Uppers, Downers, All Arounder:
I. Current Trends in Substance Abuse
II. Evolving Science of Addiction & Recovery

NAADAC 2013 Atlanta

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CNS Productions, Inc. & Addictions Recovery Center
Part I - Uppers, Downers, All Arounders: New Faces on The Usual Suspects 2013 Update

Uppers, Downers, All Arounders
Monitoring Tools

National Survey on Drug Use and Health 2011 (NSDUH)

Monitoring The Future 2010 (MTF), U of Michigan

22\textsuperscript{nd} Annual Partnership Attitude Tracking Study (PATS) April 2011
In 2009 Illegal Drug Use Increase by 9%

U.S. marijuana, methamphetamine, ecstasy (MDMA) use in 2009 highest ~decade and continued to increase through 2011

Perception of illicit drug use as harmful lowest in ~decade

~300,000 treated for primary marijuana abuse in 2007

Gil Kerlikowske SAMHSA 9/27/12
NSDUH 2011 results

SAMHSA 4/1/09
Treatment Episode Data Set (TEDS)
In 2010 Past Month Use of Marijuana by Teens > Cigarette use

Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes and Marijuana, 1975 to 2010

SOURCE: University of Michigan, 2010 Monitoring the Future Study
Correlation of Perceived Risk and Marijuana abuse

SOURCE: University of Michigan, 2010 Monitoring the Future Study
17 States and D.C with Medical Pot Laws & 2 (Co., Wa.) permit Recreational Use as of 2013

2012 Meta Analysis of National Surveys: Residents of Med. Pot States have:
• Higher rates of Pot Use
• Higher rates of Pot abuse/dependence
• Much Lower Adolescent Perception of Pot being Harmful and
• Much Higher Adolescent Average Pot Use
As compare to States with no Med. Pot Laws

2011 Past Month Illicit Drug Use
Youth Age 12 - 17  NSDUH

- Overall 10%; age 18-20 overall is 22.2%
- 7.9% used marijuana
- 2.8% used prescription drugs non-medically
- 1.0% used inhalants
- 0.9% used hallucinogens (e.g. ecstasy)
- 0.3% used cocaine
- 0.2% used methamphetamine
Past-Year Use of Illicit Drugs and Pharmaceuticals among 12th Graders

<table>
<thead>
<tr>
<th>Drug/Category</th>
<th>Illicit Drugs</th>
<th>Pharmaceutical</th>
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</thead>
<tbody>
<tr>
<td>Marijuana/Hashish</td>
<td>36.4%</td>
<td></td>
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<tr>
<td>Synthetic Marijuana</td>
<td>11.3%</td>
<td></td>
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<tr>
<td>Adderall</td>
<td>7.6%</td>
<td></td>
</tr>
<tr>
<td>Vicodin</td>
<td>7.5%</td>
<td></td>
</tr>
<tr>
<td>Cough Medicine</td>
<td>5.6%</td>
<td></td>
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<tr>
<td>Tranquilizers</td>
<td>5.3%</td>
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<tr>
<td>Hallucinogens</td>
<td>4.8%</td>
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<tr>
<td>Sedatives*</td>
<td>4.5%</td>
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<tr>
<td>Salvia</td>
<td>4.4%</td>
<td></td>
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<tr>
<td>OxyContin</td>
<td>4.3%</td>
<td></td>
</tr>
<tr>
<td>MDMA (Ecstasy)</td>
<td>3.8%</td>
<td></td>
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<tr>
<td>Inhalants</td>
<td>2.9%</td>
<td></td>
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<tr>
<td>Cocaine (any form)</td>
<td>2.7%</td>
<td></td>
</tr>
<tr>
<td>Ritalin</td>
<td>2.6%</td>
<td></td>
</tr>
</tbody>
</table>

SOURCE: University of Michigan, 2012 Monitoring the Future Study
Past Month Alcohol Use 2011
Underage Drinkers age 12 – 20  NSDUH

• 25.1% of age group (~10.4 million youths)
• 15.8% (6.9 million) engaged in Binge Drinking
• 4.4% (2.1 million) engaged in Heavy Drinking
• Teen males are more often current drinkers (29% v. 26%), Binge Drinkers (21% v. 16%) and Heavy Drinkers (7% v. 4%) than teen females
2010 PATS Demonstrate Much Greater Teen Drug Abuse

- Ecstasy (MDMA) past year use increased 67% from 6% in 2008 to 10% in 2010
- Marijuana past year use increased 22% from 32% in 2008 to 39% in 2010
- 62% reported first alcohol use by age 15, with average age of first use being 14
- Rx (esp. pain) meds abused by 25%, 11% abused OTC cough meds in past year
- Past year meth 5%, cocaine 9%, inhalant 10%, heroin 4% (heroin is lifetime use by teens)
% of Teens Who Have Used a Substance Not Prescribed to Them

- Alcohol 77%
- Nicotine 53%
- Marijuana 37%
- Inhalants’ 10%
- Vicodin 18%
- OxyContin 10%
- Ritalin or Adderall 10%
- Cough Med. (DXM) 10%

(PATS, 2010; University of Michigan, 2010)
% of Teens Who Have Used a Substance Not Prescribed to Them

- Cocaine or crack: 9%
- Ecstasy (MDMA): 10%
- Methamphetamine: 5%
- LSD: 6%
- Ketamine: 5%
- Heroin: 4%

(PATS, 2010; University of Michigan, 2010)

Despite the wide variety of psychoactive substances they all affect perception, mood, and states of consciousness by mimicking or modulating the natural excitatory (ups) or inhibitory (downs) or all around (psychedelic) natural chemistry of our brain.
Periodic Table of the INTOXICANTS

Dr. Kevin McCauley
Review: Brain Cell Communication Mechanism

Neurotransmitters Released by Brain Cell Axons

Slot into Receptor Sites on Dendrites and/or Neuron Cell Bodies Resulting in Synapse
Courtesy, Takeichi Laboratory, Nagoya, Japan
By Age 6 100 Billion Neurons and Initiated Development of a Quadrillion Synapses
Electron Microscopy of Neurons, Dendrites and Axons

Professor Terry Wiseth, Northland College
Synapse @ 50,000x Electron Microscopy

Courtesy of Thomas Deerinck, NCMIR/Photo Researchers, Inc.

