
 - internal cues, feeling down, distressed, bored
 - external cues, using friends, money, product or using devices

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What are the effects of chronic use on function and structure?

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The Brain & Craving



Craving:

– “reflexive” memories of powerful emotions and states

Grant et al., 1996

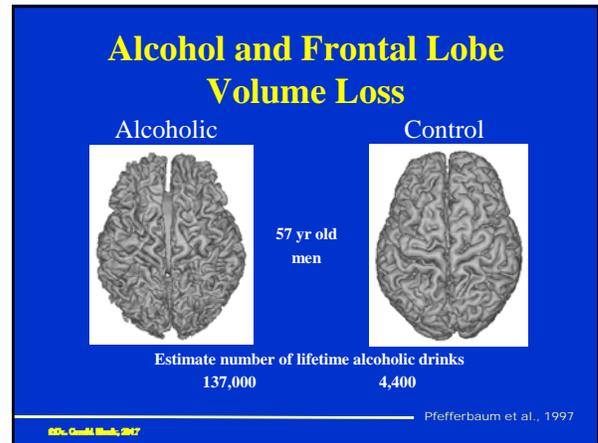
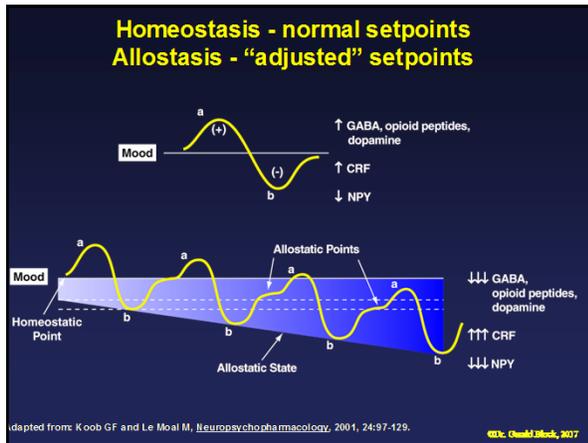
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Chronic Use Changes Brain Function & Structure

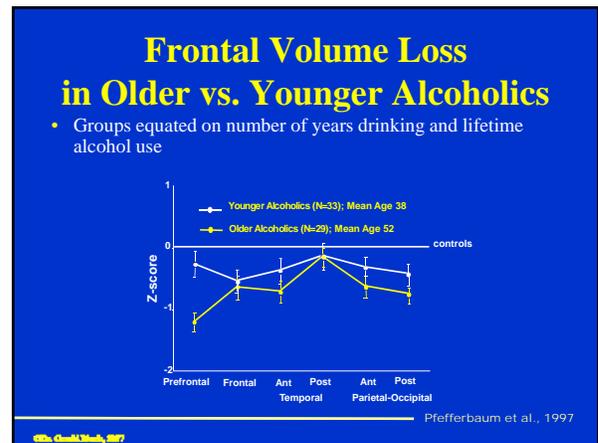
- Neuroadaptation
 - Down Regulation
 - ↓ neurotransmitter levels and fewer active receptors
 - withdrawal, tolerance
 - Allostasis instead of Homeostasis
 - loss of pleasure from normal activities
- Neurotoxicity
 - Neuron damage or death
 - Signs:
 - Persistent ↓ cognitive ability (attention, memory, judgement)
 - Substance Induced Dementia and Amnesic Disorder
 - (Alcohol, Sedatives/Anxiolytics)
 - Persistent Substance Induced Psychosis
 - (Stimulants, Hallucinogens, Cannabis)

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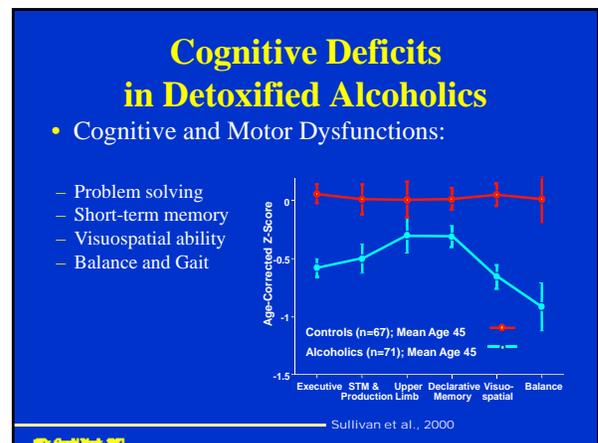
With Abstinence - neurotransmitter levels, some neuron damage reversed
- neuroplasticity



- ### Long-Term Effects
- Alcohol
 - Marijuana
 - Cocaine
 - Methamphetamine
- © 2017, Oxford Health, 2017



