Snapshot of what research is telling us about treatment and prevention

Timothy P. Condon, Ph.D.
Research Professor
Center on Alcoholism, Substance Abuse and Addictions
University of New Mexico

3rd International Consortium of Universities for Drug Demand Reduction

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Disclosures

- The Presenter:
- Chief Science Advisor. TASC-IL
- Faculty, National Judicial Collegge
- Member Scientific Advisory Committee, Recovery Centers of America
- Receive free medication from Alkermes for NIH/Arnold Foundation Clinical Trial

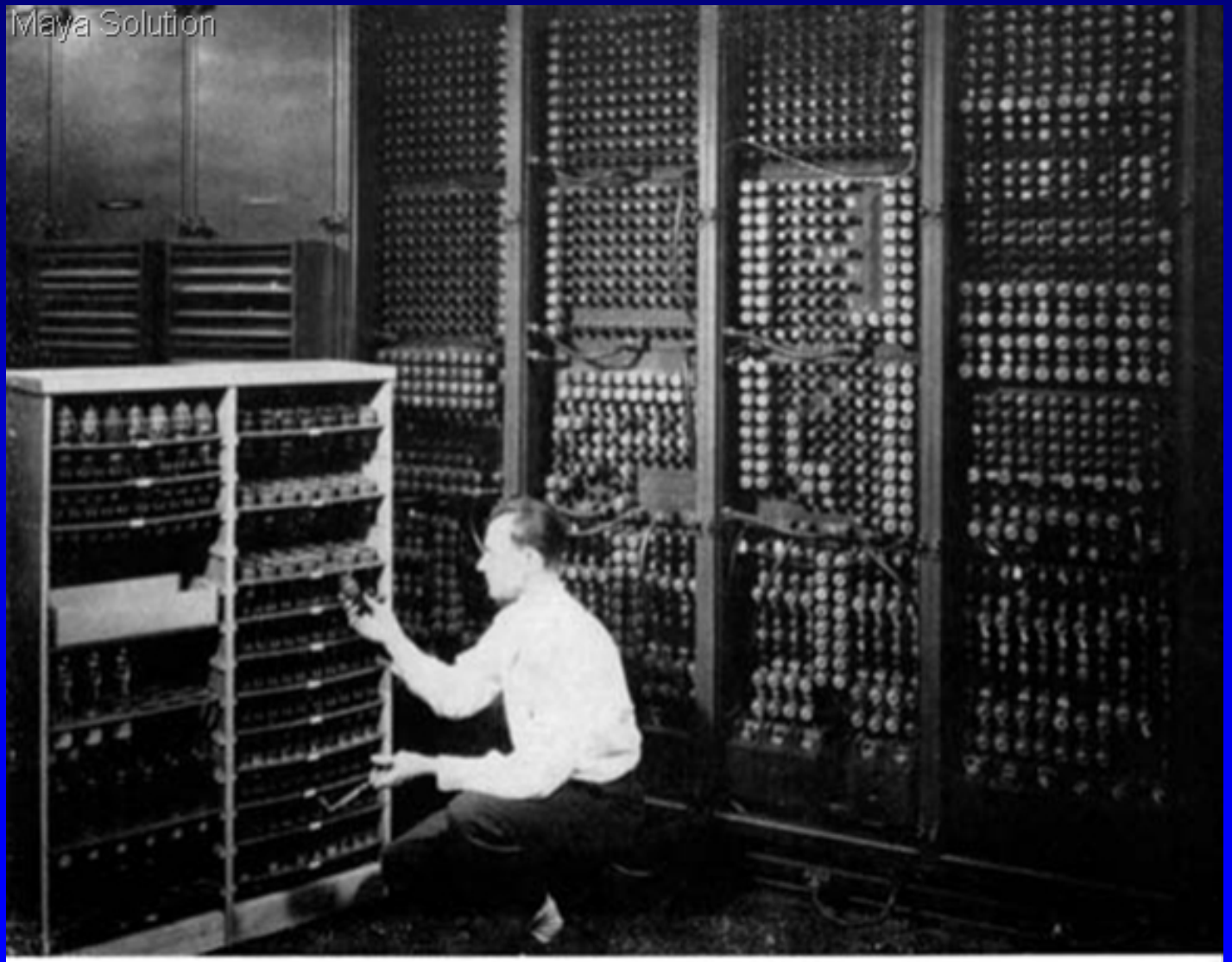
Advances in Science
Have Revolutionized Our
Way of Life…
And Our Fundamental Views of
Drug Abuse and Addiction

Remember Ohura's Communicator?

Science Fiction?

Or Science Fact?

Then…



Replacing a bad tube meant checking among ENIAC's 19,000 possibilities.

And Now


cingular
12:34 PM
SMS
Text
Tuesday
9
Calendar
Photos
Camera
Calculator
Stocks
Maps
280
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Weather
Notes
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Phone
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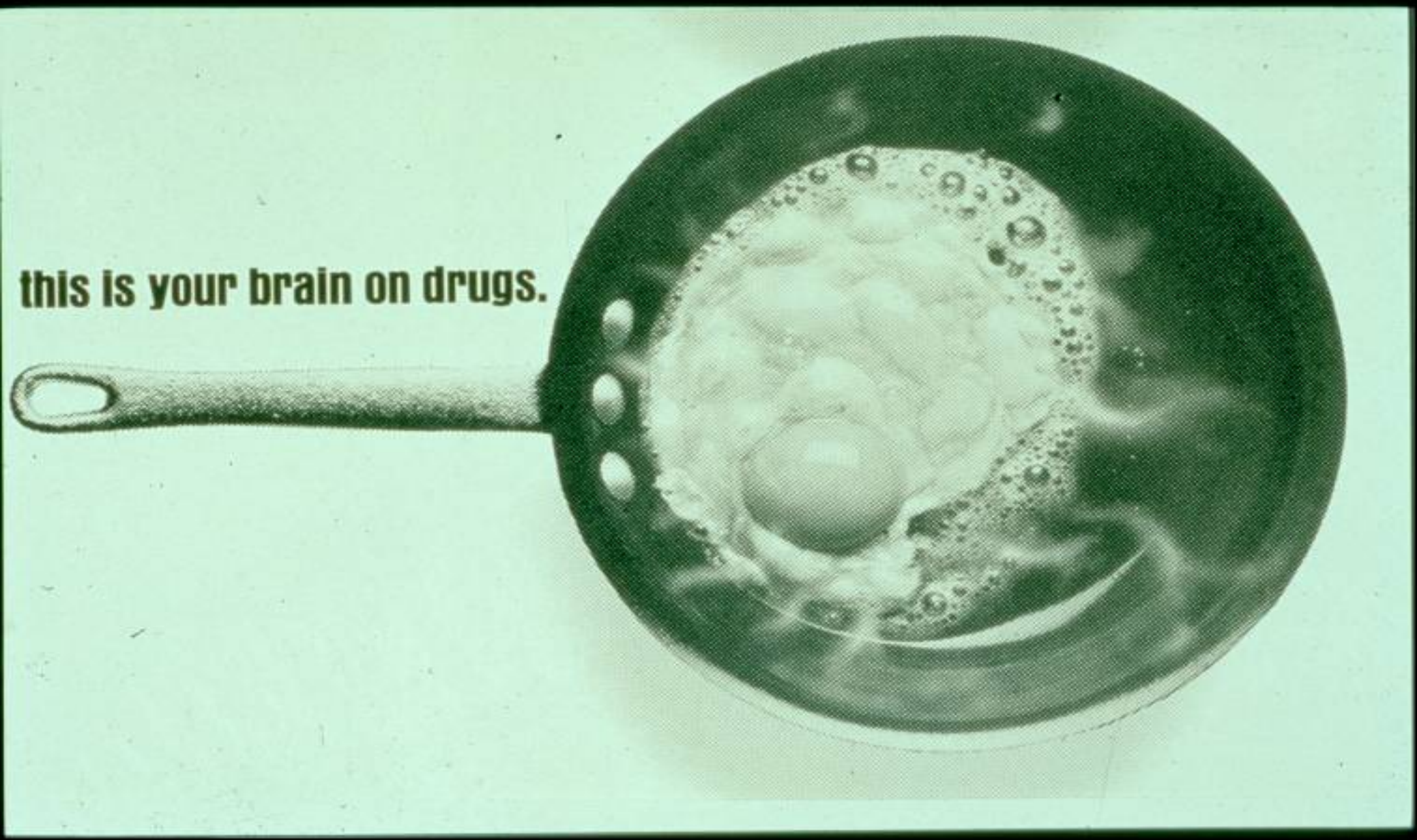
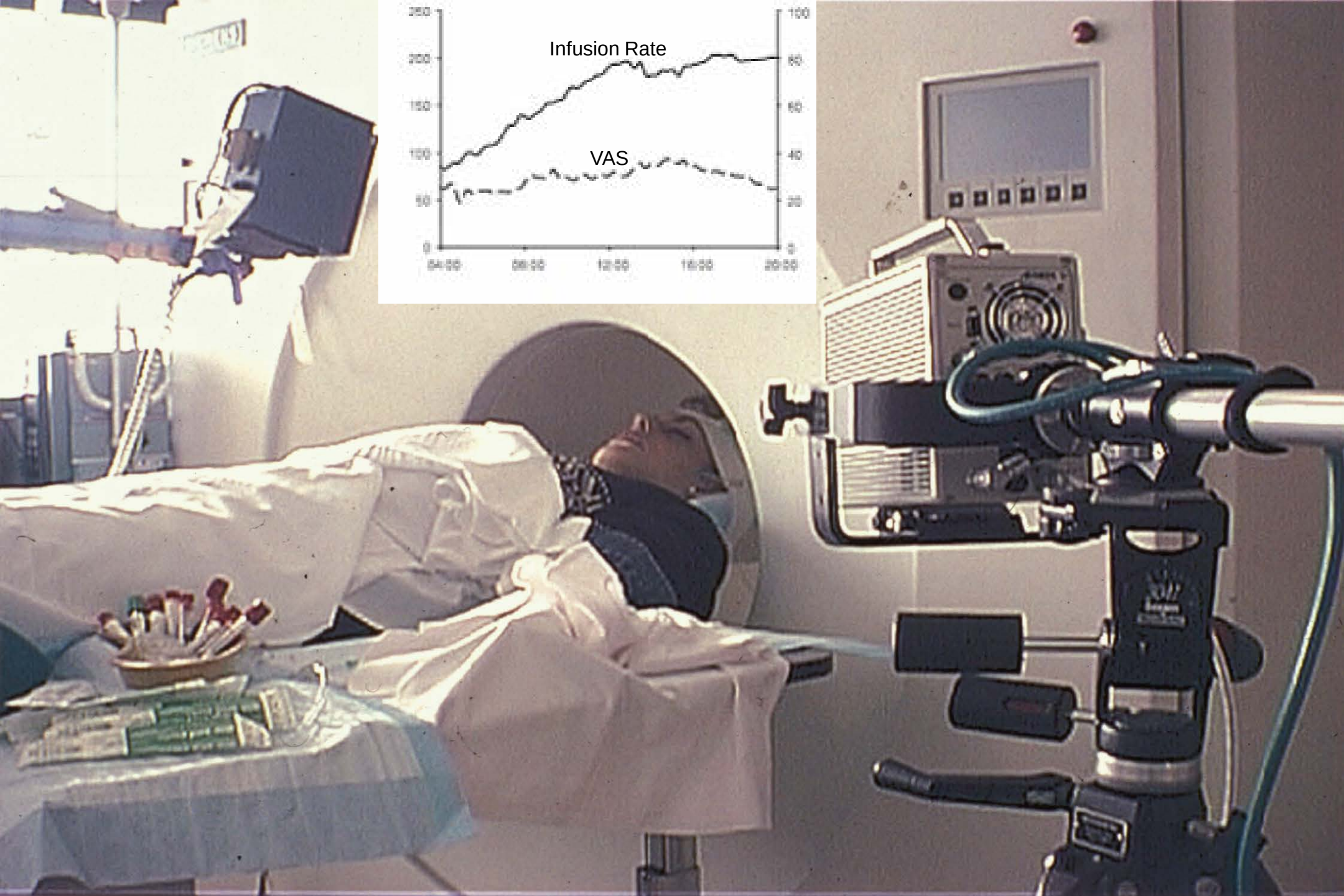
iPod