Professor Terry Wiseth, Northland College
Synapse @ 50,000x Electron Microscopy

Courtesy of Thomas Deerinck, NCMIR/Photo Researchers, Inc.
Psychoactive Drugs Affect Perception, Mood, and States of Consciousness by Mimicking or Disrupting the Natural Chemistry of the Brain

Expanded Definition of Addiction 2013 = Any Behaviors (e.g. Gambling) that Alter Moods and Affect the Brain’s Addiction Circuitries and Pathways
Drugs Mimic, Modify, Disrupt, or Block Neurotransmitters

SOME EXAMPLES -

UPPERS: Catecholamines (Norepinephrine, Epinephrine, Dopamine) + Serotonin and Acetylcholine

DOWNERS: Endorphin, Enkephalin, Dynorphin, GABA, Serotonin, Histamine

PSYCHEDELICS: Serotonin, Acetylcholine, Alpha Psychosin, Norepinephrine, Dopamine, Anandamide, 2-AG
Cocaine Forces Neurotransmitter Release

- Cocaine
- Blocks reuptake port
Heroin inhibits Substance "P" Pain Message

Nerve impulse

Substance "P"

Secondary terminal containing endorphins

Heroin
All Addictive Substance Involve Dopamine Activity
2012 UCSF Research Confirms Role of Endogenous Opioid Neurotransmitters in Reward Circuitry as well as Dopamine
Also Excess Nor Epinephrine (Nor Adrenaline) and Less Transporters in Pathological Gamblers
Expanding Role of GABA & Glutamate

Gamma-aminobutyric acid (GABA) - Inhibitory

Glutamate (glutamic acid) - Excitatory
Serotonin aka 5-hydroxytryptamine also involved with all addictions?
Taking one: *Uptown, Downtown and “Outatown”*

- **CNS Stimulants** increase the electrical and chemical activity of the brain (caffeine to ‘Ice’)
- **CNS Depressants** decrease the electrical and chemical activity of the brain (‘booze’ to ‘benzos’ to opioids)

- **All Arounders (Psychedelics)** distort and interfere with brain perceptions to produce delusions, illusion, hallucinations, & synesthesia (DXM=‘Robo’ to ‘paka-lolo’ to Sylvia d)
- **Misc:** Inhalants, Anabolic Rhoids, Behaviors
The New Faces of Abused Drugs

Overwhelming developments, but still all are basically:

• Uppers
• Downers
• All Arounders
Uppers, CNS Stimulants

All Stimulants Increase the release of the catecholamine neurotransmitters:

- epinephrine (adrenaline)
- norepinephrine (noradrenaline) and
- dopamine
- serotonin and acetylcholine are also released
“Bath Salts” – Synthetic Cocaine/Methamphetamine: 
Ivory Wave, Vanilla Sky, Bliss, Purple Wave, Cloud 9, et al.

Mephedrone: methylmethcathinone, methylenedioxy pyrovalerone (MDPV), MDMC, 4-FMC, 3-FMC, et al.
Federal Legislation Banned 10 “Bath Salt” chemicals on 7/9/12

• Law also bans 21 specific synthetic marijuana chemicals
• Some 24-30 “bath salt” chemicals available
• Various States ban different chemicals, now harder to cross state lines to get these drugs
• Also bans any synthetic chemicals that produce the same effects now or in future?
• Bars sales on-line as well as in retail outlets
Bath Salts also sold as plant foods, glass cleaners & energy boosters

- Synthetic CNS stimulants, “Uppers”, - “not for human consumption” or “for novelty use only”
- Sold in “head or smoking shops”, convenience stores and even gas station marts. (new law bans sales of bath salts)
- Cost: $20 - $50 / 25-300 mg. packet
- Dose: Usually ~5 mg but great variability depending on active ingredient(s)
Origins of MDPV, Mephedrone, Methyllone, et al.: aka Bath Salts

Khat, Qat

Indigenous to East Africa

- *Catha edulis* bush
- “African Salad”
- Harvested all year
- Alleged quick chemical degradation post harvest
“Designer Drugs” aka “Club Drugs”

• Modifications of existing molecules of abuse (isomers, analogs, isosteres, et al.), drugs laws specifically name a molecule and not the modifications of such molecules.

• Finding molecules with entirely different chemical structures that produce similar effects to illegal recreational molecules (Structure-Activity Relationship).

2013 internationally referred to as: New Psychoactive Substances
Worldwide use of Synthetic and Designer Drugs (e.g. “Bath Salts” and “Spice” Increased >50% from 2009 to 2012

2013 World Drug Report UN Office of Drug and Crime

United Nations Office of Drug and Crime now refer to these abused drugs as New Psychoactive Substances rather than “Designer, Club or Synthetic” Drugs
Methylenedioxy-Pyrovalerone (MDPV)

Methylenedioxymeth-Amphetamine (MDMA)

Methylmethcathinone, Mephedron (4-MMC)
Pump-It Powder
Energy Boost and/or Plant Food

Pump-it Energy contains Geranamine (methylhexanamine)
Mephedrone plant food contains methylmethcathinone
Jewelry Cleaner or Glass Cleaner

Cosmic Blast contains MDPV and Naphynone, Eight Ballz originally contained MDPV but changes its ingredients often to keep ahead of the laws.
2013 “Benzo Fury” 5- or 6-APB
5- or 6-(2-aminopropyl)benzofuran
Effects

- Dopamine/Norepinephrine/Serotonin reuptake inhibitor like E, meth and cocaine
- ↑ BP, HR, Palpitations, body temperature – MDPV 10 times more powerful and addictive than methamphetamine or cocaine
- Neuropharmacology 71:130, 2013
- agitation, anxiety, panic, paranoia, seizures, HA, dry mouth, insomnia, addiction, suicidal/homicidal ideation, deaths: ~6,000 ER & Poison Control contacts per year
- 6 to 8 hour duration of action, taken orally, nasally, by injection or by smoking
Media History of Bath Salts
Horror Stories