- ### Alcohol
- Brain atrophy range from mild to severe
 - Age Factor
 - prenatal & senior brain vulnerable
 - recent concerns about teenage brain
 - Brain Regions
 - entire brain vulnerable to atrophy ↓
 - frontal lobe & cerebellum vulnerable
 - frontal lobe, cerebellum & limbic system very vulnerable to thiamine deficiency (vitamin B₁)
 - Severe brain damage
 - Substance Induced Delirium / Wernicke's Encephalopathy
 - Acute life neurologic disorder caused by thiamine deficiency
 - severe confusion, severe coordination difficulties esp. walking
 - nutrient treatment reverses many of the acute symptoms
 - Substance Induced Persisting Amnesic Disorder / Korsakoffs
 - Impaired ability to create new memories
 - Impaired executive function
- Oscar-Berman 2003
Martin 2003 © 2017, Oxford Health, 2017



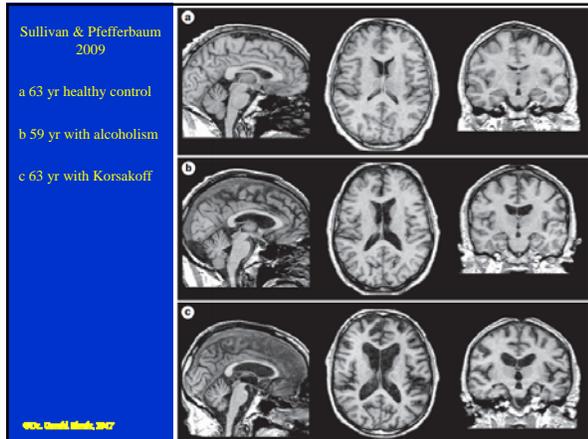
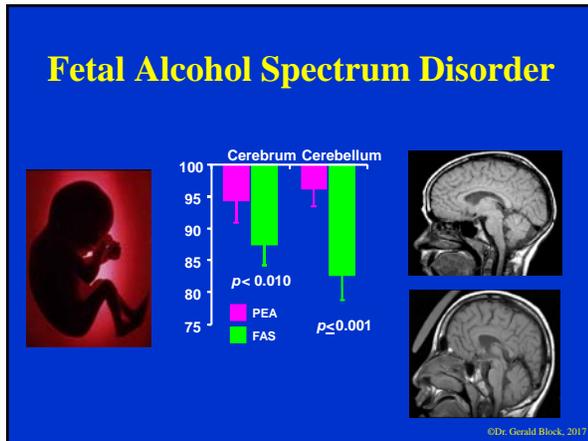


Table 1. Percentage changes in risks for males and females of premature death from 12 alcohol-related illnesses according to typical daily alcohol intake

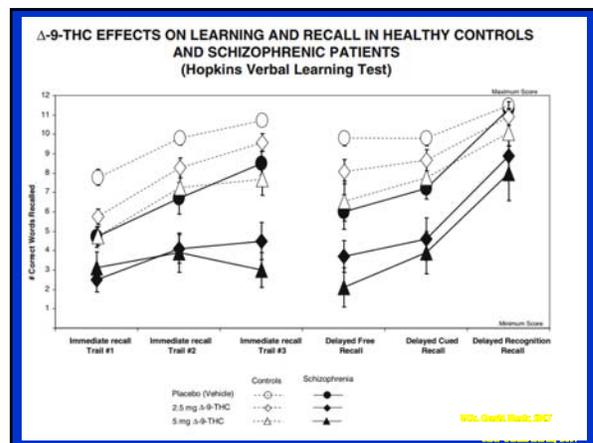
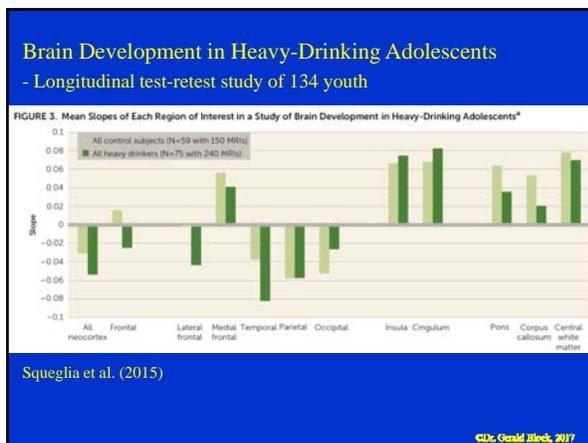
Type of Illness or Disease	Proportion of All Deaths, 2002-2005	Percentage Increase/Decrease in Risk				
		1 Drink	2 Drinks	3-4 Drinks	5-6 Drinks	+ 6 Drinks
Tuberculosis	1 in 2,500	0	0	+194	+194	+194
Oral cavity & pharynx cancer	1 in 200	+42	+96	+197	+368	+697
Oral esophagus cancer	1 in 150	+20	+43	+87	+164	+367
Colon cancer	1 in 40	+3	+5	+9	+15	+26
Rectum cancer	1 in 200	+5	+10	+18	+30	+53
Liver cancer	1 in 200	+10	+21	+38	+60	+99
Larynx cancer	1 in 500	+21	+47	+95	+181	+399
Ischemic heart disease	1 in 13	-19	-19	-14	0	+31
Epilepsy	1 in 1,000	+19	+41	+81	+152	+353
Dysrhythmias	1 in 250	+8	+17	+32	+54	+102
Pancreatitis	1 in 750	+3	+12	+41	+133	+851
Low birth weight	1 in 1,000	0	+29	+84	+207	+685

