Neurobiology of Substance Use Disorders

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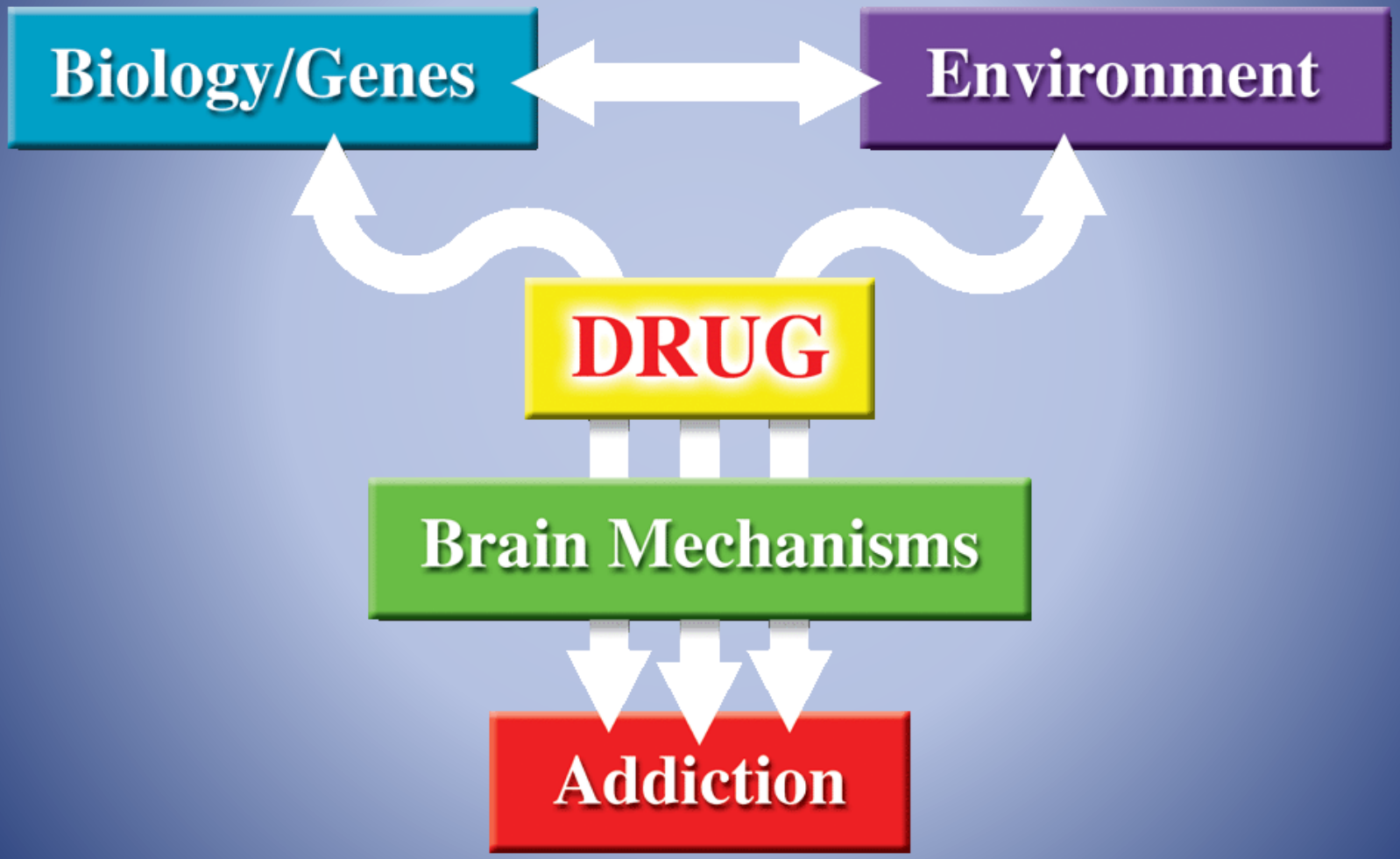
How does substance abuse develop?



Background

- Addiction is a chronic disease of brain reward, motivation, memory and related circuitry.
- The harmful use of alcohol results in 3.3 million deaths each year.
- Smoking kills at least 5 million every year
- Some 31 million persons have drug use disorders.
- Almost 11 million people inject drugs

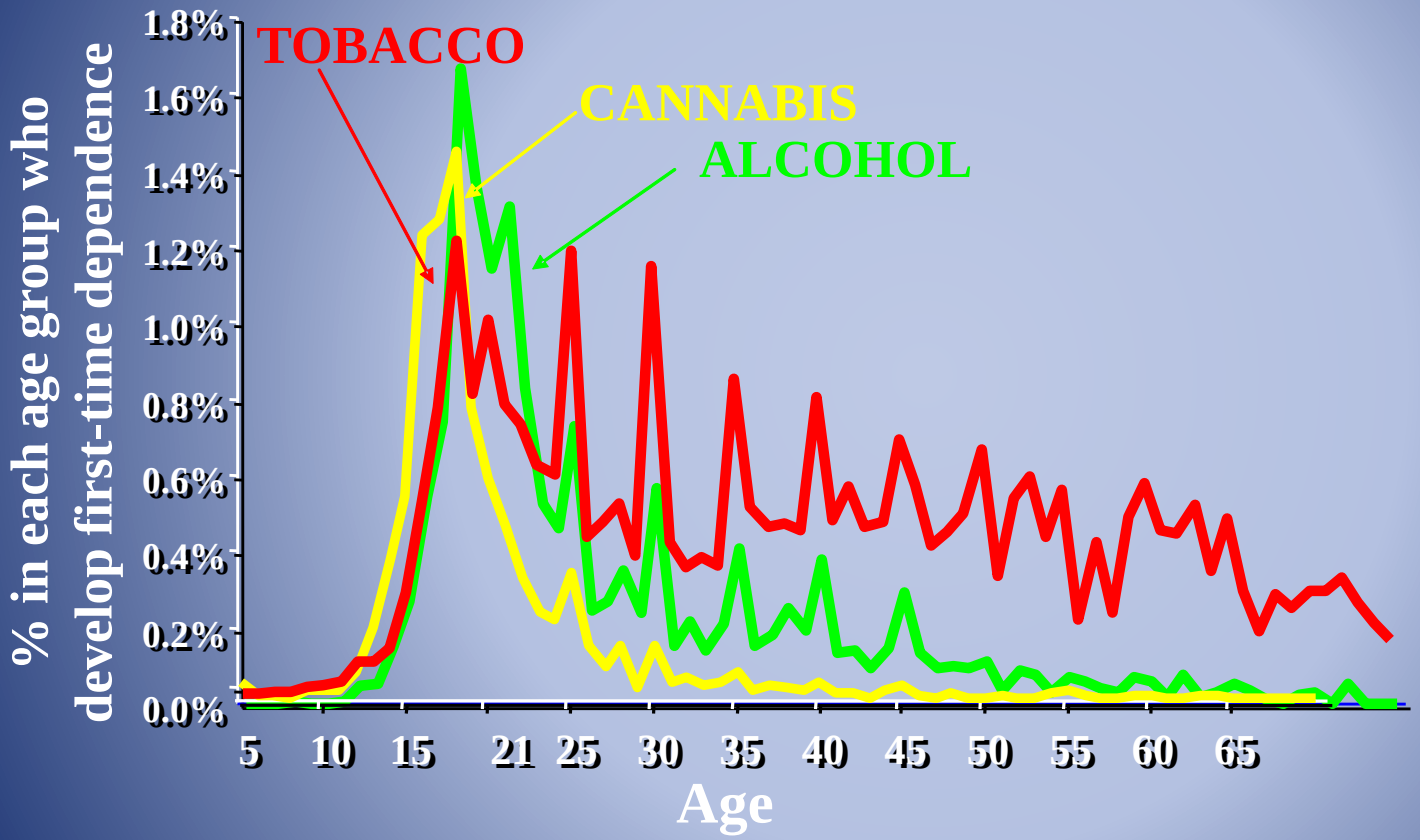
Common Substances of Abuse

- Alcohol/Sedatives (hypnotics, BNZ, etc..)
- Narcotic Opiates (tramadol, heroin, oxycodone)
- Stimulants (amphetamines, cocaine)
- Recreational drugs (MDMA, ketamine, Ecstasy)
- THC cannabis marijuana
- Nicotine (waterpipe, cigarettes, e-cigarrtes)
- Caffeine
- Inhalants (nitrous, butane, glue)
- Herbals (salvia)
- Behavioral Addictions: gambling, pornography, gaming

Most common substances

- Alcohol dependence: 100 million estimated cases
- cannabis dependence: 22 million cases
- opioid dependence: 20 million cases