- October 2009, Sarah F (35) dies taking “Ivory Wave” to lose weight for her London wedding
- May 2011, Dateline NBC story of adolescent suicide after taking “bath salts”
- January 15, 2012, 34 y.o. New Orleans Woman develops severe necrotizing fasciitis from I.V. “bath salt” abuse
- May 29, 2012, face-eating naked cannibal high on “bath salts”?? killed by police in Miami, Fl. but only cannabinoids reported by toxicology.
9-State Analysis of Designer Stimulant, “Bath Salt”, Hospital Visits Reported to Poison Control Centers


- 1633 ER visits between Nov. 1, 2010 to Nov. 30, 2011 for use of “Bath Salts”
- 16% were in critical condition or died
- Age range 1 day to 61 yo, 48% 18-29 yo
- 68% male, 26% used with other drugs (opiates, pot, alcohol)

States: Illinois, Indiana, Kentucky, Michigan, Minnesota, North Dakota, Ohio, South Dakota, and Wisconsin
SAMHSA 2013 Bath Salts & Hospital ED Report (Covers 2011)

- 22,904 cases in US Hospital Eds 2011
- 67% had other drugs involved, 15% of these were marijuana or synthetic pot
- Medical reasons for ED visits: heart problems, high blood pressure, seizures, addiction, suicidal thoughts, psychosis, death (especially when combined with other drugs)

Cocaine - Methamphetamine

Cocaine Paste – Oxidado, Oxi, Rust, Pasta, Basay (2 times stronger than cocaine)

“Shake and Bake” Methamphetamine
ADD, ADHD Medications

[Image of Concerta and Ritalin LA medication bottles]
ADD/ADHD Amphetamine Meds

Adderall is a combination of amphetamine and dextroamphetamine.

<table>
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<th>Strength</th>
<th>Color</th>
<th>Shape</th>
<th>PDU</th>
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<tr>
<td>5 mg</td>
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<td>Round</td>
<td>AD</td>
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<tr>
<td>7.5 mg</td>
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<td>10 mg</td>
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<td>D</td>
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<td>12.5 mg</td>
<td>Yellow</td>
<td>Round</td>
<td>D</td>
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<td>15 mg</td>
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<td>20 mg</td>
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<tr>
<td>25 mg</td>
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<td>30 mg</td>
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<tr>
<td>10 mg</td>
<td>Blue</td>
<td>capsule</td>
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<tr>
<td>15 mg</td>
<td>Blue</td>
<td>capsule</td>
<td>D</td>
</tr>
<tr>
<td>25 mg</td>
<td>Blue</td>
<td>capsule</td>
<td>D</td>
</tr>
</tbody>
</table>
Amphetamine congeners
Explosion of legal OTC Energy Drinks and Bar Energy Drink Cocktails
2012 Frito-Lay Cracker Jack’d
Jelly Belly Extreme Sport Beans
Kraft MiO Energy

70 mg/2 oz package
50 mg/1 oz bag
60 mg/container
Nicotine Vaporizers
Downers: CNS Depressants

Downers Exaggerate or mimic the action of the brain’s inhibitory neurotransmitters: Endorphin, Enkephalin, Dynorphin, Gamma Amino Butyric Acid (GABA), Serotonin, Histamine
Concern over Kratom: “Legal Phyto-Vicodin?”

Alleged 15X Concentrated mitragynine and 7-hydroxymitragynine extracted from Kratom leaves
Captain Kratom
“Synthetic Vicodin”
Kratom, Ithang, kakuam, thom, & Ketum
Mitragyna speciosa

Thailand, Malaysia, Indonesia, et al.

7-hydroxymitragynine, speciogy-nine, paynantheine, mitraphyl-line, & about 2 dozen others

Various commercial concentrated 15X to 250x extracts
Kratom Pharmacology

• Low Dose = Yohimbe-like stimulant
• Higher doses = Mu-opioid receptor agonist
• Effects (4 gms = 4 hours of euphoria)
  – Analgesia, cough suppression
  – CNS depressant, ↓ blood pressure
  – Quick onset and lasts ~ 1 – 4 hours
• Acute side effects: dry mouth, ↓ appetite
  – Constipation
  – No n/v, ↓ blood sugar
• Opioid-like full physical addiction
In 2010 U.S. Prescription Drug Deaths (primarily opioid pain medications) were Greater than Auto Accident Deaths! Methadone represented 30% of these deaths in 2010 yet only amounted to only 2% of all pain medications prescribed.
Endogenous Opioid Peptides

- Endorphins, β-Endorphin, Gamma-Endorphin
- Enkephalins
- Dynorphins
- Adrenorphin, amidorphin
- Opiorphin
- et al.
New Oxycontin® Formulation to Mitigate Abuse April 2010

So, by 2012:
1. Freeze Oxy or
2. Opana®

Or, 3. Heroin

Oxycodone

Oxymorphone
Methadone (Dolophine, Methadose) Leading Cause of Rx OD Deaths 2010-2011
Heroin: making a big comeback in 2010 on!

Batches of Heroin can be as different as night and day.

Texas “Cheese Heroin”: Black Tar Mixed with Tylenol PM

Black “Tar Heroin”

“Gunpowder Heroin” = fentanyl with tar heroin?
“Krokodil” & “Baker’s Brew”

Krokodil
Desomorphine is made from codeine with iodine, lighter fluid, oils or gasoline, et al.

Poppy Seed Tea
Seeds are crushed or blended, steeped in boiling water, strained and then mixed with grapefruit extract
Sedative-Hypnotics (downers)

• Benzodiazepines
  Xanax, Valium, Halcion, Librium, Ativan
  Rohypnol, Klonopin, Restoril, phenazepam

• Barbiturates
  Seconal, Nembutal, Amytal
  Phenobarbital

• Others
  chloral hydrate, GHB, Z-hypnotics, etc
Benzodiazepines

The Molecule

29 types in Clinical Use
Other Downers

- Antihistamines
- Skeletal muscle relaxants
- Over-the-counter downers
- Look-alike downers

Downers mimic or interact with the neurotransmitters: GABA (gamma amino butyric acid), histamine, serotonin, et al.
## OTC Antihistamines abused as Sedatives