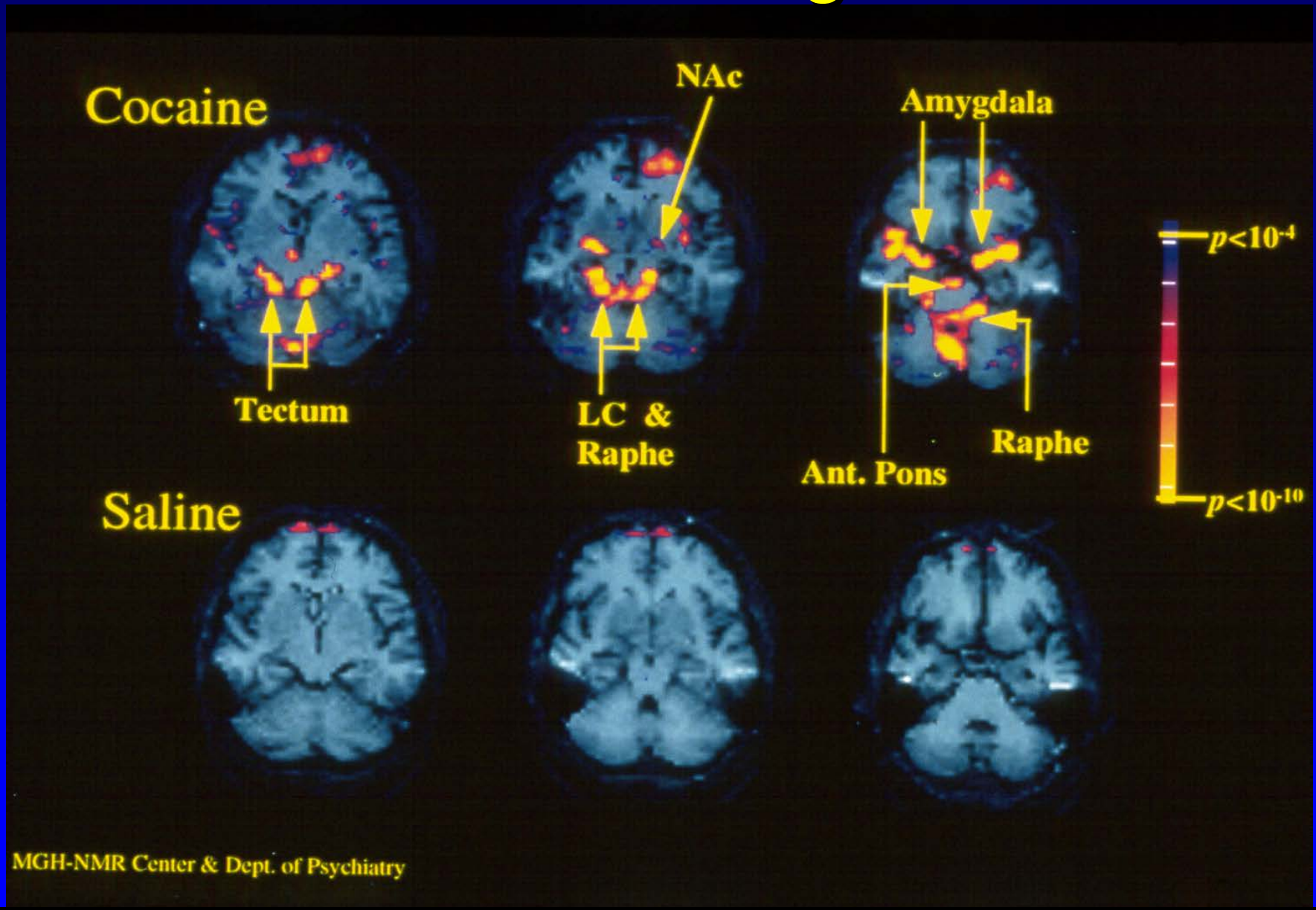
Advances in Science Have Revolutionized Our Fundamental Views of Alcohol and Drug Abuse and Addiction

Your Brain on Drugs - Then




Infusion Rate
VAS

Your Brain on Drugs – *Now*



Source: Breiter & Rosen, Ann N Y Acad Sci 1999

So..What have we learned?