Canadian Centre on Substance Abuse
Centre canadien de lutte contre les toxicomanies

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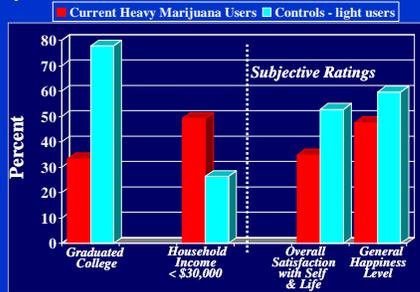


- ### Marijuana
- **While using (Acute Impairment)**
 - Attention, learning, and memory reductions
 - **After 1 month of no use**
 - No discernable difference between cannabis users and non-users
 - Meta-analysis of 13 studies (reviewed in Volkow 2016)
 - Concern about the long-term effects of cannabis use on youth.
 - **Associated with Onset of Psychosis**
 - Link could stem from direct causality, gene-environment interaction, or shared etiology
 - **Reduced Education, Income and Happiness**
 - Long-term heavy users:
 - complete less post-secondary education,
 - have reduced income level
 - reduced satisfaction with life
- ©Dr. Gerald Block, 2017



Education, Income and Satisfaction with Life in Heavy vs. Light Marijuana Users

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Source: Gruber, AJ et al., Psychological Medicine, 33, pp. 1415-1422, 2003.

Your View of Addiction is Important in Helping others Pursue Recovery?

If addiction is seen as:

- a moral failing - it will be condemned
- acceptable - it will be tolerated
- illegal - it will be prosecuted

a behavioural & brain based disorder

- education about the condition will be provided
- recovery skills will be taught
- leverage will be used to assist people with recovery

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Cocaine

- With use:
 - ↓ number of dopamine transporters & receptors
 - ↓ speed of processing, memory, and judgement
- With abstinence:
 - subtle speed of processing, memory & decision making difficulties persist after 1 month abstinence
 - difficulties more noticeable with chronic heavy use (3g/wk)
 - orbitofrontal cortex (OFC) volume - neuron loss
 - abnormal activation of OFC during decision making task after 1 month abstinence

Bolla 1999, 2003; Matochik 2003

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Does addiction treatment work?

How is effective treatment defined?

How well do our current treatment systems address addiction as a chronic condition?

Can treatment systems be developed to address the chronic nature of addiction?

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Methamphetamine

With use:

- ↓ number dopamine & serotonin transporters & receptors
- ↓ attention, motor, memory & and judgment
 - but still within normal limits
- damage to dopamine & serotonin dendrites
 - demonstrated in animal and autopsy studies
- cell death not documented

With abstinence:

- dopamine transporters ↑ in some but not all regions
 - thalamic, but not frontal, nucleus accumbens, caudate
- continued difficulties with decision making after 1 month
- partial recovery from attention, memory & motor difficulties after 14 month

Wang & Volkow, 2004; Paulus 2001

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Effectiveness of Treatment: A Provider's Perspective

- Effective treatment available
 - no cure, no quick fixes
- Addiction treatments as effective as treatment for mental health disorder (depression, anxiety) and medical conditions (hypertension, diabetes, asthma)
- Considerable research being done on increasing the effectiveness of addiction treatment given its well established chronic nature

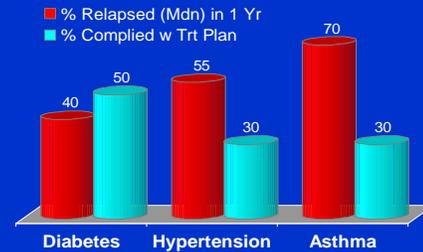
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Old Treatment Outcome Model

- Treatment should result in abstinence
 - abstinence the sole or primary focus
- Assumptions:
 - Some finite amount, intensity and duration of treatment adequate for successful and sustained abstinence.
- Based on this model there is considerable disappointment regarding abstinence rates
- Supporting this view are robust findings regarding abstinence rates

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Relapse Rates & Tx Compliance for Medical Conditions