<table>
<thead>
<tr>
<th>Antihistamine</th>
<th>Brand Names</th>
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<tbody>
<tr>
<td>brompheniramine</td>
<td>Dimetane, Dimetapp</td>
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<tr>
<td>chemastine</td>
<td>Tavist</td>
</tr>
<tr>
<td>chlorpheniramine</td>
<td>Coricidin, Chlor-Trimetton</td>
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<tr>
<td>dimenhydrinate</td>
<td>Dramamine</td>
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<tr>
<td>diphenhydramine</td>
<td>Benadryl, Adios?</td>
</tr>
<tr>
<td>doxylamine</td>
<td>Nyquil</td>
</tr>
<tr>
<td>pheniramine</td>
<td>TussiRex</td>
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</tbody>
</table>
Soma®

Carisoprodol tablets (generic Soma)
AWOL – Alcohol Without Liquid Ethanol Inhalant Devices

Banned in many States
Dry Ice ‘Smoking’ Alcohol

Images from KCTV via New York Times and Nub TV via YouTube Videos
Jenkem – “Ass Gas”

Human or Animal excrement fermented to methane gas said to be a ~ psychedelic?
All Arounders: Psychedelics, Hallucinogens, Entactogens, Enteogens, Psycho Stimulants, Empathogens, Psychotogens, et al.
All Arounders/Psychedelics: Modulate various neurotransmitters - Serotonin, Acetylcholine, Alpha Psychosin, Norepinephrine, Dopamine, Anandamide, 2-AG

Ecstasy, E = MDMA-Methylenedioxy methamphetamine comes in a wide variety of street tablets. Also “Thizz”, “Flatliners” & MDMA analogs. Now, “Extreme Ecstasy” or “Meth X” = meth & XTC
New Designer Ecstasy-Like Psychostimulants

Benzo Fury

5-APB [5-(2-aminopropyl)benzofuran]

Or,

6-APB [6-(2-aminopropyl)benzofuran]

Compare these to Ecstasy or MDMA (3,4-methylenedioxy-N-methylamphetamine) molecule
Marijuana “Pot”

Three Species, infinite varieties/hybrids with wide concentrations of some 420 chemicals ~60 of which are psychoactive (plus their metabolites) cannabinoids; $\Delta_9$THC (tetrahydrocannabinol) considered to be responsible for most effects

- Cannabis sativa
- Cannabis indica
- Cannabis ruderalis

Sinsimilla and growth manipulations
Origin of “420, 4/20, 42°”
Street Code for Marijuana

• Hitler’s birthday: April 20, 1889
• Teatime in Holland
• Police code for marijuana abuse in progress
• SB420 California’s Medical Pot initiative
• Multiplier product of a Bob Dylan song #s
• The 5 ‘Waldos’ (they hung out at a certain wall) of San Rafael HS 1971. 4:20pm was meeting time on 4/20 during harvest season to go rustle someone pot patch
Cannabis sativa
Cannabis Indica
Cannabis ruderalis
Sinsemilla: Sp. for no seeds
Sinsemilla: female seedless flower top
Buds: flowering buds of Cannabis
3 species but infinite number of variants & hybrids
Endocannabinoid Neurotransmitters

- Anandamide (arachidonoylethanolamine or AEA) — mainly CB₁ Central & some CB₂ periferal
- 2AG (2-arachidonoyl glycerol) — CB₁ & CB₂
- Nolandin Ether (2-arachidonoyl glycercyl ether) — CB₁ mainly some CB₂
- N-arachidonoyl-dopamine (NADA) — CB₁ selective
- Virodhamine (O-arachidonoyl-ethanolamine or OAE) — CB₂ some CB₁
Incidence & Perspective
(Johnson Monitoring the Future; DAWN; et al)

• 12-18 yo: 40% tried, 14% current, 3% daily
• 18-25 yo: 48% tried, 5% daily use of pot

• Other Drugs by US high school seniors:
  Alcohol: 88% tried, 5% daily use
  Nicotine: 27% tried, 17% daily use
  Methamphetamine/cocaine: ~6% tried, <1%
  Ecstasy (MDMA): 10% tried, < 0.1 daily use
More Potent Pot
Marijuana Potency Monitoring Project University of Mississippi

Average Potency of US street marijuana

- 1976 – 2% THC
- 1983 – 4% THC
- 2005 – 5.2% THC
- 2007 – 7.3% THC
- 2008 – 10.1% THC
<table>
<thead>
<tr>
<th>THC Content of Cannabis</th>
<th>Range</th>
<th><em>Avg.</em></th>
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<tbody>
<tr>
<td>Marijuana</td>
<td>0.4% to 9.5%</td>
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<tr>
<td>Sinsemilla</td>
<td>6.0% to 14%</td>
<td>6.66%</td>
</tr>
<tr>
<td>Hashish</td>
<td>up to 14%</td>
<td>5.69%</td>
</tr>
<tr>
<td>Hash oil</td>
<td>up to 40%</td>
<td>10.30%</td>
</tr>
</tbody>
</table>

*Department of Justice*
“Dabbing” butane hash oil (BHO) aka “wax, shatter, honey oil” et al.

Alleged to result in a waxy product containing 70-90% THC!
New Cannabis Substances also produced with butane, nitrous oxide, alcohol, carbon dioxide and even cold water

“Ear Wax Weed, Butane Hash Oil (BHO), Cannabis Oil, Honey Oil, Shatter, Wax, Bubble Hash”, et al. Extraction process is known as “Dabbing”
Also Commercial Products (e.g. PureGold) via Tetralabs CA. et al.
sold as medical marijuana

Sold as liquid, gel cap, gel Ampoule and solution for E-Cigarette Use

Alleged 95% cannabinoid with 75% $\Delta_9$ THC
Synthetic Marijuana (THC) aka Synthetic Cannabinoids (SC) Analogs sold as Herbal Incense

“Not For Human Consumption!”