The earlier the exposure to a substance the likelihood of Addiction is higher



Age at tobacco, alcohol, and cannabis dependence per DSM IV

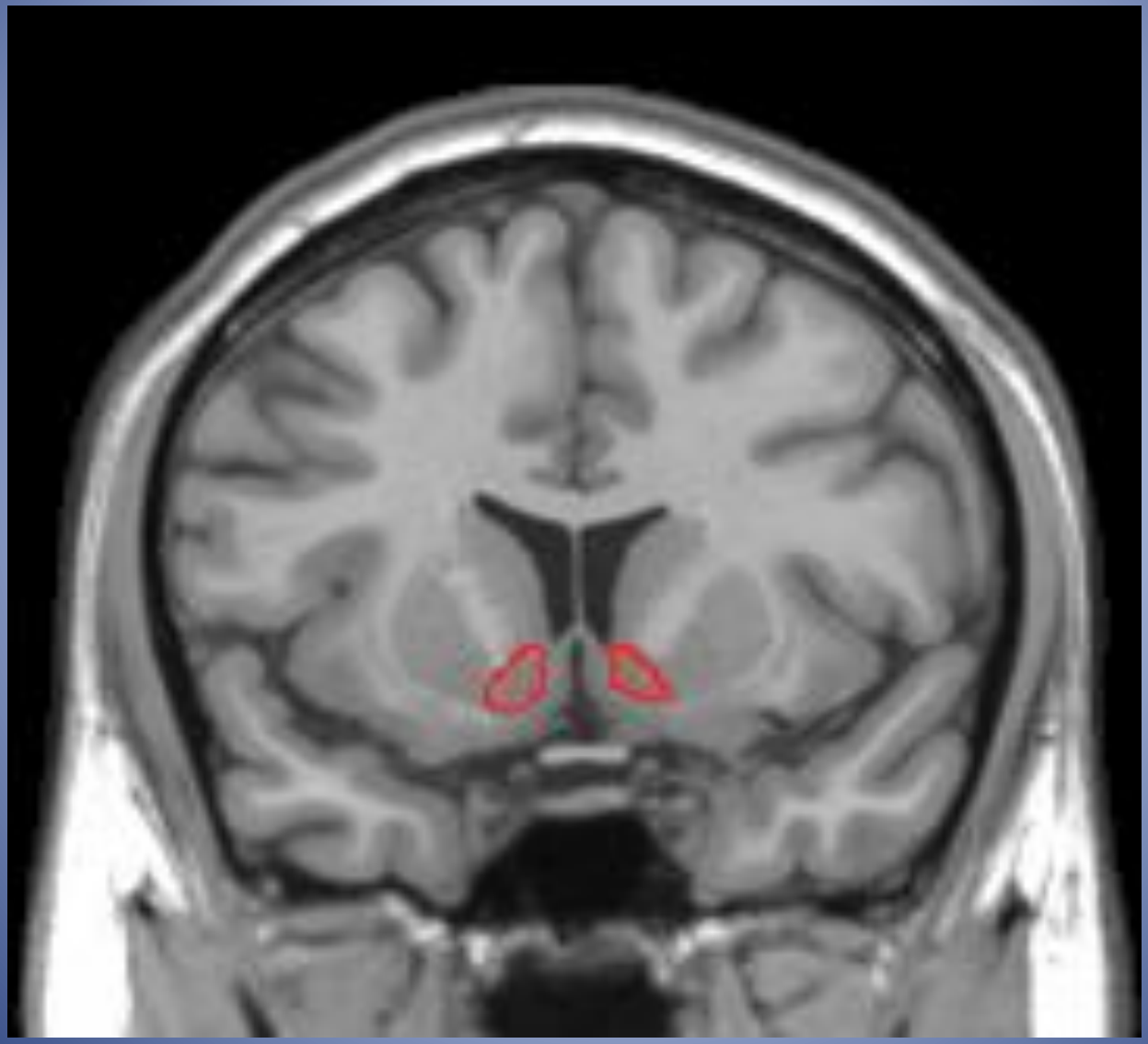
National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

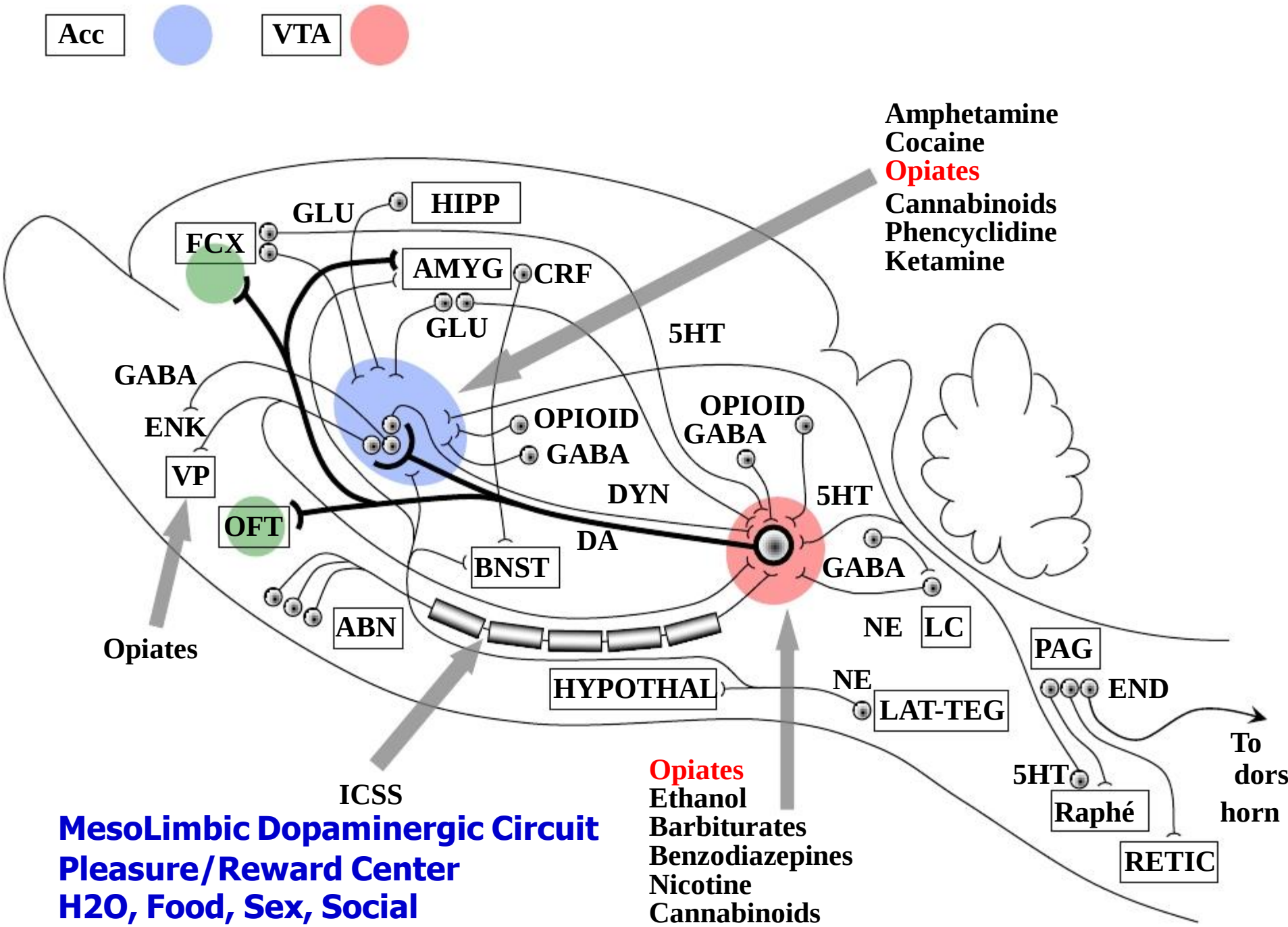
NIDA

Neurobiology of Substance Abuse

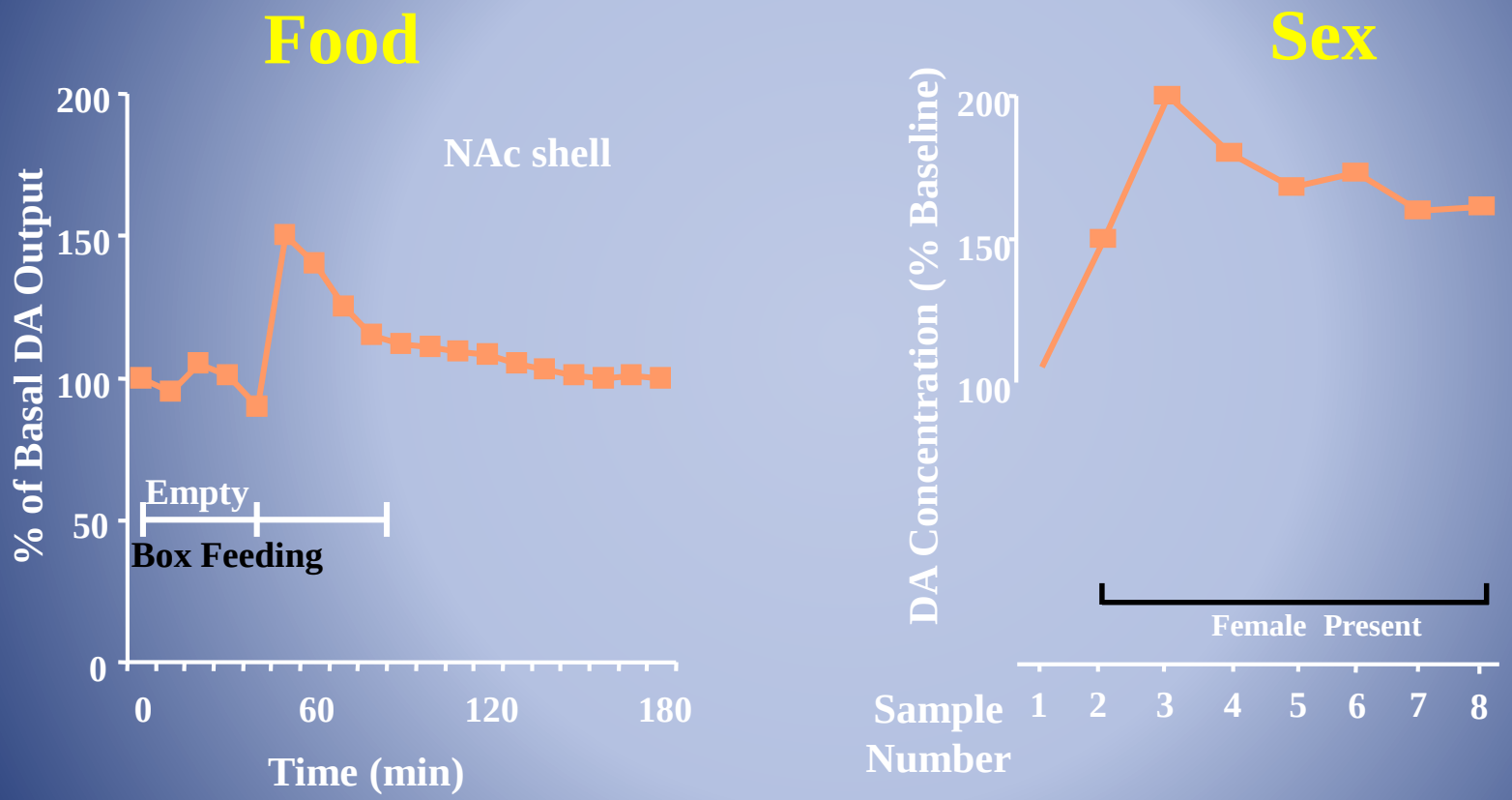
- **Limbic** system of the brain is involved
- Drugs/alcohol activate the brain “reward” system
- The central part of the addiction pathway is the **Nucleus Accumbens** and the VTA ventral tegmental area in the brain
- Main neurotransmitters involved in the addiction pathways are **DOPAMINE and SEROTONIN**