Drug Abuse Is A Preventable Behavior

Drug Addiction Is A Treatable Disease

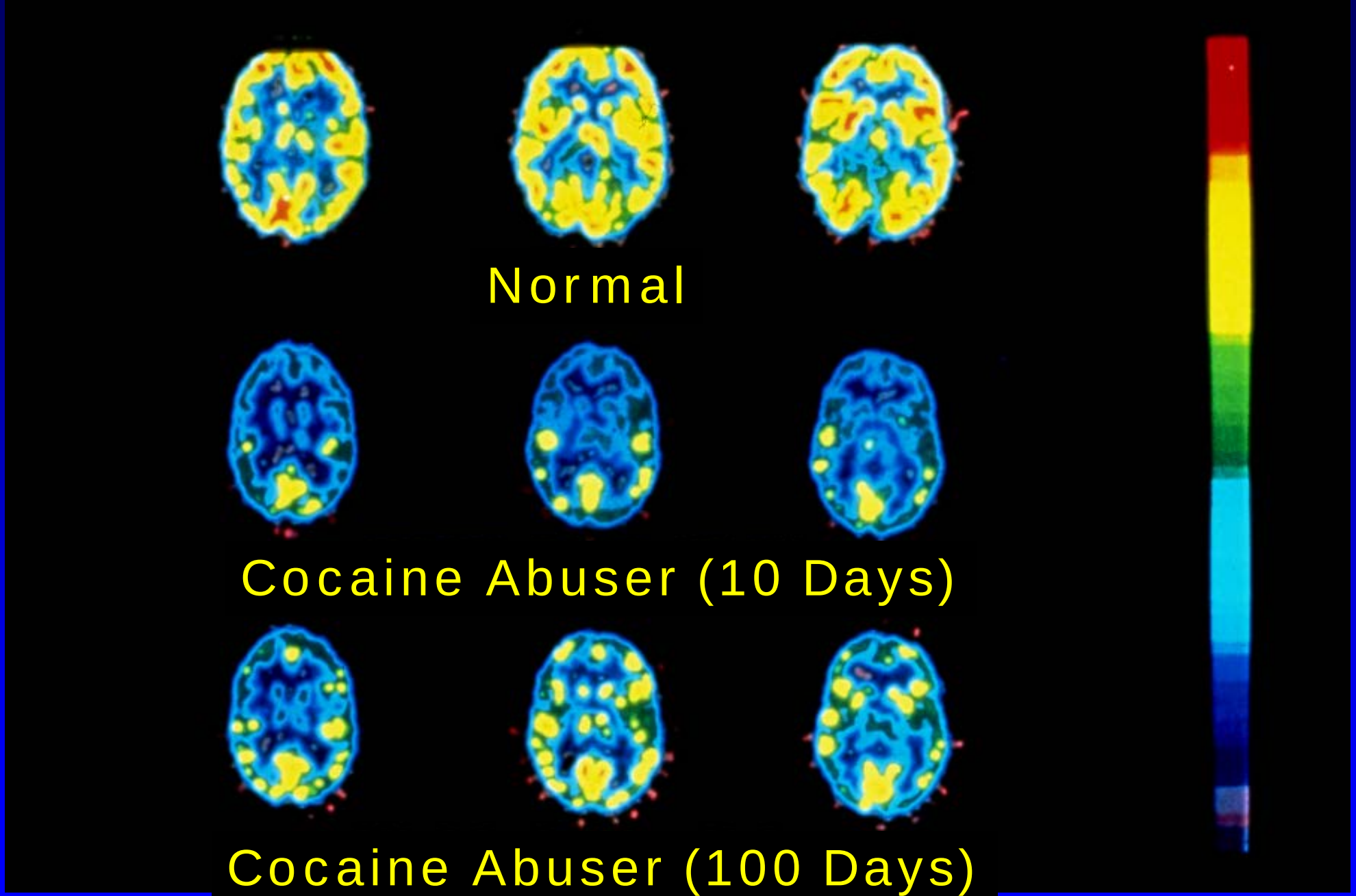
Partnership for a Drug Free America

Initial Drug Use Is A *Voluntary* Behavior…

A Person *Chooses* to Take a Drug for the First Time

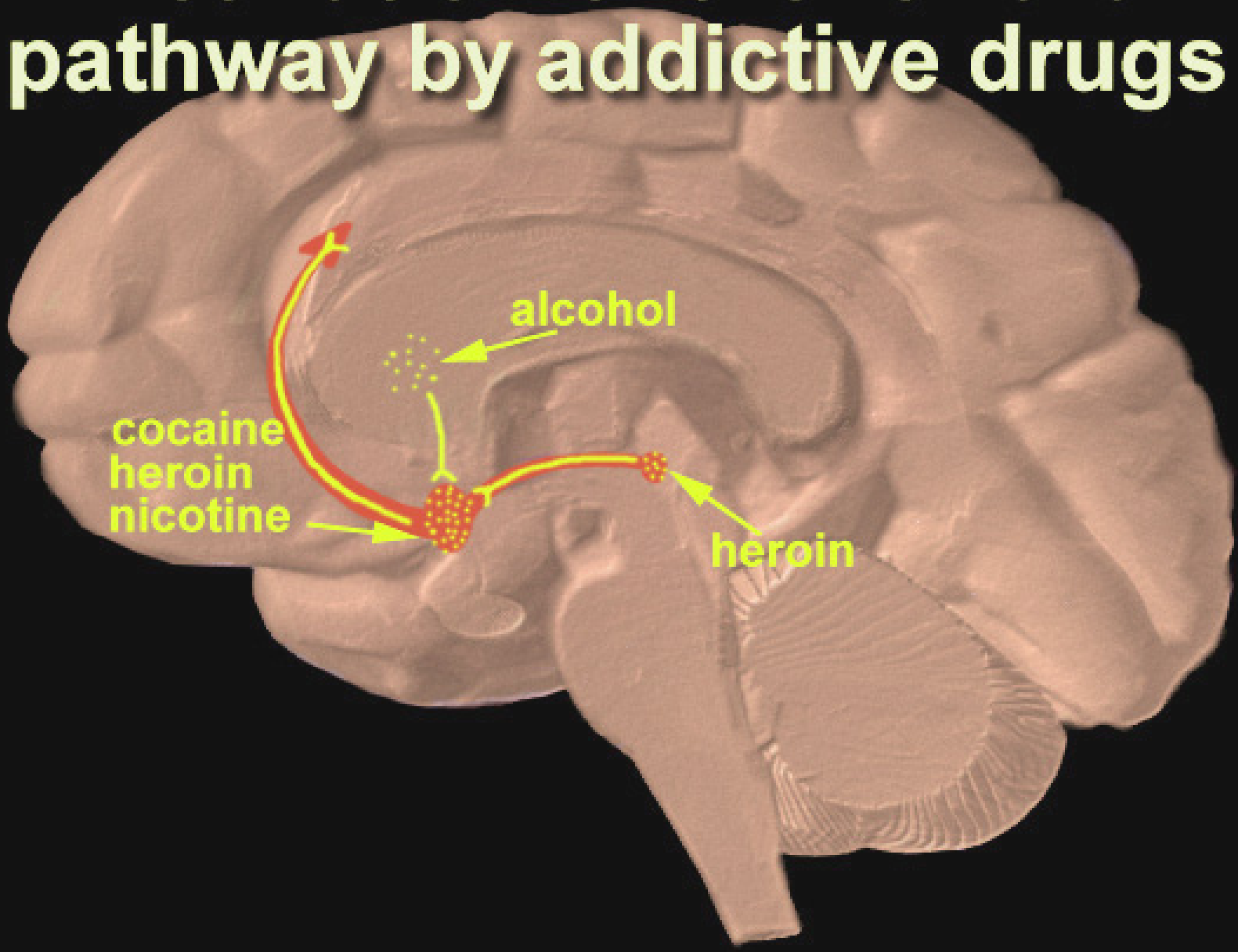
Science Has Generated A Lot of Evidence Showing That…