$30 to $40 per 3-3.5 gm packets
2000’s Synthetic Cannabinoids

Herbal “Incense”

K₂, K₉, Spice Gold or Silver or Diamond, Budda Blend, Yucatan Fire, et al contain JWH-015, HU-210, WIN-55/212-2, CP-47/497/C6 or other THC agonist. By 2012 about 100 such molecules. These “designer pots” are anywhere from 5 to 800 times more potent than THC. UA test for JWH series in 10/10. Also THC Antagonist: rimonabant (Accompli)
Cannabinoids – 3 Types

• **Endocannabinoids**: 5 ligands, main ones - anandamide and 2-AG

• **Phytocannabinoids** (botanical): 60 at least, tetrahydrocannabinol, cannabidiol, and cannabinol are main ones

• **Synthetic Cannabinoids (SC)**: 6 chemical families - naphthoylindoles, naphthylmethylindoles, naphthoylpyrroles, naphthylmethylindened, phenylacetylindoles, cyclohexyphenols. These can be 5 to 800 times more potent and have 6 to 12 duration of action
Illegal 1\textsuperscript{st} in 12 States, then in U.S. 2010

- Some of these synthetic cannabinoid products (eg K\textsubscript{2} and Spice) are now illegal in 12 States (Ala, Ark, Geo, Ill, LA, Mcg, Miss, NJ, NY, OH, Tx) and many communities as well
- On 10/13/10 Oregon Board of Pharmacy adopted “Temporary Rule” classifying K\textsubscript{2} and Spice as Schedule I Controlled Substance
- Federally 21 banned on 7/9/12 as well as anologs with same effects used as such
Synthetic Cannabinoids more Toxic than Phytocannabinoids

- Reports of anxiety, dry mouth, tolerance, increased HR, increased blood pressure, confusion, psychosis, paranoia, coma, seizures, kidney failure and even deaths.

Cannabinoid Hyperemesis Syndrome

- Developing Drug Tests: JWH-018, -073, -019, -250 and for AM-2201 now available. Tests for others continue to be developed.

- Cost: $17.00 to $35.00 for the complete UDS screen of available standards.
So, Now Legal Potpourri

- Green Grenade
- Clown Loyal
- Natural Spirits
- Super Kush
And, Chill Spice: marketed as aromatherapy incense

Suspected to contain JWH-200, -250, and/or CP-47, -497
Also new oral pot street products
Marijuana Gel Caps: Pot + Olive Oil Blended and Capsulized
Medables: responsible medical marijuana?

NORML medical marijuana outlet in Medford promotes safer less harmful processes:

- “medables” (edible marijuana products) e.g. cookies, butter, lollipops, candy, ice cream, sorbet, soft drinks, Gel caps
- spray, drop, vaporization inhalation of pot or alcohol extracts for oral or vaporization mist
- marijuana ointment, cream, salve, tincture
Vaporizers
How do vaporizers work?

• When cannabinoids are heated to between 285 °F (140 °C) and 392 °F (200 °C) they literally boil and vaporize.

• Studies show that vaporization is most effective at around 338 °F (170 °C)

• A vaporization temperature over 392 °F (200 °C) will burn the cannabis, creating unwanted smoke.
Dextromethorphan: DXM, Robo
OTC Antitussive dextromethorphan abused as a Psychedelic
Salvia divinorum
SALVIA Methods of Use:

Traditional
  Macerate leaf
  Extract juice
  Tincture

Chewing “quid” method

Smoke dried leaves

(inactivated by GI acids)
Pharmacology of Salvinorin A
(located in the leaves not the plant’s flower)

• Kappa-opioid receptor agonist
• Partial agonist dopamine receptor (D₂)
• Hallucinogen
  – Psychotomimetic, dysphoric, bad trips & HPPD
  – Fast onset, duration 30-60min (but users often experience this as days or weeks)
• No activity 5-HT2A Serotonin Receptor that is the major receptor for LSD
• May also Inhibits intestinal motility, decreases gut inflammation, and have antispasmodic properties
Ketamine diverted from Hospital and Veterinary Stock Rooms Now Abused as a Psychedelic

“K or Special K in U.S.; “Roflcopter” in U.K.”
New Age Psychedelics & PsychoStimulants

~ infinite number of potential analogs isomers, Isosteres, or other chemical modifications
DEA Drugs and Chemicals of Concern

2C-T-7  Tripstasy, Blue Mystic
2C-B    Nexus
2C-1    Smiles (also 2C-E, 25-I & 25b-Nbome)
5-methoxy diisopropyltryptamine  Foxy Methoxy
alpha methyltryptamine           Spirals
N-benxylpiperazine                BZP
dimethyltryptamine                DMT
bromobenzodifuranylpropylamine    Bromo-DragonFly
Expanding Diversion and Abuse of Prescription Medications
The Under – Over Medication Pendulum

Anxiolytics – benzodiazepines

Treatment of ADD/ ADHD – analeptics

Especially Analgesics – opiate and opioids
  morphine, methadone, Oxycontin, Vicodan and now Zohydro advocacy
Center for Disease Control Evaluation of Rx Drug Abuse Problem

- Unintended Rx drug OD death every 19 minutes in 2007
- Each Rx opioid OD death = 9 detox admissions, 35 ER visits, 161 abusera/addicts, & 461 reports of nonmedical use of Rx opioids
- 9 million U.S. long-term medical Rx opioids users and 5 million annually report nonmedical use
- Pharmacy U.S. distribution of Rx opioids rose 600% from morphine equivalent of 96 mg. in 1997 to 700 mg. per capita in 2007
Abusing Prescription Drugs

Prescription drug abuse is the nation’s fastest growing drug problem. Drug overdoses are the leading cause of accidental death in 16 states and D.C.

**Painkillers dominate**

Prescription opioid painkillers, such as OxyContin, caused the largest share of accidental overdose drug deaths in 2007.

- **Total deaths**: 27,658
- **42%**: Opioid painkillers
- **58%**: All other drugs

**Comparing killers**

Deaths from prescription opioid painkillers were almost twice as high as those from cocaine; in thousands.

- Opioid painkillers: 11,499
- Cocaine: 5,943
- Heroin: 2,137

**Drug overdose deaths**

Per 100,000 population, 2007

- Less than 9.0
- 9.0-10.9
- 11.0-13.9
- 14.0 or more

Highest

W.Va. 21.1

Source: U.S. Centers for Disease Control and Prevention, McClatchy Washington Bureau
Graphic: Judy Treible

© 2011 MCT
June 2012 US Senate Caucus on International Narcotics Control

• Rx drugs now second most common form of drug abuse in the U.S.
• Now responsible for most OD deaths, greater than heroin and cocaine combined
• Violent pharmacy robberies increased 82% between 2006 and 2011
• NSDUH data indicates 70% or Rx drugs were supplied by friends or relatives
July 2013 CDC Report: More Rx med death than car crash death in U.S.