O'Brien & McLellan, 1996 The Lancet; McLellan et al 2000, JAMA ©Dr. Gerald Block, 2017

Categorical Abstinence Rates

- Only approximately 25% of clients who complete addiction treatment programs remain abstinent during the year following treatment
 - regardless of the type of treatment provided (Miller 2001, McLellan 2005)
- 75% return to substance use
- If abstinence is the **sole focus**, addiction treatment will be viewed as ineffective

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New Treatment Outcome Model

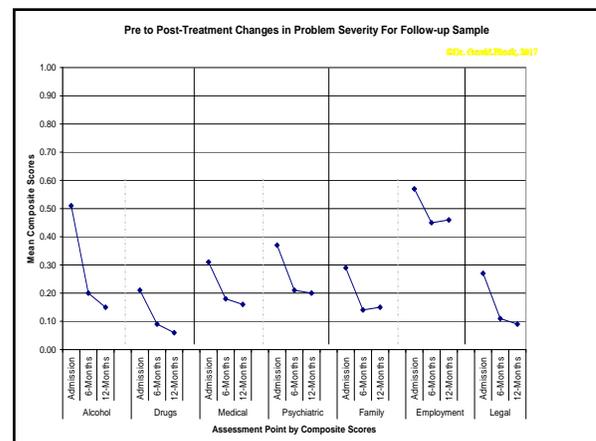
- **Need to look beyond abstinence rates**
 - 75% of clients who participate in addiction treatment programs show a large and statistically significant decrease in substance use & related problems
 - supports the need for broader view of effectiveness
 - **Effective addiction treatment** results in a reduction of alcohol, drug & associated problems (medical, social, legal).
- Need to compare effectiveness of treatment for both addiction & medical disorders involving behaviour change
 - diabetes, asthma, heart conditions

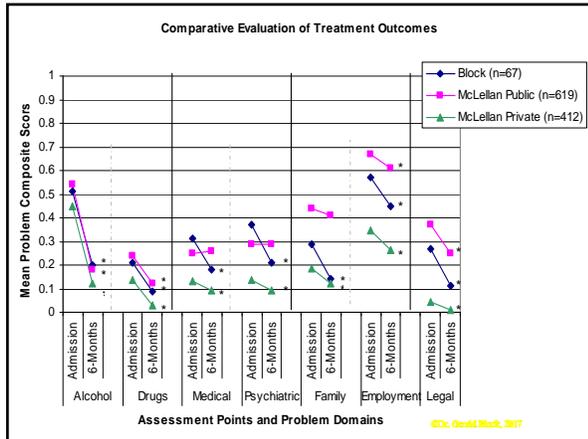
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Addiction vs Medical Conditions

- NB differences & similarities between trt of addiction and chronic medical conditions
 - behaviour change is essential for meaningful & sustained recovery
 - if diabetes patient does not monitor blood glucose levels or follow recommended diet changes effectiveness of pharmacological treatment is reduced
 - relapse frequently associated with lack of behaviour change rather than the pharmacological trt or medical directives
- With addiction treatment
 - knowledge of available supports and recovery strategies not sufficient, action is required to use supports and skills learnt

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- ### Continuum of Addiction Treatment Services
- 1) Self-Help Support Groups (AA, NA, ALANON)
 - 2) Detoxification
Home, Brief, Social, Medical, Psychiatric
 - 3) Outpatient Addiction Counselling
Outpatient Addiction Physician
 - 4) Outpatient Day Program
 - 5) Residential Addiction Treatment Program (2-6 weeks)
- Addiction Counselor, Multi-Disciplinary Professionals
 - 6) Long-Term Residential Addiction Treatment (3-6 mo)
 - 7) Telephone Continuing Care
- ©Dr. Gerald Block, 2017

- ### The Treatment Challenge
- clients who engage detoxification often do not engage other treatment supports and continue using
 - clients who engage outpatient or residential treatment often do not complete treatment
 - Clients who complete treatment often relapse within 6 months
 - Growing support of the need for continuing care for at least 1 year
 - A strategy used in the treatment of chronic conditions
- ©Dr. Gerald Block, 2017

- ### Effectiveness of Treatment from a Client's Perspective
- Why do most people with a substance dependence not engage addiction treatment services?
 - Top Reasons

1) No problem / Can handle things	58%
2) No confidence in treatment	51%
3) Bad experience with treatment	31%
4) Disagree with abstinence-only trt	31%
- Rapp 2005; Stanton 2004 Appel 2004 Tsogia 2001
- ©Dr. Gerald Block, 2017

Can the effectiveness of addiction treatment be improved by adopting strategies used in treating chronic medical conditions?

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- ### When Nothing is Working
- "I care about your health"
 - "I am concerned about you"
 - "I will be here for you"
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