Prolonged Drug Use Changes the Brain In Fundamental and Long-Lasting Ways

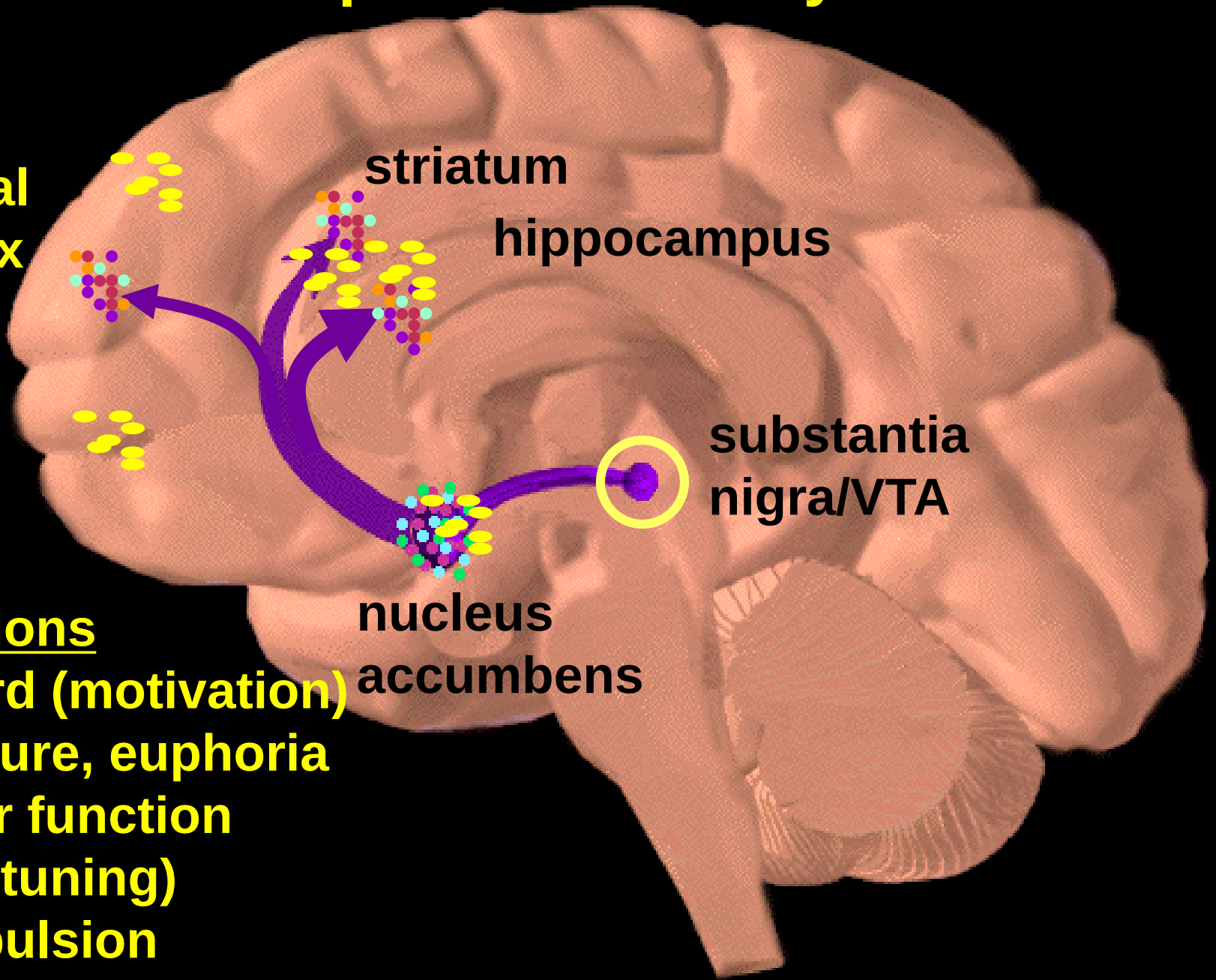


(Volkow et al., 1992; 1993)

Activation of the reward pathway by addictive drugs

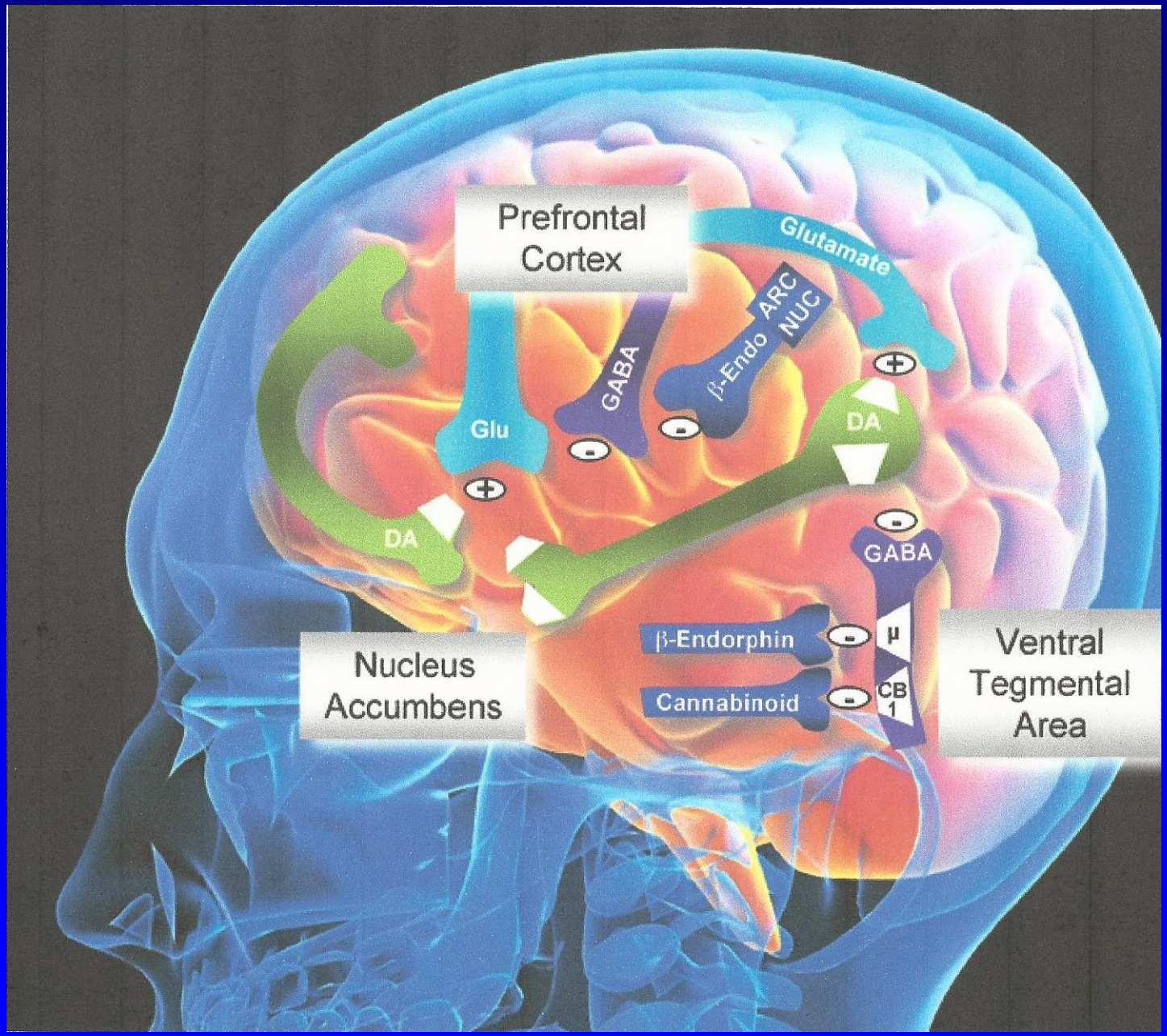


Dopamine Pathways

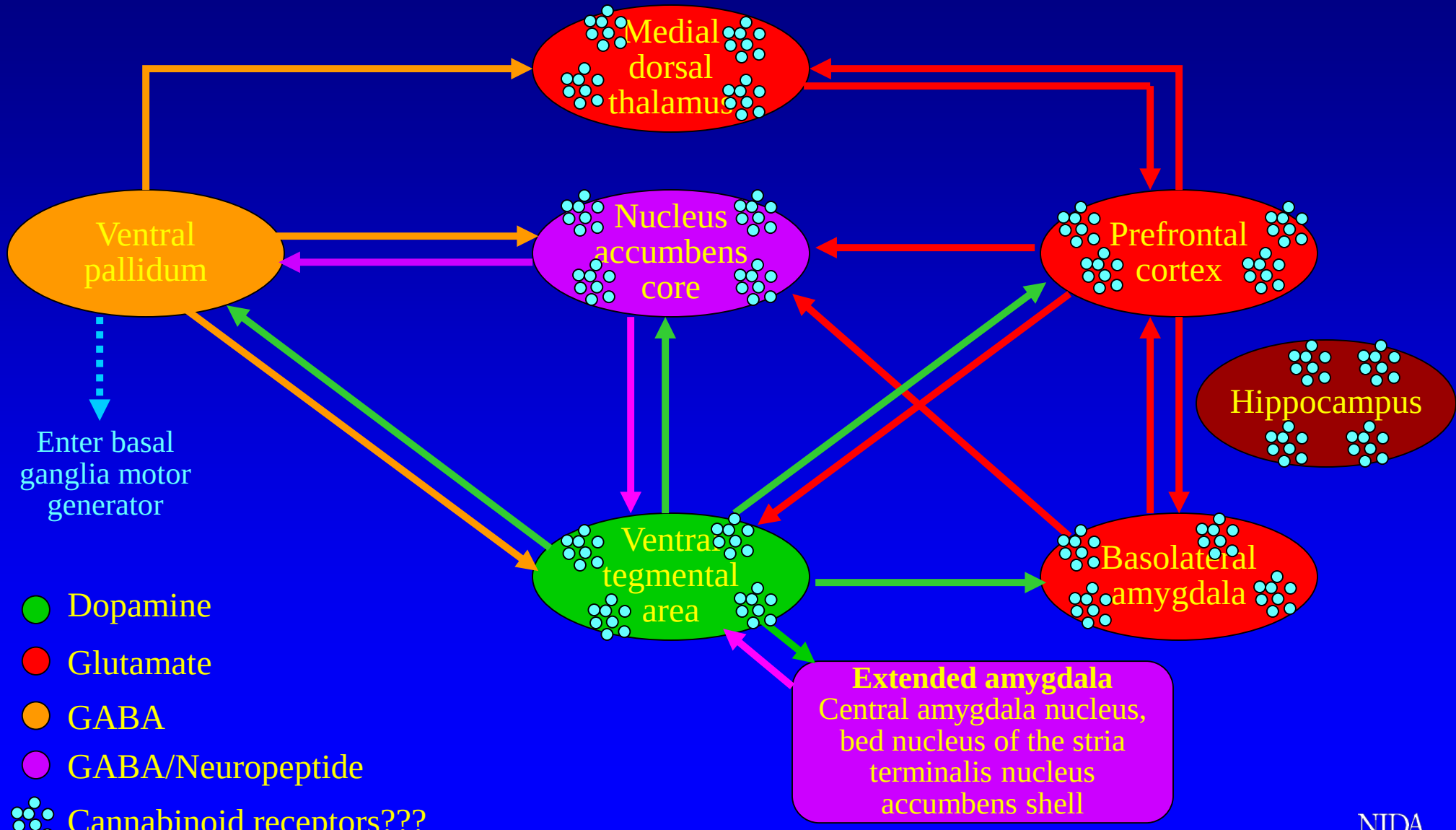


Functions

- reward (motivation)
- pleasure, euphoria
- motor function (fine tuning)
- compulsion