Nucleus Accumbens




Acc
VTA
Amphetamine
Cocaine
Opiates
Cannabinoids
Phencyclidine
Ketamine
HIPP
GLU
FCX
AMYG
CRF
GLU
5HT
GABA
ENK
VP
OPIOID
GABA
OPIOID
GABA
DYN
5HT
OFT
DA
BNST
GABA
ABN
NE
LC
PAG
Opiates
HYPOTHAL
NE
END
LAT-TEG
To
dors
horn
5HT
Raphé
RETIC
ICSS
Opiates
Ethanol
Barbiturates
Benzodiazepines
Nicotine
Cannabinoids
MesoLimbic Dopaminergic Circuit
Pleasure/Reward Center
H2O, Food, Sex, Social

Euphoria (feeling good) is related to Dopamine: Natural Rewards



Di Chiara et al., Neuroscience, 1999.,Fiorino and Phillips, J. Neuroscience, 1997.

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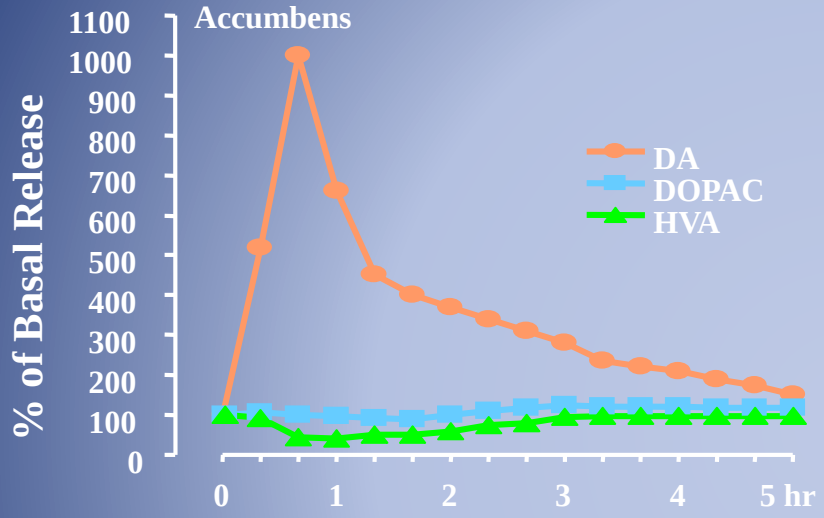
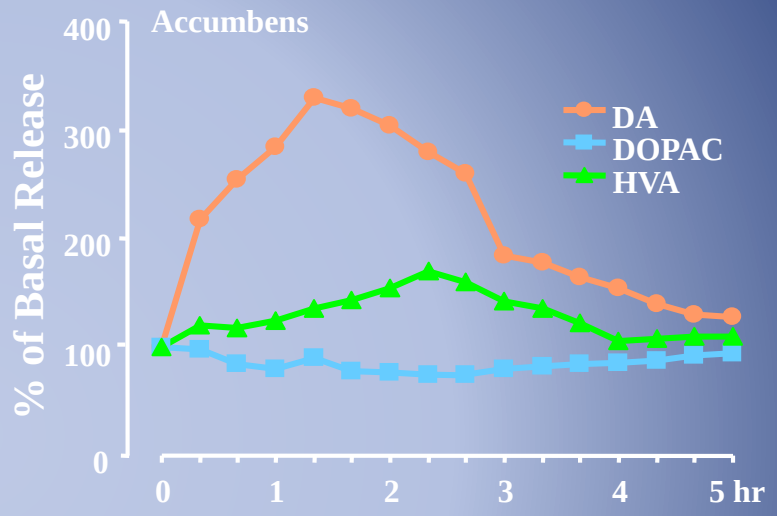
Effects of substances on Dopamine

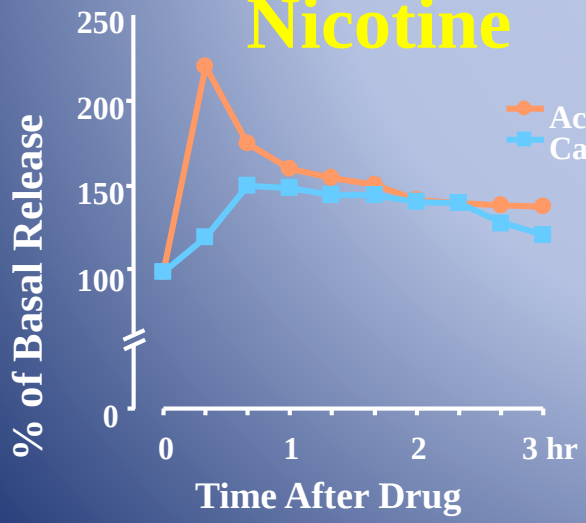
Amphetamine



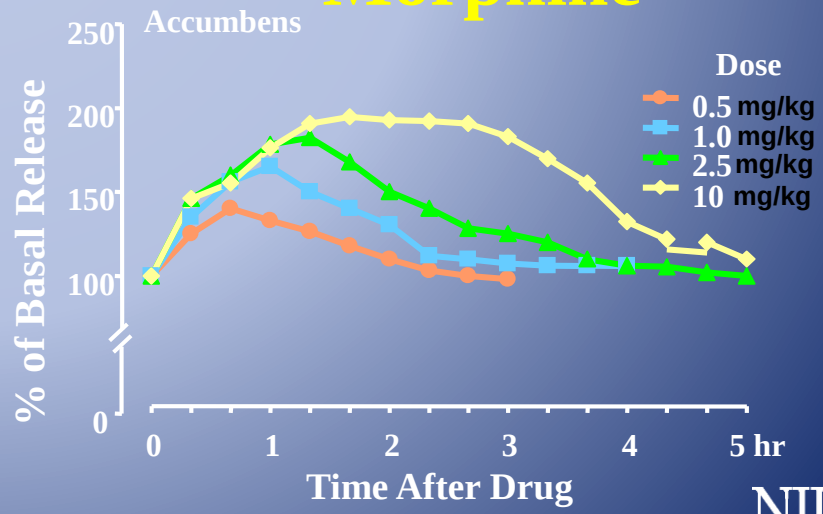
Cocaine



Nicotine



Morphine



Di Chiara and Imperato, PNAS, 1988

NIDA

Vulnerability factors for Addiction:

1. High reactivity to stress
2. High novelty seeking/High impulsivity
3. Intrinsic reward deficiency (low dopamine state)

The above can manifest clinically as:

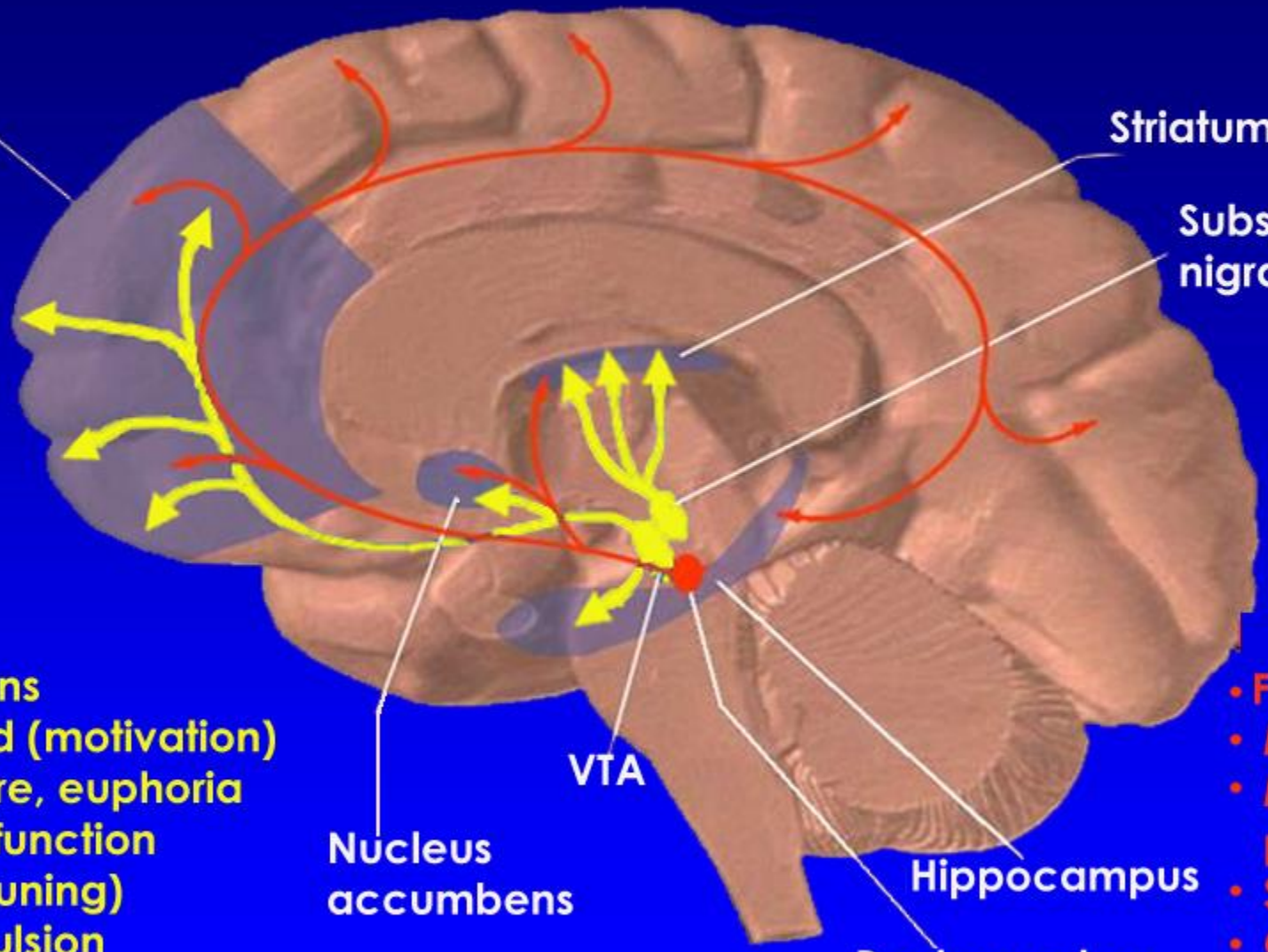
Conduct Disorder, MDD, and ADD/ADHD

WHY is ANY SUBSTANCE USE RISKY?