- 1999-2010 Rx Opioid OD death increased 400%, in women, 265% in men. 18 women deaths every day!
- Rx meds (esp. Oxycontin & Vicodin) comprised 34% of suicide deaths in women and 8% in men
- >200,000 women ER visits were due to misuse or abuse of these drugs, ~one every three minutes
- Rx Opioid OD deaths were greater than 4 times as many cocaine and heroin deaths in women
- Dr. Thomas Frieden, CDC Director now estimates 42 women deaths each day from Rx Opioid ODs
Some Unethical, Unwise, and Over-Prescribing of Opioids

Many horror stories and tabloid reports especially when a public figure is involved or overdoses (e.g. This dog X-ray used in a sting to get pain meds)

But:
Most diverted opioid and other prescription drugs are obtained from friends or family members
Also many horror stories of overzealous restriction of such medications from appropriately medical uses – Pseudo Addictions

- Hyperalgesia– PAF activation of chemokines (i.e. cytokines) release with nociception
- Neuropathic Pain (Hyperpathia – peripheral nerve and spinal dorsal horn sensitization
- Allodynia – temperature or touch pain
- Development of opioid tissue dependence
New era of ‘Designer Drugs’ and the discovery of ‘New Age Intoxicants’:

- Usher in an era of infinite numbers of new drugs of abuse and addiction
- Circumvent Drug Testing, Drug/DUI Laws
- Produce new addiction concerns
- Present drug toxicities that have not been reported or vetted but all lead to impaired driving as well as major health problems
- Pose a great threat to maintenance of sobriety and recovery (propagates denial)
End Part I: Current Trends in Substance Abuse

NEW BEGINNINGS

Every journey begins with a single step, but a little foresight would do you some good. In all honesty, most ventures are doomed from the start and spring from poor planning and heavy drinking...like you, for instance. (probably)

Questions? / Comments?
Afternoon Break?
Part II: Evolving Science of Addiction & Recovery: Dispelling The Stigma

Darryl S. Inaba, PharmD., CATC V, CADC III
Director of: Clinical and Behavioral Health Services - Addictions Recovery Center
Research and Education - CNS Productions, Inc. Medford, Oregon

NAADAC 2013 Atlanta Georgia
Substance-Related and Addictive Disorders

- Misconceptions, Misunderstandings, Myths & Stigma [weak, bad, stupid, crazy]
- 60% illicit drugs sold in suburbia or rural US
- 75% Hard-Core drug users: actively employed
- <5% Alcoholics fit “Wino” stereotype
- US lifetime prevalence = 30% (Inc. Mensa)
Disease/Disorder

A pathological impairment of health or a condition of abnormal functioning associated with specific symptoms and signs caused by internal or external factors that result in an expected (predictable) set of discomforts or dysfunctions.
Disease Characteristics

- Chronic (persistent)
- Progressive
- Relapsing
- Incurable but Treatable/Manageable and often Preventable
- Fatal if untreated

Diabetes analogy to Addiction Disorders
Pathomimetic Symptoms 3 Polys / 6 Cs
Mental Health Parity and Addiction Equity Act Oct. 2008

- Addiction is a biologic & psychological Medical Disorder due to anomalous neurocellular, neuro-chemical & neuro-functional features of vulnerable individuals.

- 10 U.S. Addiction Medicine Residency programs launched on 7/1/11; 15 as of May 2013.
DSM V – May 18 2013
Impulse Control Disorders of DSM IV-TR redefined as Substance-Related and Addictive Disorders
Pathological Gambling (Inc. Internet Gambling) accepted as such
Compulsive Buying?
Compulsive Sexual Behavior maybe
Internet or Compulsive Computer Use?
Others: Trichotillomania, Kleptomania, Pyromania, Intermittent Explosive Disorder
Brain Imaging Revealing Anomalies Of Process Addictions: Gambling
Internet Including Gaming and Gambling On-Line
Addiction Pathway
Brain Circuits & Processes

- **Reward/Reinforcement (Go)**
  
  *[I prefer Survival/Reinforcement]*
  
  *Hyperactivity then Hypoactivity*

- **Control (Stop)**

  *Impaired, dysfunctional or disconnection of Go and Stop*

Bill Cohen: Overactive go, Damaged Stop & Lack of Communication between them
Relapse Related Brain Circuits and Processes

- Stay Stopped (Slip Decisions)
- Emotional Memory (Cravings)
- Stress Hormone Cycle (Hypersensitivity)
Neurons in Earth’s Fossil Record: Spinal Cord to Diencephalon to Mammalian-Meso Cortex to Neo Cortex

Earth 4.5 Billion Years, Life from 4 Billion Years
reward/reinforcement pathway

Prefrontal Cortex
Nucleus Accumbens
Lateral Hypothalamus
Amygdala
VTA
Brain on Cocaine

Minutes after shooting or smoking

1-2 Min
3-4
5-6
6-7
7-8
8-9
9-10
10-20
20-30

Courtesy of Nora Volkow, Ph.D.
Cocaine affects addict’s brain differently than a Normies brain.

Glucose metabolism in Prefrontal Cortex & Cingulate Gyrus
Diabetes = Pancreas Beta Cell Anomaly
3. Addiction is a disease of the brain as other diseases it affects the tissue function.

Decreased Brain Metabolism in Drug Abuse Patient

Control  Cocaine Abuser

Decreased Heart Metabolism in Heart Disease Patient

Healthy Heart  Diseased Heart

Sources: From the laboratories of Drs. N. Volkow and M. Schelbert.
VTA Dopamine Cells of Opiate Addict vs. Non Addict Rat
Medial Prefrontal Cortex: Value
Lateral Prefrontal Cortex: Consequence
Control Circuitry = Stop Switch

- Orbital Prefrontal Cortex – Especially left ventral medial OFC
- Fasciculus Retroflexus (anterior)
- Lateral Habenula (posterior and mesocortex terminal)

Age of first use correlation to future addiction
Diffusion Tensor Imaging
Acute Reinforcing Effects
Courtesy of Dr. John Hart

Limbic Area
- Role: Drive Generation (SURVIVAL)
- Intervention: Pharmacotherapy

Prefrontal Cortex
- Role: Executive Function
- Intervention: Counseling
Prefrontal Cortex

Nucleus Accumbens

Arcuate Nucleus

Ventral Tegmental Area

Brain Reward Pathways

Dopamine
Glutamate
Opioid Peptides

Courtesy of Dr. John Hart, Portland, Oregon
Brain Processes of Relapse

A. Slip/Stay
Stopped Brain Anomalies
Courtes of Paulus, M.P.; Tapert, S.F.; and Schuckit, M.A. NIDA, Archives of General Psychiatry, 62(7), 2005


Right Insula

Right Inferior Parietal Lobule

Right Middle Temporal Gyrus

Left Caudate/Putamen

Left Cingulate Gyrus
RELAPSERS, NONRELAPSERS MAKE DECISIONS DIFFERENTLY

During a decision-making exercise, nonrelapsers activated five brain regions that relapsers did not.