Prefrontal Cortex
Glutamate
ARC NUC
β-Endo
GABA
Glu
DA
DA
GABA
β-Endorphin
μ
Cannabinoid
CB 1
Nucleus Accumbens
Ventral Tegmental Area

Nuclear Circuitry Mediating the Activation of Goal-Directed Behavior



Adapted from Kalivas and Volkow, Am J Psychiatry 162:8, Aug 2005

NIDA

	Response
Binge/intoxication	
Dopamine[15]	Increase
Opioid peptides[16]	Increase
Serotonin[17]	Increase
γ-aminobutyric acid[18]	Increase
Acetylcholine[19]	Increase
Withdrawal/negative affect	
Corticotropin-releasing factor[20]	Increase
Dynorphin[21]	Increase
Norepinephrine[22]	Increase
Hypocretin (orexin)[23]	Increase
Substance P[24]	Increase
Dopamine[25]	Decrease
Serotonin[17]	Decrease
Opioid peptide receptors[26]	Decrease
Neuropeptide Y[27]	Decrease
Nociceptin[28]	Decrease
Endocannabinoids[29]	Decrease
Oxytocin[30]	Decrease
Preoccupation/anticipation	
Dopamine[31]	Increase
Glutamate[32]	Increase
Hypocretin (orexin)[23]	Increase
Serotonin[17]	Increase
Corticotropin-releasing factor[33]	Increase

Table 1: Neurotransmitter systems involved in the neurocircuitry of addiction stages and functional domains

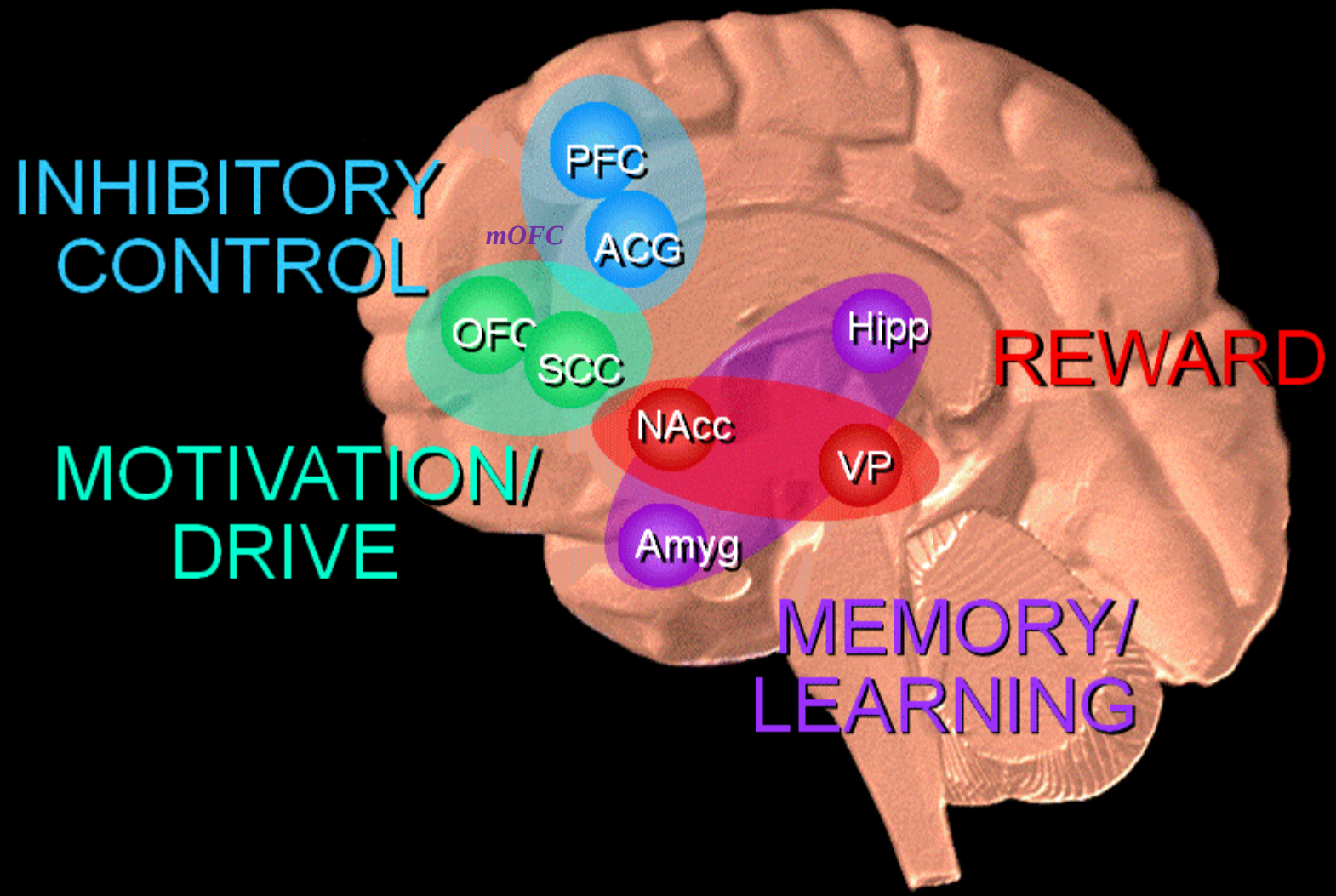
	Neurotransmitter
Binge/intoxication	
Ventral tegmental area (circuit 1)[43]	Glutamate
Ventral tegmental area (circuit 2)[44]	γ-aminobutyric acid
Dorsal striatum (circuit 3)[45]	Dopamine
Dorsal striatum (circuit 4)[46]	Glutamate
Withdrawal/negative affect	
Ventral tegmental area (circuit 5)[47]	Corticotropin-releasing factor
Central nucleus of amygdala (circuit 6)[20]	Corticotropin-releasing factor
BNST (circuit 7)[22]	Norepinephrine
Nucleus accumbens shell (circuit 8)[21]	Dynorphin
Habenula (circuit 9)[48]	Acetylcholine
Central nucleus of amygdala (circuit 10)[49]	Neuropeptide Y
Central nucleus of amygdala (circuit 11)[29]	Endocannabinoids
Preoccupation/anticipation	
Prefrontal cortex (circuit 12)[32]	Glutamate
Prefrontal cortex (circuit 13)[50]	γ-aminobutyric acid
Hippocampus (circuit 14)[51]	Glutamate
Basolateral amygdala (circuit 15)[52]	Glutamate
BNST (circuit 16)[53]	Corticotropin-releasing factor
BNST (circuit 17)[53]	Norepinephrine
Insula (circuit 18)[54]	Corticotropin-releasing factor

BNST=bed nucleus of the stria terminalis.