- We cannot predict how our genes will interact with DRUGS/ALCOHOL
- We cannot predict how are brain/nervous system will be affected.
- Some of the changes that happen in the YOUNG brain can be IRREVERSIBLE

Dopamine Pathways

Serotonin Pathways



Functions

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

- Functions
- Mood
- Memory processing
- Sleep
- Cognition

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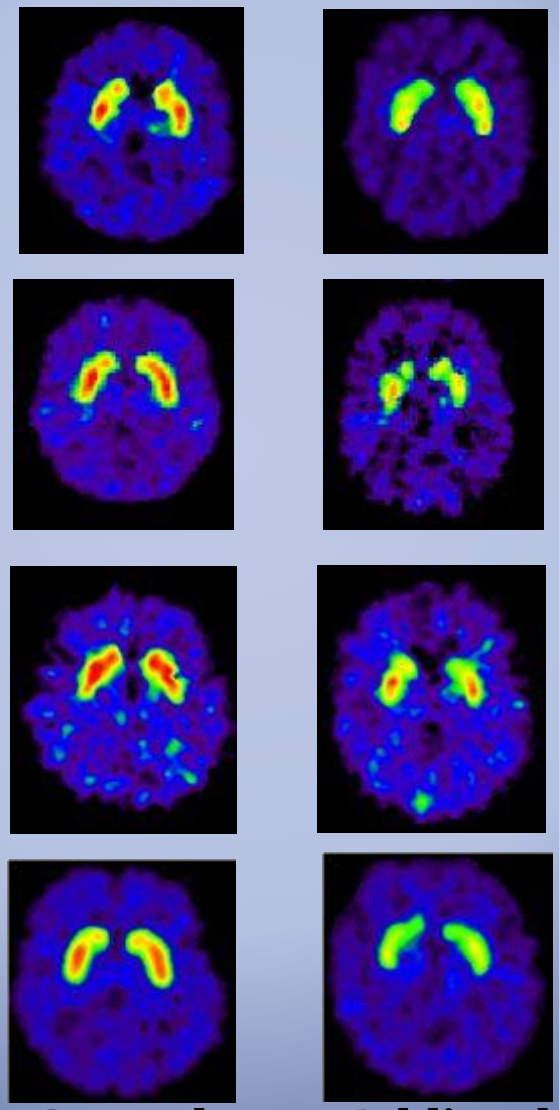
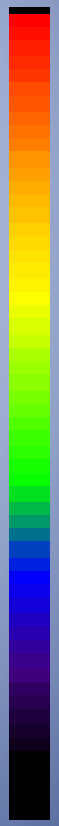
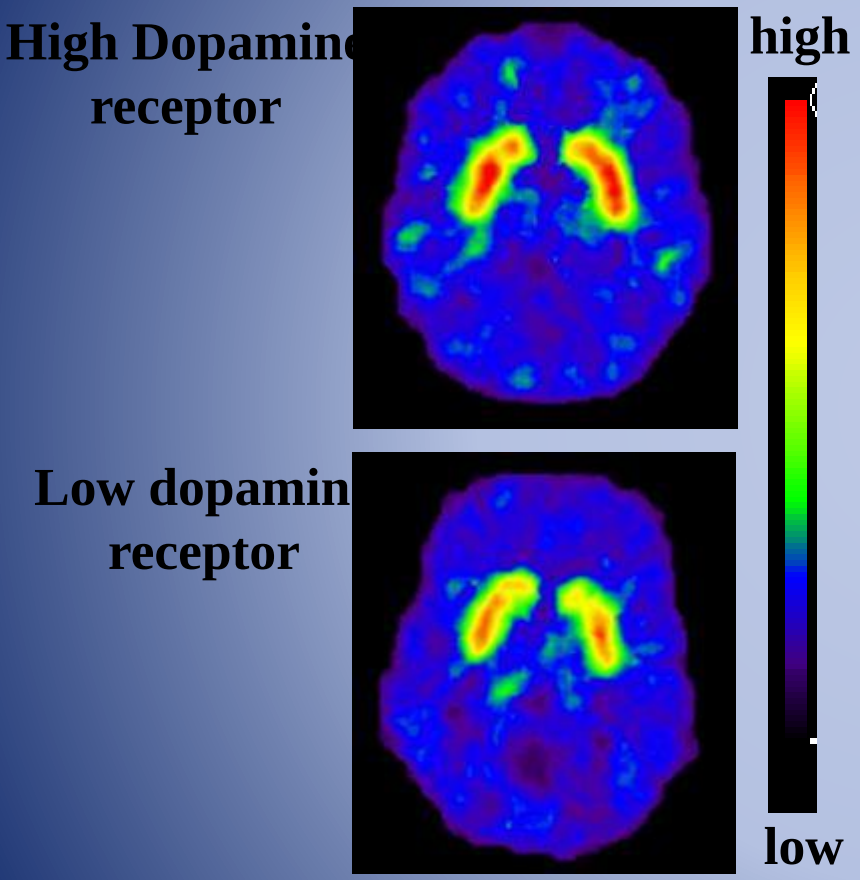
Dopamine D2 Receptors are Decreased by Addiction

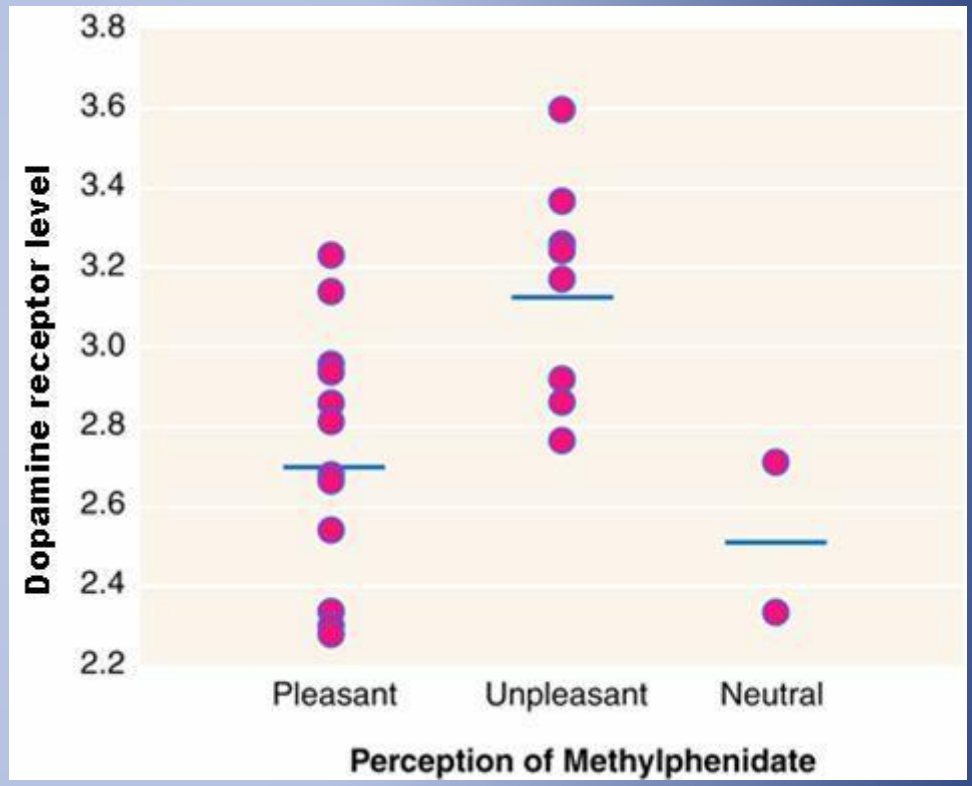




DA D2 Receptor Availability

Individual Differences in Response to Drugs: 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.