- **Right Insula**
- **Right Inferior Parietal Lobule**
- **Right Middle Temporal Gyrus**
- **Left Caudate/Putamen**
- **Left Cingulate Gyrus**

The bar graph shows the percent difference in activity during decision-making relative to activity during simple response for relapsers and nonrelapsers.
Why Can’t Addicts Just Quit?

Non-Addicted Brain

Control

Saliency ➔ Drive

NO

Memory

Addicted Brain

Control

Saliency

Drive ➔ Memory

GO

Because Addiction Changes Brain Circuits

Adapted from Volkow et al., Neuropharmacology, 2004.
Addiction is a battle between the old primal brain and the new brain.

Old Brain = Survival (5X faster and more powerful) than Neocortex = Control, Planning and Decision Making.
Brain Processes of Relapse

B. Memories

Formation & Role In Drug Cravings
Neuro-development of Memories

Dendritic spines, bumps or protrusions
Dendritic Memory Spines

• Amygdala process emotional memories, hippocampus all other memories
• Also known as Bumps, Spikes – I like the term memory protrusions = less triggering
• 4 to 6 sensory inputs of the same stimulus per hour results in development of a semi-permanent memory protrusion
• The more often a memory protrusion is activated the larger it grows and the more permanent it becomes
Courtesy of Max Planck Institute of Neurobiology
Meso-Limbic Reward-Reinforcement Circuitry of the MFB

- Phase I – Endogenous/Environmental Cue or memory triggers the Ventral Tegmental Area to release dopamine which activates core of Nucleus Accumbens Septi = anticipation of use ON A MISSION! If initiated difficult to stop

- Phase II – Cues or actual use of addictive drug activates dopamine “go” switches of lateral hypothalamus and Nucleus Accumbens (core and shell): COMPULSION FOR MORE!

- Phase III – Control circuitry of the prefrontal cortex is disrupted, is inactivated and releasing glutamate: results in LOSS OF CONTROL, CONTINUE DESPITE NEGATIVE CONSEQUENCES
Reward / Reinforcement Pathway

Stop Switch

Prefrontal cortex

Go Switch

Nucleus accumbens
Lateral hypothalamus
Amygdala
Hippocampus
Substantia nigra

Ventral tegmental area
New NIH Details on Addiction Craving Brain Pathway

• Hippocampal memory process activates
• Lateral Septum via glutamate and this in turn activates
• Ventral Tegmental Area (VTA) via gamma-aminobutyric acid (GABA) that then activates
• Nucleus Accumbens Septi ("go Switch") via dopamine

Luo, AH, et al. Science 7/15/11
Brain Processes of Relapse

C. Stress Hormone Cycle Hypersensitivity
Hypersensitivity of Stress Hormone Cycle in Addiction

1. Stress activates hypothalamus release of corticotropin Releasing factor (CRF)

2. CRF activates pituitary release of adrenocorticotropic hormone (ACTH)

3. ACTH activates kidney adrenal glands to release cortisol
“Addiction is a stress-induced defect in midbrain’s ability to perceive pleasure”

Dr. Kevin McCauley

- CRF & ACTH are neurotransmitters as well as hormones they modulate novelty-seeking and dopamine activity in the brain
- Severe stress increase risk-taking behaviors in all and suppress dopamine’s ability to perceive reward, survival reinforcement, “pleasure?” resulting in anhedonia since
- CRF & ACTH as neurotransmitters produce the unpleasant emotional reactions associated with stress
- Cortisol usually turns off these secretions to terminate a stress reaction but extreme stress overrules cortisol
Addictive drugs first release of dopamine in the midbrain fools it as being a coping mechanism for the relieve of stress

- Opiates & endorphins shown to also inhibit CRF & ACTH as cortisol would naturally do
- But, withdrawal from opiates cause increase release of CRF, ACTH and creates hypersensivity to stress that overrule cortisol’s regulation of cycle = craving
- Cocaine directly releases the CRF and ACTH mistaken as part of or covered by the rush, stimulant withdrawal also activates the stress mechanism = craving
- Research: metyrapone validation (shuts off cortisol production increasing CRF & ACTH) and CP-154,526 treatment (blocks CRF and thus suppresses ACTH release)

Heilig and Koob 2007, Lowery et al. 2008
VTA’s (ventral tegmental area): GABA-releasing neurons, dopamine-releasing neurons and Kappa opioid receptors interaction in stress. Drugs and natural satiations release dopamine in the VTA. GABA applies a brake to this via strengthening synapses (known as long-term potentiation or LTP) but stress interrupts this process leading to unabated dopamine reinforcement. Nor-BNI blocks Kappa receptors in the VTA and prevents stressed out rats from relapsing to cocaine use.

Historic Evolution of Addiction Science
Dr. Robert Heath,
Tulane University, 1959
American Society of Addiction Medicine Definition

Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry

Adopted April 19, 2011

A Brain Reward Disorder

Dr. Kenneth Blum 1990
National Institute on Drug Abuse (NIDA) View of Addiction

All drugs of abuse target the brain's pleasure center.

**Brain reward (dopamine) pathways**

These brain circuits are important for natural rewards such as food, music, and art.