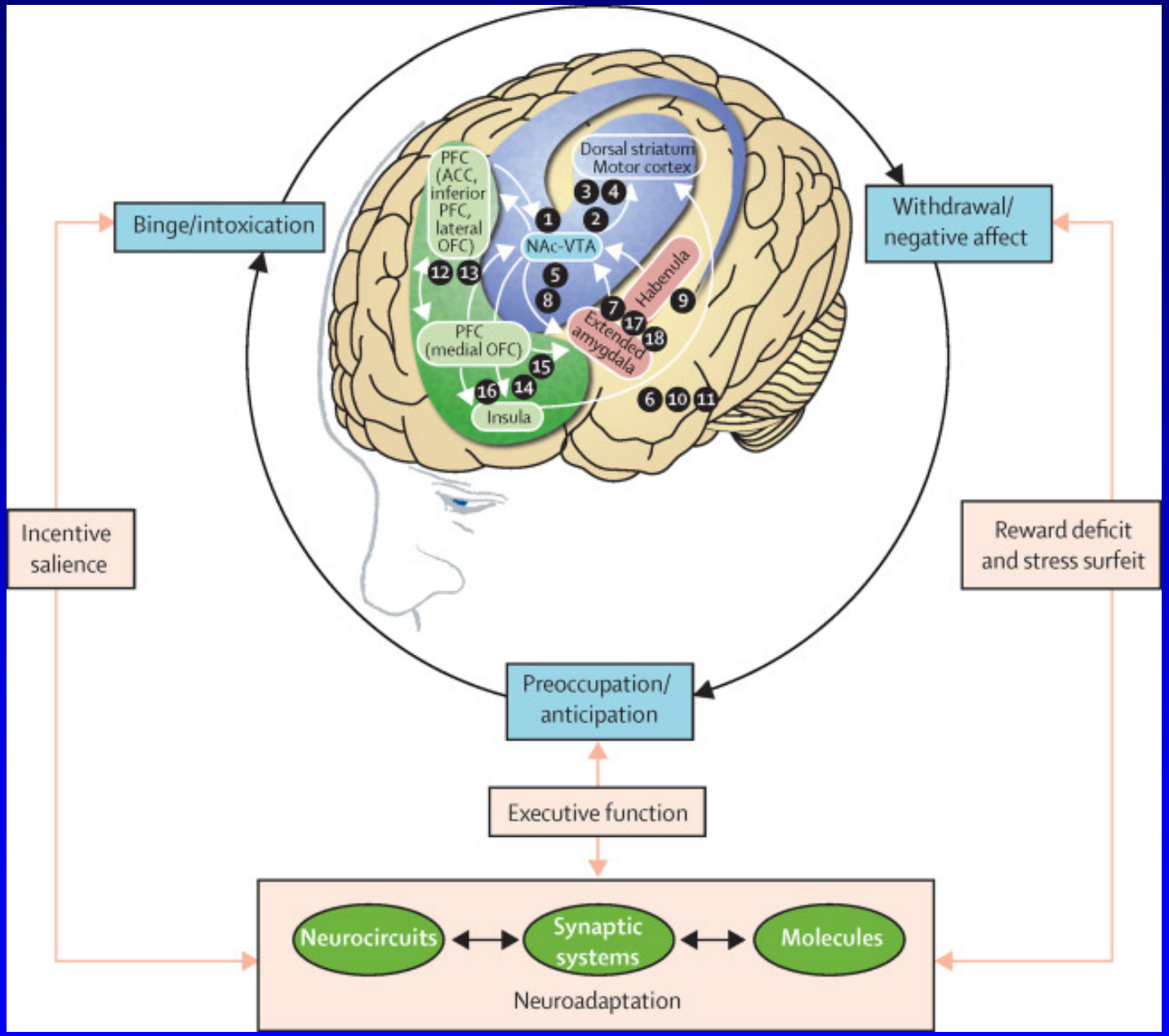
Table 2: Molecular neurocircuits as focal points for neuroplasticity in addiction

Koob and Volkow. 2016

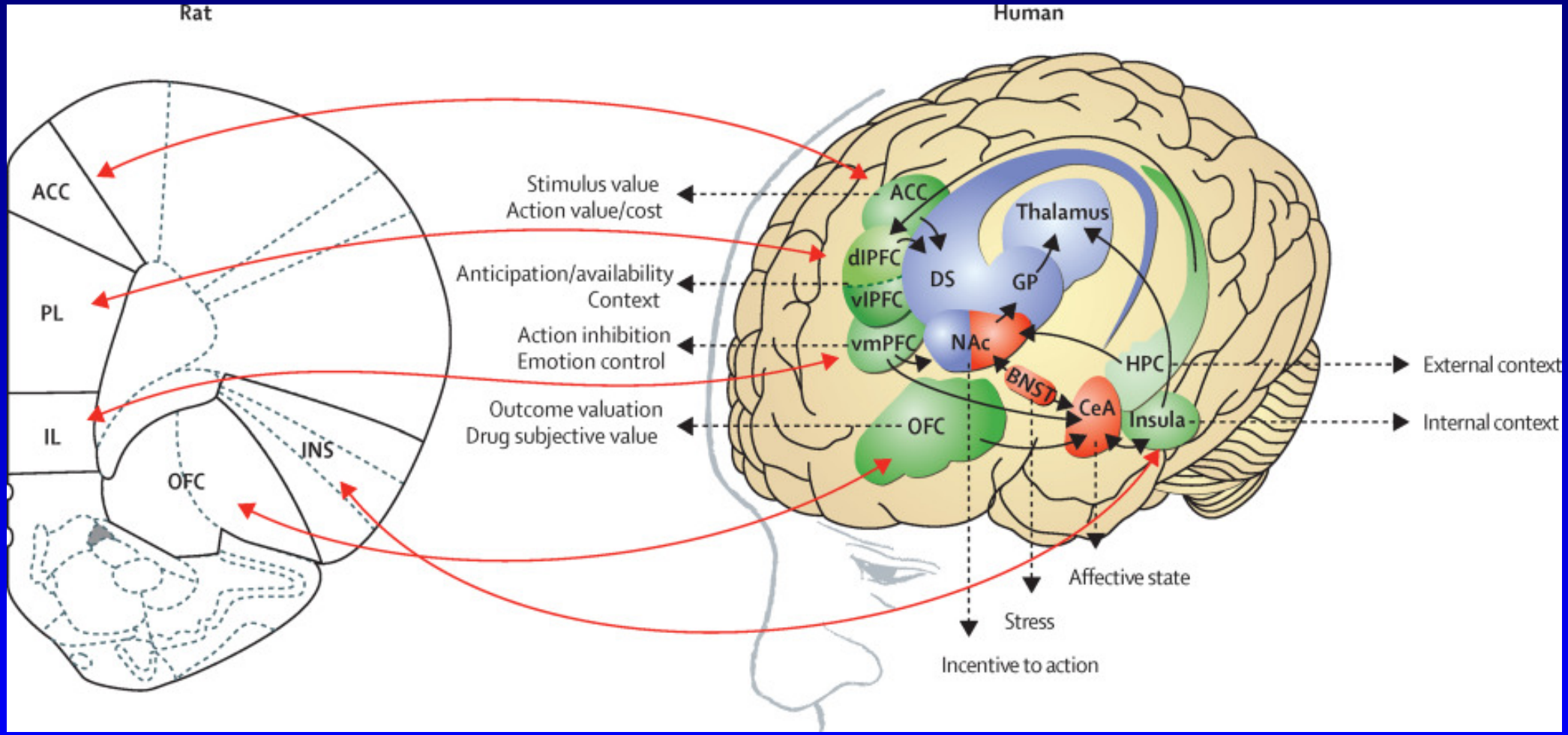
Circuits Involved In Drug Abuse and Addiction