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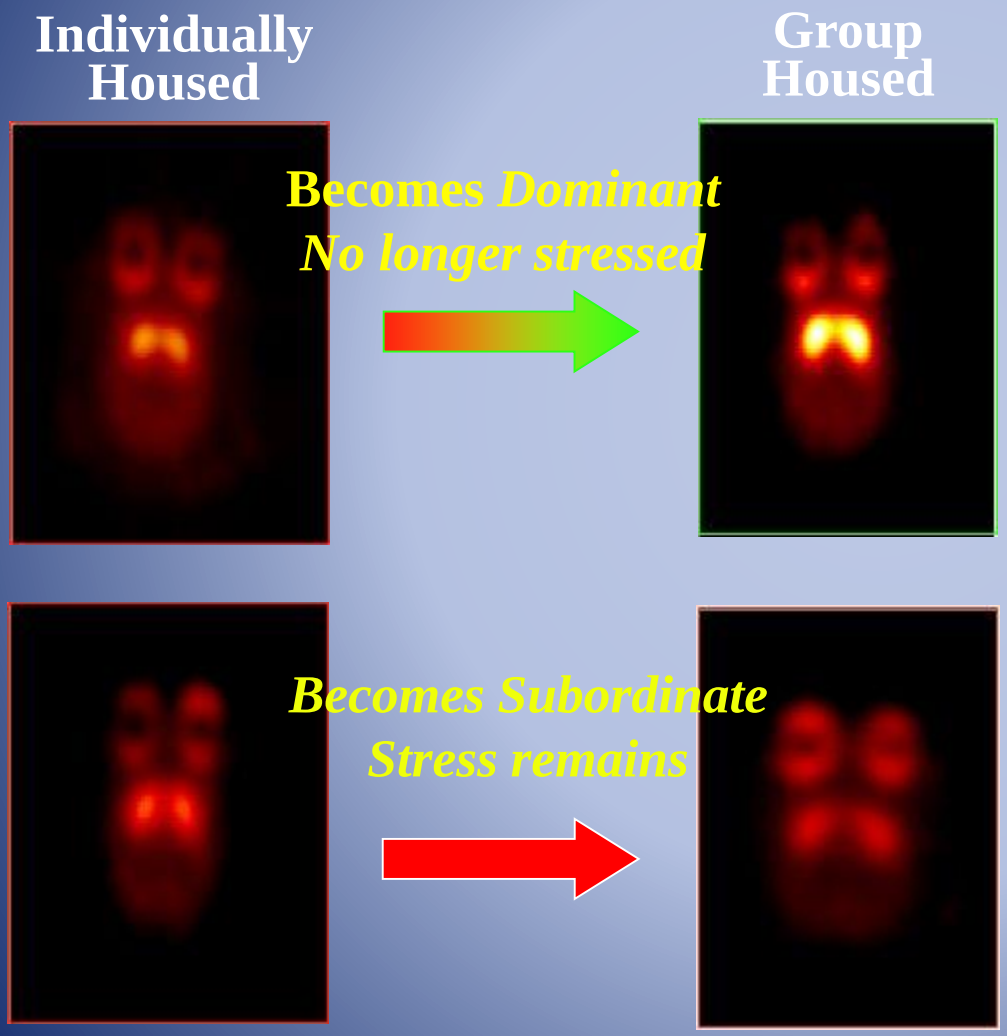
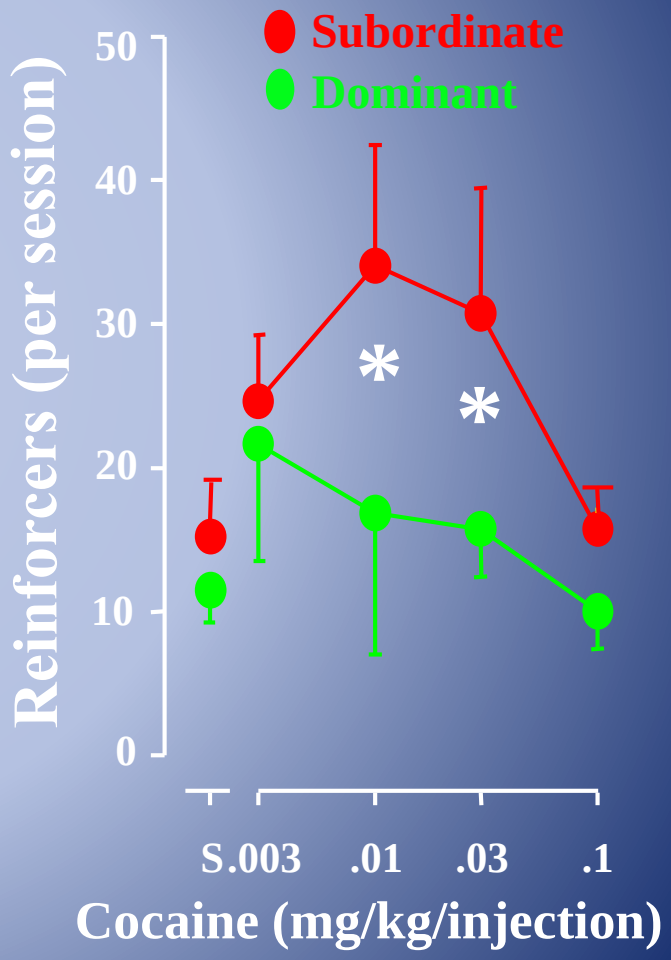
Social Stressor Affects Brain dopamine Receptors and Drug Self-Administration





Morgan, D. et al., Nature Neuroscience, 2002.

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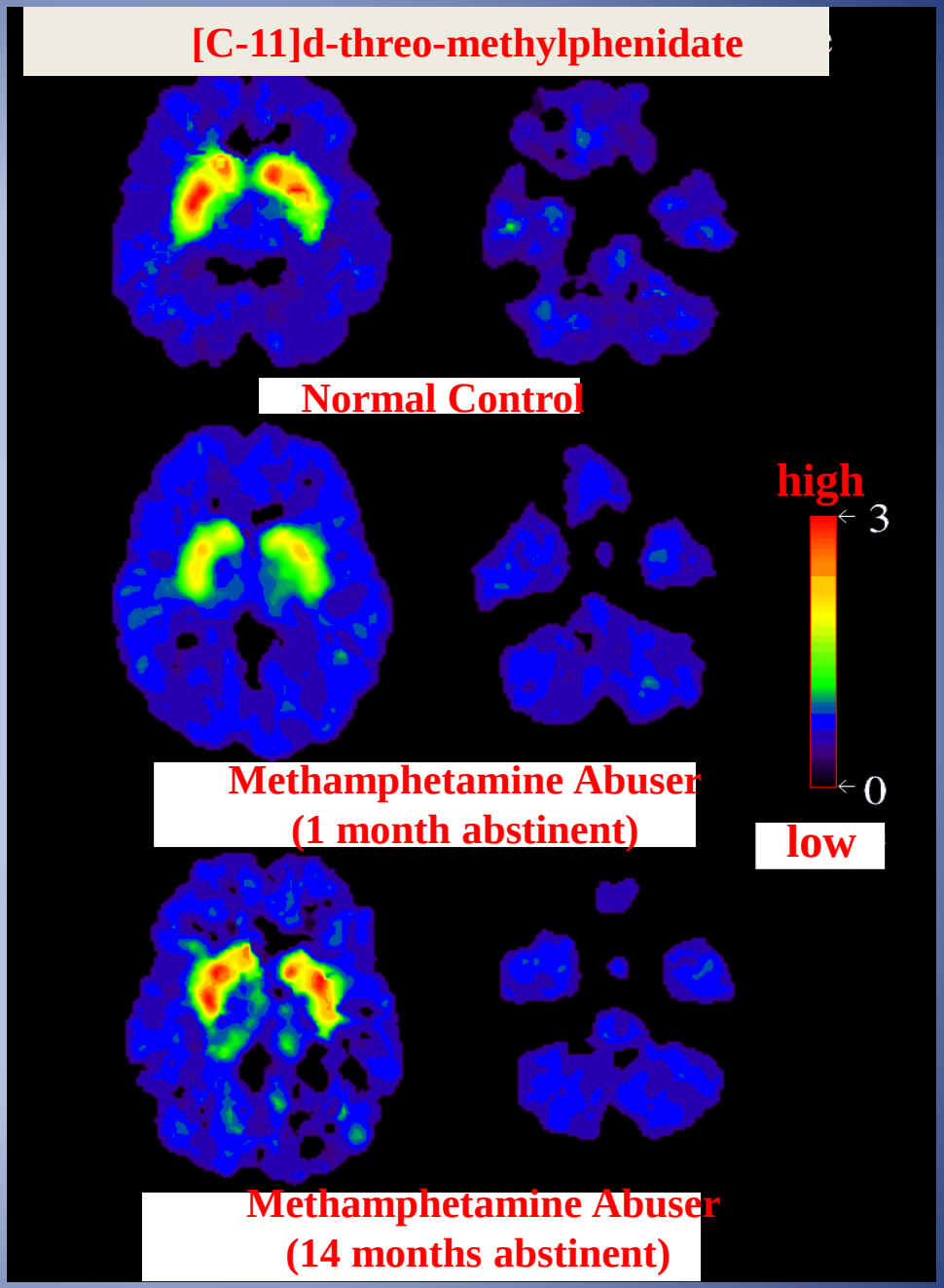
Recovery with prolonged abstinence from Methamphetamine: 12-14 month to normalize dopamine levels