**All drugs of abuse increase dopamine**

Typically, dopamine increases in response to natural rewards such as food. When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

**Food**

- Dopamine Transporter
- Dopamine
- Dopamine Receptor

**Cocaine**

- Dopamine Transporter
- Dopamine
- Cocaine
- Dopamine
Brief Review of Brain Cells and their communication processes
Neurons are the fundamental units of the nervous system. They consist of a cell body, dendrites, axon, and synapses. Dendrites receive signals from other neurons, the cell body processes these signals, and the axon transmits the signals to other neurons or to muscles and glands. Synapses are the points where signals are transmitted from one neuron to another. Electrical transmission occurs across the synapses.
By Age 6 100 Billion Neurons and then Development of a Quadrillion Synapses
Electron Microscopy of Neurons, Dendrites and Axons

Professor Terry Wiseth, Northland College
Neurotransmitters

- Acetylcholine
- Norepinephrine
- Epinephrine
- Dopamine
- Endorphin
- Enkephalin
- Serotonin (5HT)
- GABA
- Substance “P”
- Anandamide
- Glycine
- Histamine
- Nitric oxide
- Glutamic acid
- Cortisone
- Aspartic Acid
- Oxytocin

© 2007, CNS Productions, Inc.
Synapse @ 50,000x Electron Microscopy

Professor Terry Wiseth, Northland College

Courtesy of Thomas Deerinck, NCMIR/Photo Researchers, Inc.
Synapse @ 50,000x Electron Microscopy

Courtesy of Thomas Deerinck, NCMIR/Photo Researchers, Inc.
Drugs Mimic, Disrupt, or Block Neurotransmitters

SOME EXAMPLES -

UPPERS: Catecholamines (Norepinephrine, Epinephrine, Dopamine) + Serotonin and Acetylcholine

DOWNERS: Endorphin, Enkephalin, GABA, Serotonin

PSYCHEDELICS: Serotonin, Acetylcholine, Alpha Psychosin, Norepinephrine, Dopamine, Anandamide & endocannabinoids
Taking one: **Uptown, Downtown and “Outatown”**

- **CNS Stimulants** increase the electrical and chemical activity of the brain (caffeine to ‘Ice’)
- **CNS Depressants** decrease the electrical and chemical activity of the brain (‘booze’ to ‘benzos’ to opioids)
- **All Arounders (Psychedelics)** distort and interfere with brain perceptions to produce delusions, illusion, hallucinations, & synesthesia (DXM: ‘Robo’ to ‘paka-lolo’ to Sylvia d)
- **Misc**: Inhalants, Anabolic Rhoids, Behaviors
All Addictive Substance Involve Dopamine Activity
2012 UCSF Research Confirms Role of Endogenous Opioid Neurotransmitters in Reward Circuitry as well as Dopamine

Beta Endorphin

Met-Enkephalin
Also Excess Nor Epinephrine (Nor Adrenaline) and Less Transporters in Pathological Gamblers
Expanding Role of GABA & Glutamate

Gamma-aminobutyric acid (GABA)

Glutamate (glutamic acid)

Inhibitory  Excitatory
Serotonin aka 5-hydroxytryptamine also involved with all addictions?
Brain Imaging: Impact of Addiction Pathology
Brain Imaging

1980s – First MRI studies of brain development
1990s – MRI find white matter increases and gray matter decreases with age

Thus, Process of Brain Development & Impact of Addiction Pathology Revealed
Multiple Brain Imaging Techniques
Dopamine Depletion in Addiction = Endogenous Craving and Anhedonia
<table>
<thead>
<tr>
<th>Cocaine abuse</th>
<th>Alcoholism</th>
<th>Obesity</th>
<th>Tobacco</th>
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Nicotine Evokes Addictive Brain Changes With Just One Puff

SMOKING SATURATES RECEPTORS. As nicotine from a synthetic airpuff is inhaled to the peak of NAS, nociceptive receptors in the brain (a) are displaced by radioactive tracer (red and yellow indicates high levels of the tracer, green indicates intermediate levels, and blue indicates low levels). The nicotine from three puffs displaced 75 percent of the tracer from study participants’ receptors, and the nicotine from three cigarettes, nearly all.
Chronic Alcohol Abuse  
Heroin Abuse
Normal Brain | Marijuana Abuse

Courtesy of Daniel Amen, M.D.
7 years Methadone use

Deborah - Methadone 100 mg/day
Xanax 20 mg/day FOR 20 YEARS

ONLY SIX WEEKS FOLLOWING DETOX
Brain Imaging Revealing Anomalies Of Process Addictions: Gambling
Internet Including Gaming and Gambling On-Line
Internet Addictions
Cybersex
Net relationships
Net compulsions
Information
Gambling
Games
Sex Addiction

Natural Rewards Elevate Dopamine Levels

RECOVERY
The Resilient Brain

8-10 Months Rigorous Uninterrupted Treatment for Reasonable Outcomes
Implies time needed for brain to become functional
Takes up to 2 years for greater functioning to return
Courtesy of Nora Volkow (Volkow, Hitzmann, Wong, et al 1992)
ADDITION CAN BE TREATED

Partial Recovery of Brain Dopamine Transporters in Methamphetamine (METH) Abuser After Protracted Abstinence

Dopamine Transporter Binding (DAT) Recovery in Meth Addiction

DAT Recovery with prolonged abstinence from methamphetamine

Volkow et al. J. of Neuroscience 2001
Brain Recovery even after 7 years Methadone and Xanax

7 years Methadone use

Deborah - Methadone 100 mg/day
Xanax 20 mg/day FOR 20 YEARS

ONLY SIX WEEKS FOLLOWING DETOX
Dr. Ken Blum’s patented: Synapta GenX, KB220Z

Neuronutrient complex “normalization” of caudate, accumbens and putamen regions of heroin addicts demonstrated by fMRI Scan
Recovery

• Continued Abstinence
• Discovery of Natural Highs
• Recovery of neurotransmitters and of natural brain functions
• Positive lifestyles and quality of life enhancements
• Remember: Not an Event but a Process

One does not cure addiction, you treat it and manage it like any other chronic persistent medical disorder
Conclusion

• Addiction is not about morals, will power or character. It’s about anomalous neurocellular, neurochemical and neurofunctional features of vulnerable brains that hijacks their reward and control circuits resulting in behaviors that are defined as Addiction.

• Good news is that the brain is resilient, it’s plastic, it has the ability to bring itself back to healthy functionality if given the chance to.
A lot of information compressed in a very short time!

Questions?
Thank You!

Darryl Inaba, PharmD., CATC V, CADC III

Director of Clinical & Behavioral Health Services
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