NIDA



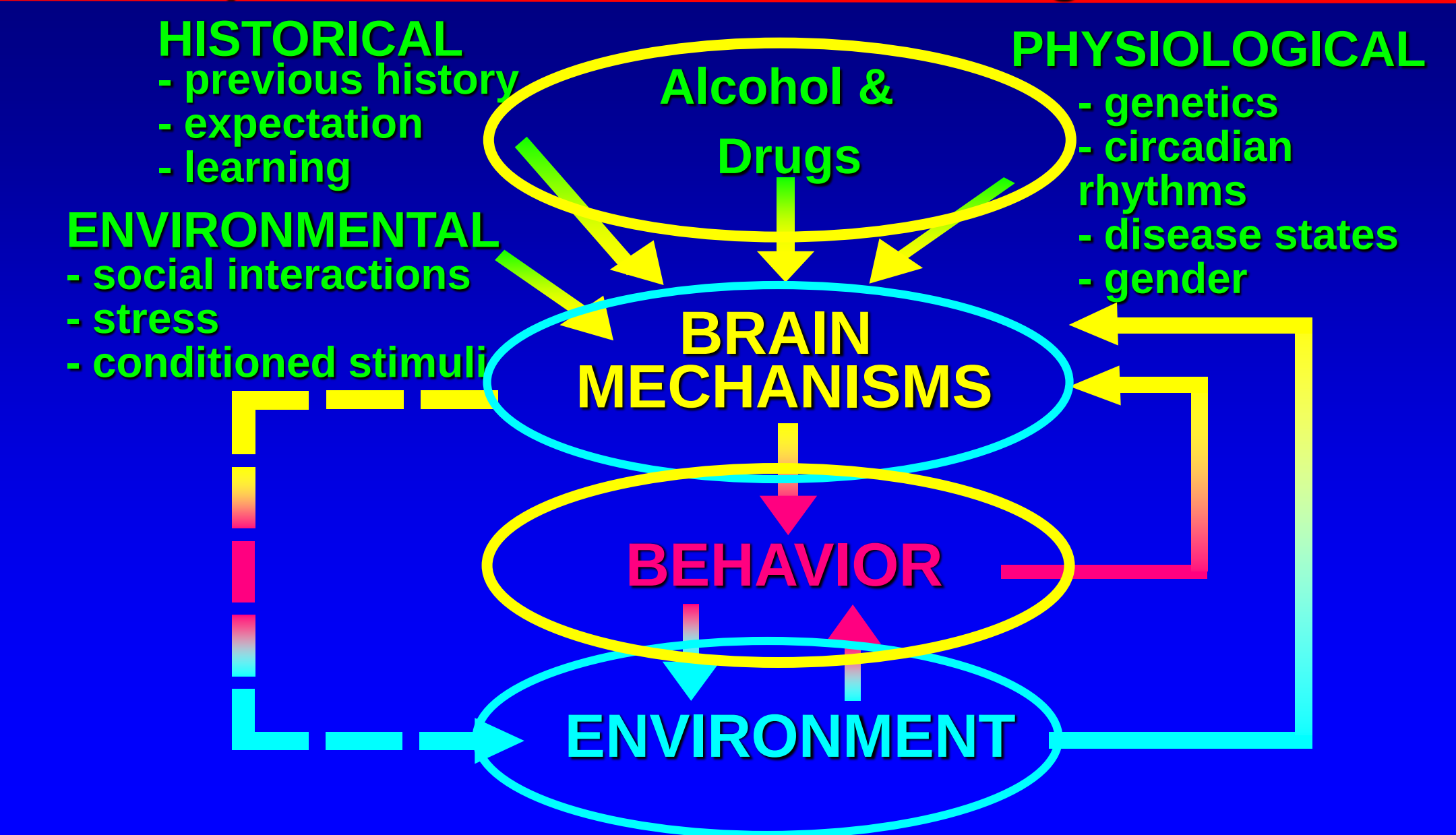
Koob and Volkow, 2016



Koob and Volkow, 2016

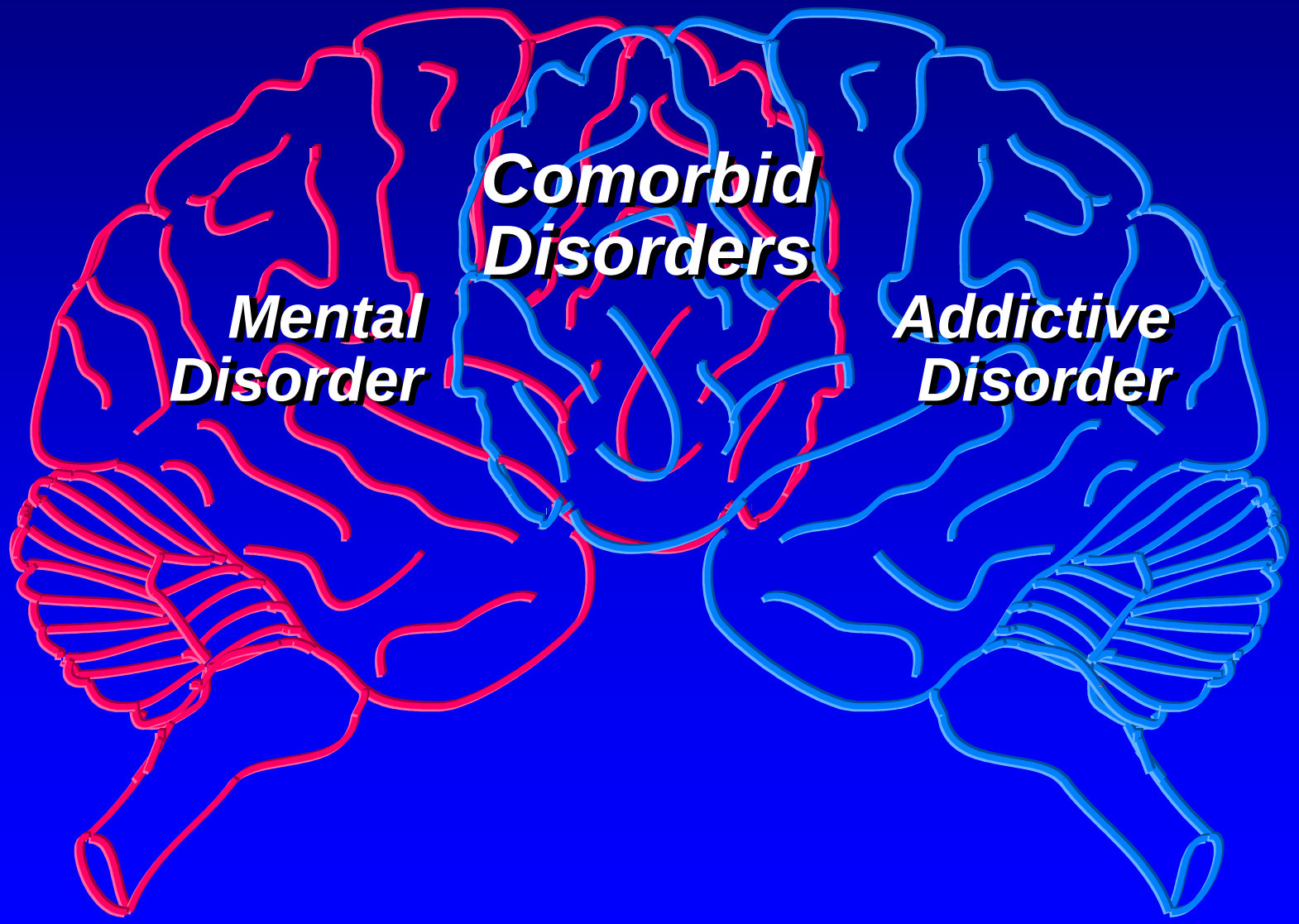
Addiction is the Quintessential Biobehavioral Disorder

Addiction:
A Complex Behavioral and Neurobiological Disorder



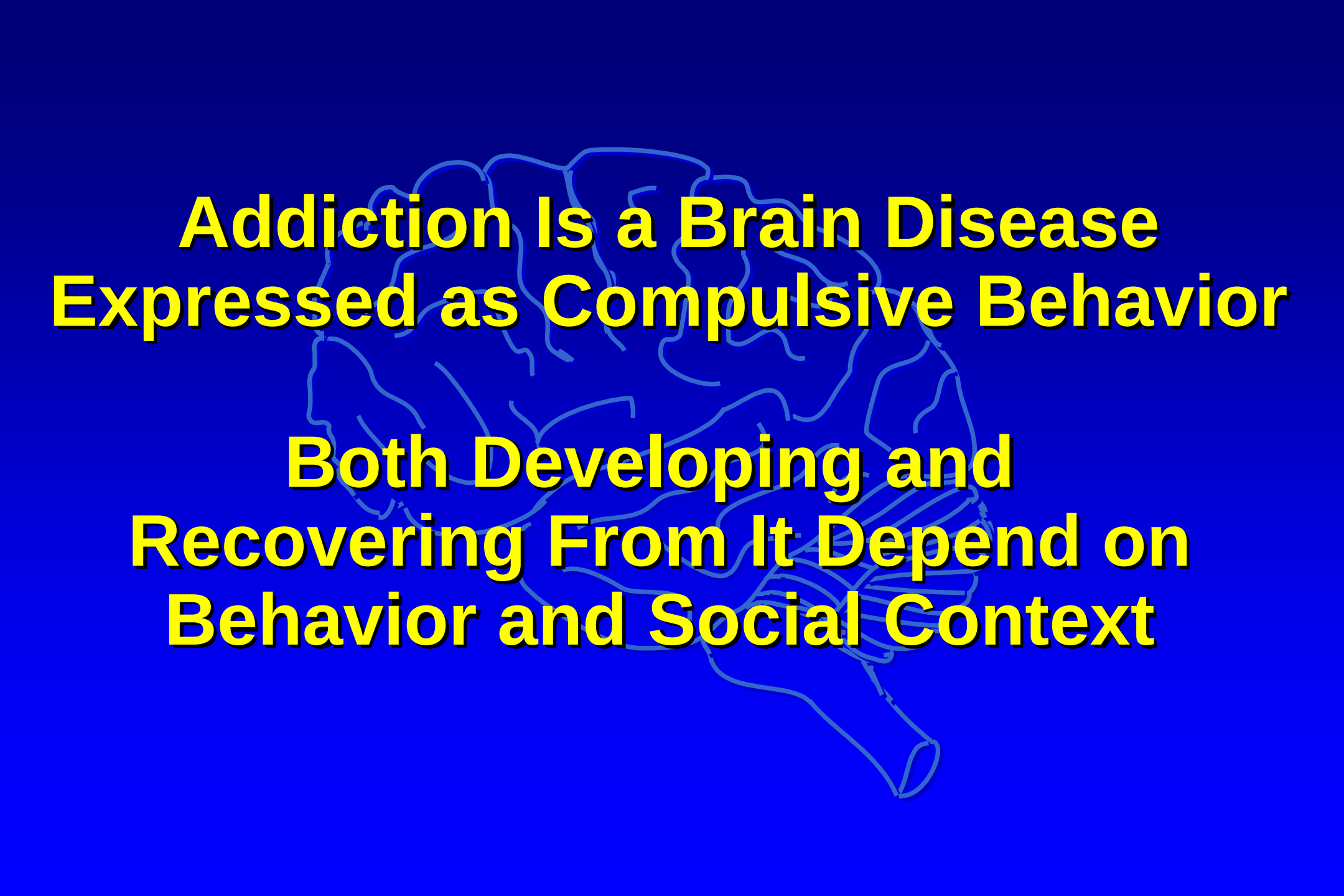
What else have we learned?