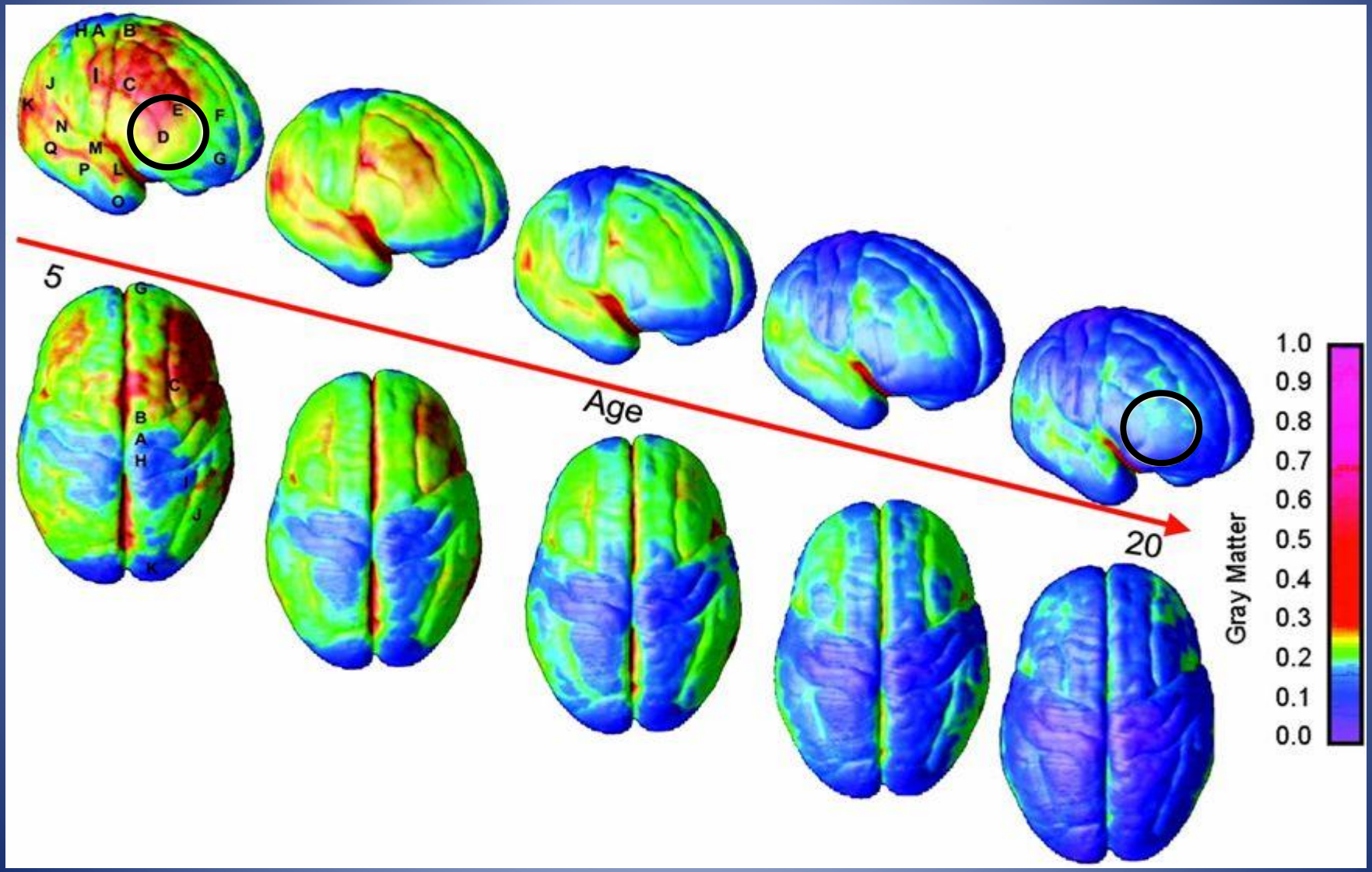
Volkow et al., J. Neuroscience, 2001.

It is important for young people to avoid drugs, because any substance can influence the growing brain.

The human brain does not complete its development until at least 21 years of age.

Exposure to drugs in the teenage years can seriously disturb brain development.

BRAIN Scans of Healthy Children and Teens Over Time



Gogtay, Giedd, et al. Proc. Natl. Acad. Sci., 2004

Why Do People Take Drugs in The First Place?

To have new:
feelings
sensations
experiences

To lessen:
anxiety
worries
fears
depression
hopelessness

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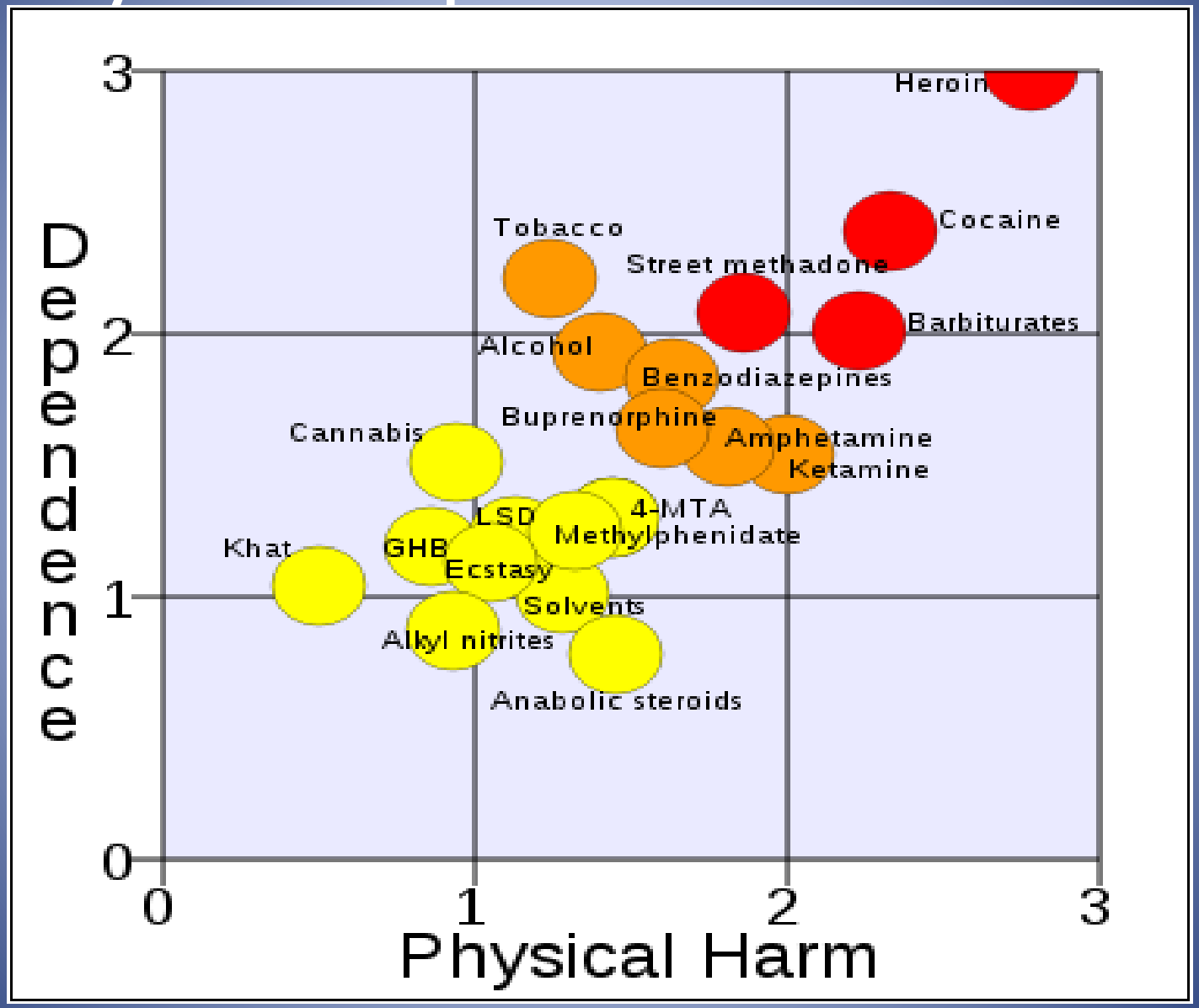
Bidirectional relationship: Addiction and Psychiatric Disorders

Psychiatric disorder causes substance use disorder

Substance use disorder causes other psychiatric disorder

Those with serious addiction problems up to 75% have a psychiatric disorder

Physical dependence vs. harm



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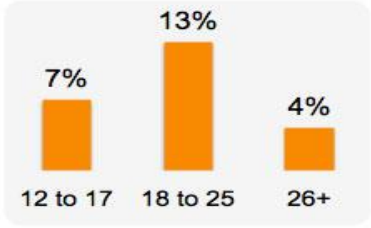
- Herbals (salvia)

Abuse of Prescription (Rx) Drugs

Affects Young Adults Most

Young adults (age 18 to 25) are the biggest abusers of prescription (Rx) opioid pain relievers, ADHD stimulants, and anti-anxiety drugs. They do it for all kinds of reasons, including to get high, or because they think Rx stimulants will help them study better. But Rx abuse is dangerous: In 2010, almost 3,000 young adults died from prescription drug (mainly opioid) overdoses—more than died from overdoses of any other drug, including heroin and cocaine combined—and many more needed emergency treatment.

PAST YEAR USE



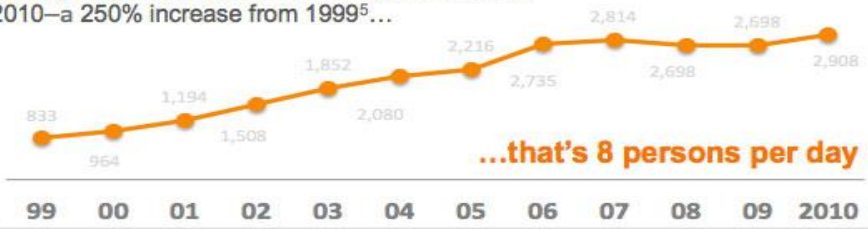
The nonmedical use of prescription drugs is highest among young adults.[1]

MOTIVATIONS FOR USE

Most young adults say they use Rx drugs to[2,3,4]

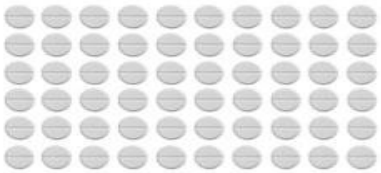
CONSEQUENCES

3,000 young adults died from Rx drug overdose in 2010–a 250% increase from 1999[5]…



Among young adults, for every death due to Rx drug overdose, there were

17 Treatment Admissions[6]



66 Emergency Room Visits[7]

Teens Mix Prescription Opioids with Other Substances

Nonmedical use of prescription (Rx) opioids by teens remains high, and a new study shows that 7 out of 10 teen nonmedical users combine opioid medications with other drugs and/or alcohol. This puts teens at much greater risk of overdose.

7 out of 10 teen nonmedical users combine Rx opioids with other substances[1]

The substances most commonly co-ingested were…

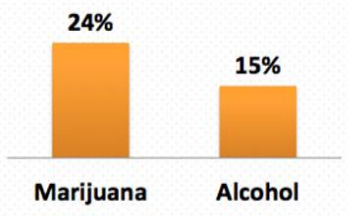
marijuana	alcohol	cocaine	tranquilizers	amphetamines
58.5%	52.1%	10.6%	10.3%	9.5%

Teens who reported co-ingestion of Rx opioids with other drugs were[2]…

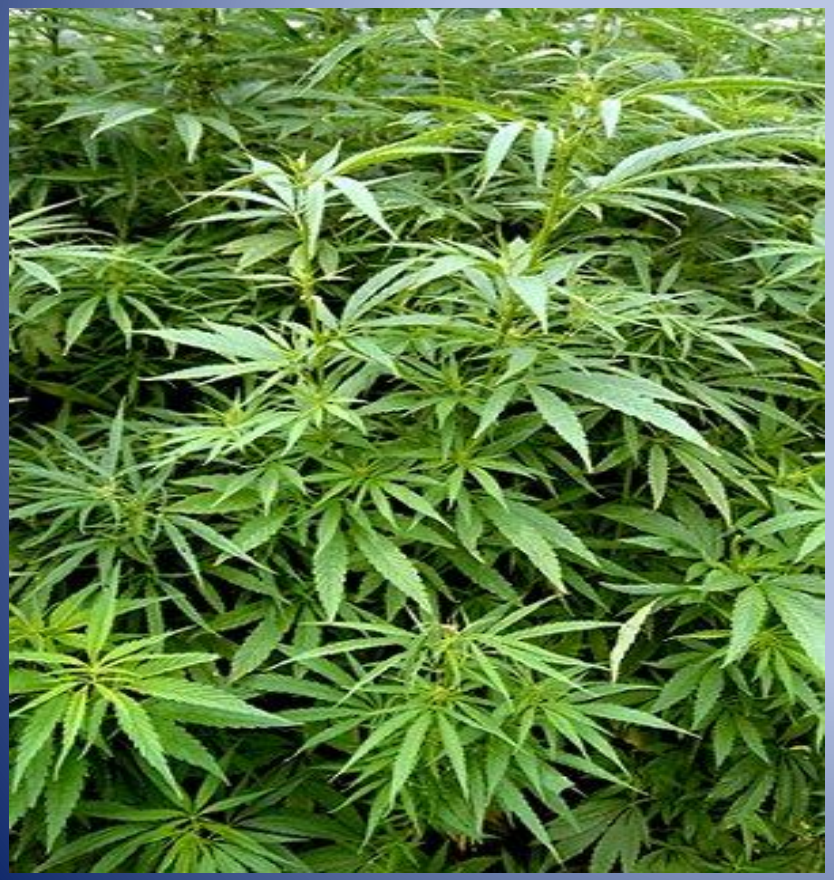
8X more likely to report abusing marijuana

4X more likely to report being drunk ≥ 10 times

Percent of teens that usually or always combine Rx opioids with marijuana or alcohol[3]



Cannabis: **tetrahydrocannabinol** (**THC**) exists in 2 types dried plants (weed/pot/Marijuana) and resin (Hashish/Hash) then smoked



Mental effects

- Euphoria and relaxation
- Memory impairment
- Concentration problems
- Slower reflexes
- Paranoia or Panic
- Loss of motivation syndrome?
- Can increase risk of serious psychiatric problems: Depression and Schizophrenia

Physical effects

- Fast heart rate
- Dizziness
- Dry Mouth
- Red eyes
- Appetite increase and weight gain
- Low testosterone!

Is cannabis addictive: YES

Approximately 10% of people who use marijuana will become addicted.

The risk increases in people who start using in their teens.

CANNABIS

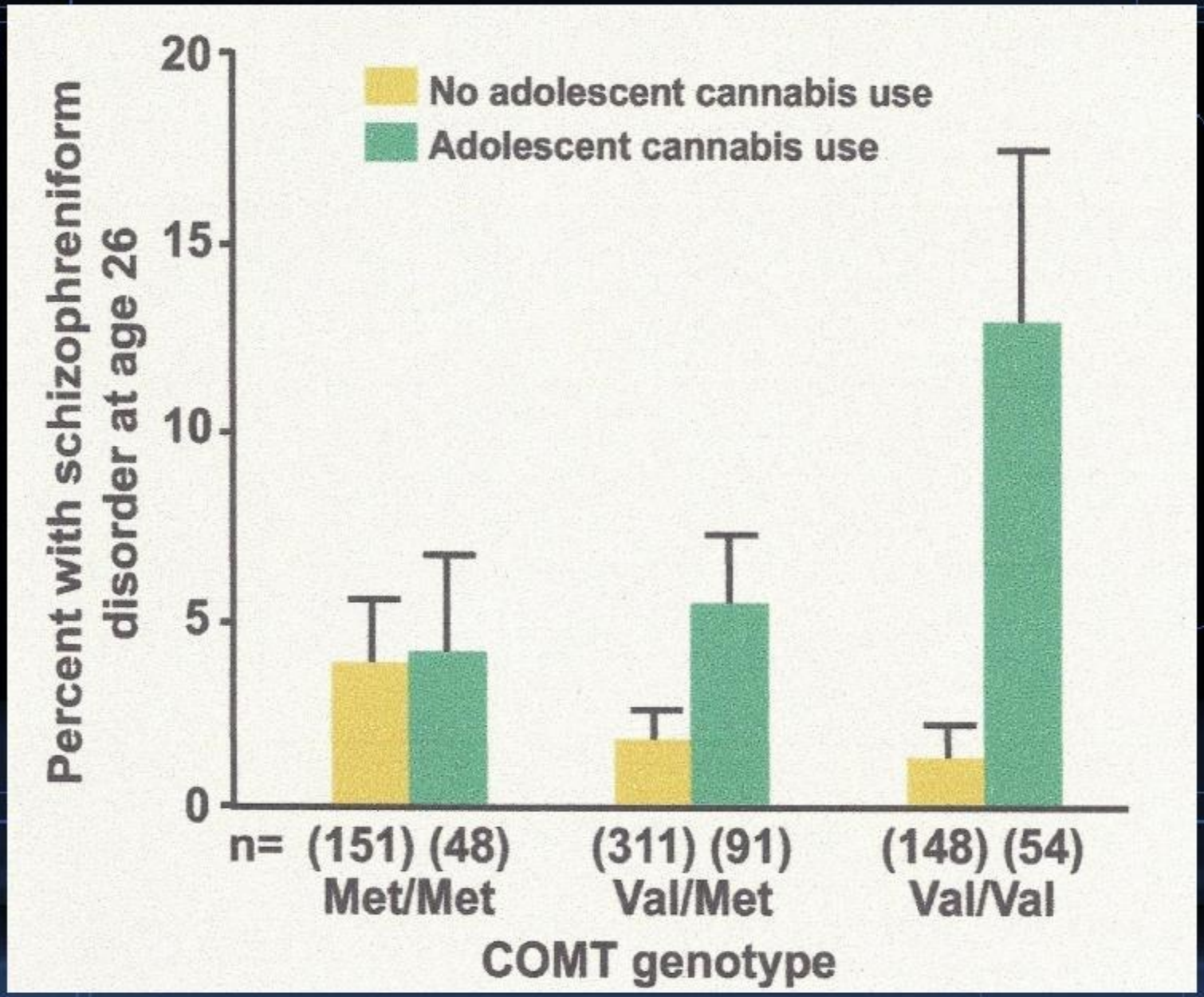
- **activates** CB1 (brain), CB2 (body) cannabinoid receptors
- Increases GABA (sedative) and Dopamine (euphoria)
- **Cannabis withdrawa**l is listed now in DSM V: can occur with insomnia, irritability, anxiety, poor appetite

CANNABIS cont.

- **Chronic cannabis use** can lead to development of schizophrenia (or psychotic disorders) independent of other risk factors. (ODDS Ratio) 4:1

- **May develop into a permanent disorder**

Psychosis: hard to predict vulnerability. Those with COMT gene homozygous for Val/Val genotype are at much greater risk for psychosis than those with Met/Met



Caspi, *Biol Psychiatry*, 2005

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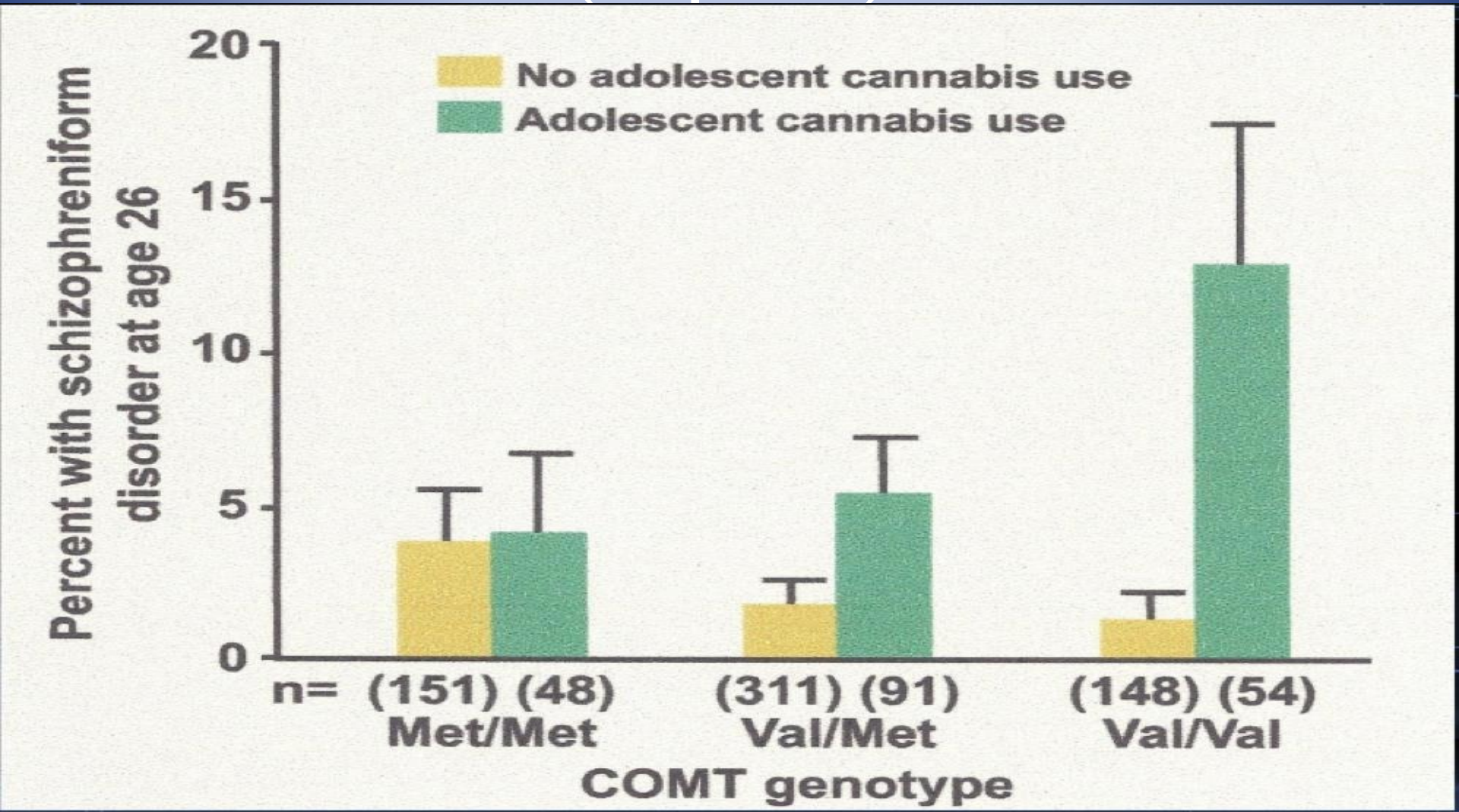


Synthetic Marijuana Lands Thousands of Young People in the ER, Especially Young Males

Since bursting on the scene a few years ago, synthetic marijuana (MJ)—often called "Spice" or "K2"—has become the second most popular illegal drug among American teenagers, after MJ. It is especially popular among teenage boys. Sometimes touted as a "natural," "safe," and (until recently) legal alternative to pot, this very *un-natural* class of designer chemicals has shown itself to be a dangerous threat. Thousands of teens and young adults, mostly young males, are ending up in emergency rooms with severe symptoms that may include vomiting, racing heartbeat, elevated blood pressure, seizures, or hallucinations.

How Many Teens Are Using Synthetic MJ?

In 2012, 11% of American high school seniors used synthetic marijuana in the past year.[1]

11,406 ER Visits In 2010 Were Associated With Synthetic MJ.[2]

75% were among adolescents and young adults ages 12-29.

22.5% of these visits involved females, and 77.5% involved males.

1. Monitoring the Future Survey, 2012; 2. Drug Abuse Warning Network, 2012

Salvia


Healthy
Suplements
Hierbas
Secas
SALVIA
(Sage Leaves)
Wt. 3/8 OZ (10.6 G.)

SALVIA

- Causes hallucinations
- Kappa opioid receptor activators
- It is a plant dried leaves smoked
- Perceived as safe
- Not detected in drug testing
- Causing psychotic episodes
- Is addictive

Opioids (Morphine/Heroin/codeine)

Heroin

Opiates/Heroin/Tramal/Codeine

- Can cause overdose: slowing heart rate and low blood pressure and decreased breathing rate
- Activates the opiate system in the central nervous system
- **Can cause death and serious infections: HIV and Hepatitis from injections**
- **Causes severe withdrawal**


FARBENFABRIKEN
vorm.
FRIEDR. BAYER & Co
ELBERFELD.
Heroin
Nom déposé

Cocaine

COCAINE: Powder and Crack (solid)

Cocaine

- increases adrenaline and dopamine to dangerous levels
- Can cause heart attacks and brain clots causing death
- Cocaine and alcohol combo is very toxic
- Can cause violence, aggression, and psychosis (hallucinations)
- nose damage and nasal bleeds


COCAINE
TOOTHACHE DROPS
Instantaneous Cure!
PRICE 15 CENTS.
Prepared by the
LLOYD MANUFACTURING CO.
219 HUDSON AVE., ALBANY, N. Y.
For sale by all Druggists.
(Registered March 1885.)
See other side.

Amphetamines (meth)

- Amphetamines are stimulants.
- Abuse is increasing globally
- Increase dopamine levels
- Can cause psychosis

Methamphetamine: crystals

HALLUCINOGENS: MUSHROOMS and LSD

- Naturally occurring: Peyote cactus Psilocybin Mushroom
- Synthetic agents : LSD

- Can trigger intense visual hallucinations by affecting brain serotonin leading
- Can cause panic
- Flashbacks to hallucinations may persist after use

Psilocybin Mushrooms - Schedule I

MDMA (XTC or Ecstacy)

- Euphoria and increased energy, but one of the more dangerous drugs

- Illusions, synthesia, sensitivity of touch, taste/ smell altered, "oneness with the world", tearfulness, euphoria, panic, paranoia

- unpleasant side effects, can cause Parkinsonism, hyperthermia, dehydration, seizures, KIDNEY failure, seizure, death

Caffeine is addictive and harmful In large amounts (more 400 mg/day): anxiety and sleep problems

Tobacco (NICOTINE): MOST ADDCITIVE! CAUSES CANCER, HEART and LUNG DISEASE: 5 MILLION DEATHS WORLWIDE!

The first drug usually abused by young people and gateway to other drugs!

Waterpipe

- MORE DANGEROUS THAN CIGARETTES
- ALL Tobacco smoking causes serious health problems
- Addiction to Nicotine can develop in 3-4 weeks and lasts for 25 to 30 years

Electronic cigarettes, heated cigarettes (IQOS), and Juul

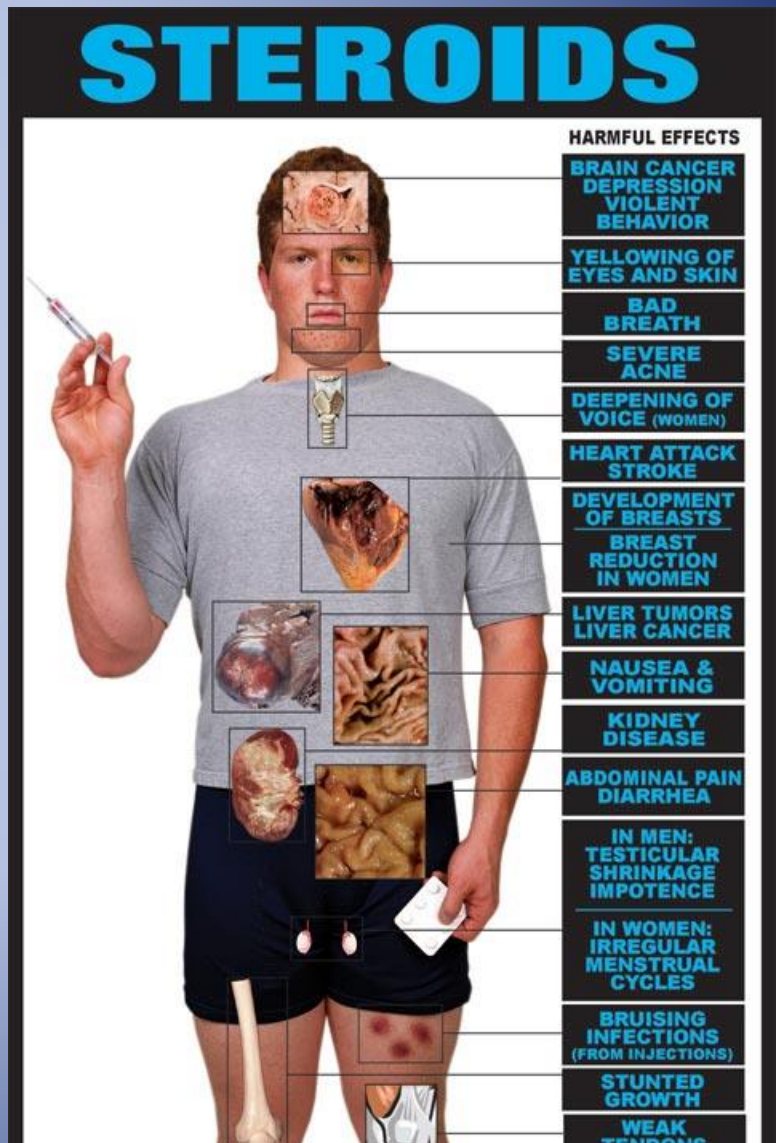
- All are very addictive, eventually young people shift to regular cigarettes.
- Chemicals and toxins are dangerous in these products
- Juul is especially addictive very high dose nicotine
- Sometimes used to smoke cannabis via the devices


JUUL
the alternative for adult smokers
JUUL device
USB charger
4 pod multipack
5% strength
JUUL
innr


JUUL


.MICKO PLUS
VEIIK

Steroids: addictive and cause physical and behavioral problems/violence



Inhalants and solvent abuse: huffing and sniffing chemicals

Extremely dangerous can be FATAL can cause irreversible brain damage and sudden heart attacks in young people and lung damage

Alcohol can be very dangerous in young people: can cause serious health problems and risky behaviors as well as risk of dependence

Depression and anxiety worsen.

BLACKOUTS (loss of memory and awareness from binging causes serious accidents)

Addiction/Dependence risk

Risk of Addiction

	Ever Used (%)	Addicted (%)	Risk (%)
Tobacco	75.6	24.1	31.9
Cocaine	16.2	2.7	16.7
Heroin	1.5	0.4	23.1
Alcohol	91.5	14.1	15.4
Cannabis	46.3	4.2	9.1

Anthony et al, 1994.

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