ADDICTIVE DISORDERS OFTEN CO-EXIST WITH MENTAL DISORDERS



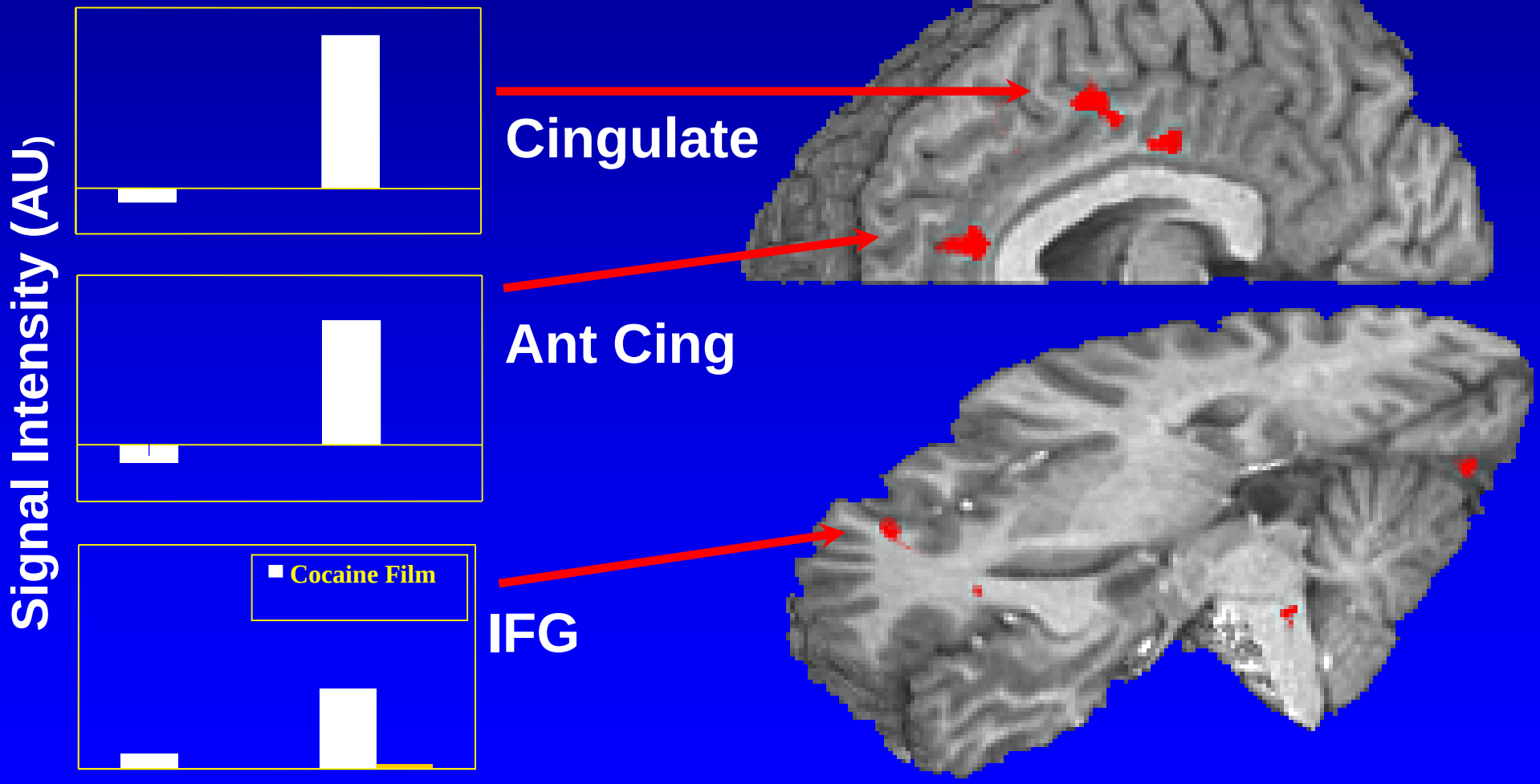
Comorbidity Is a Reality

AND WHAT ELSE?


Addiction Is a Brain Disease
Expressed as Compulsive Behavior
Both Developing and
Recovering From It Depend on
Behavior and Social Context

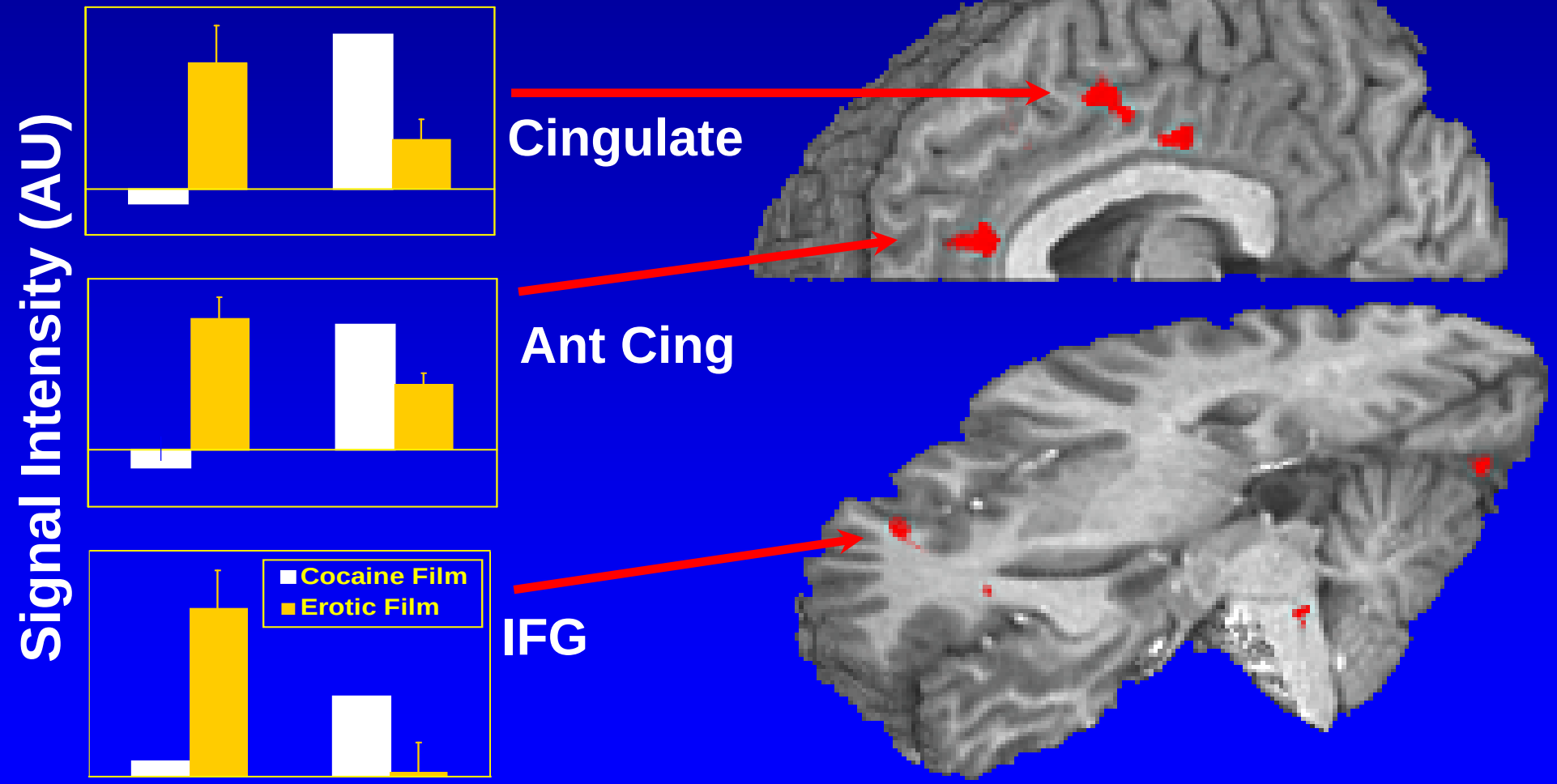
Cocaine Craving:

Population (Cocaine Users, Controls) x Film (cocaine)



Cocaine Craving:

Population (Cocaine Users, Controls) x Film (cocaine, erotic)



Garavan et al , A. J. Psych 2000

This Results in "Motivational Toxicity" and Compulsive Drug Use (Addiction)

Because…

Their ***Brains***

have been

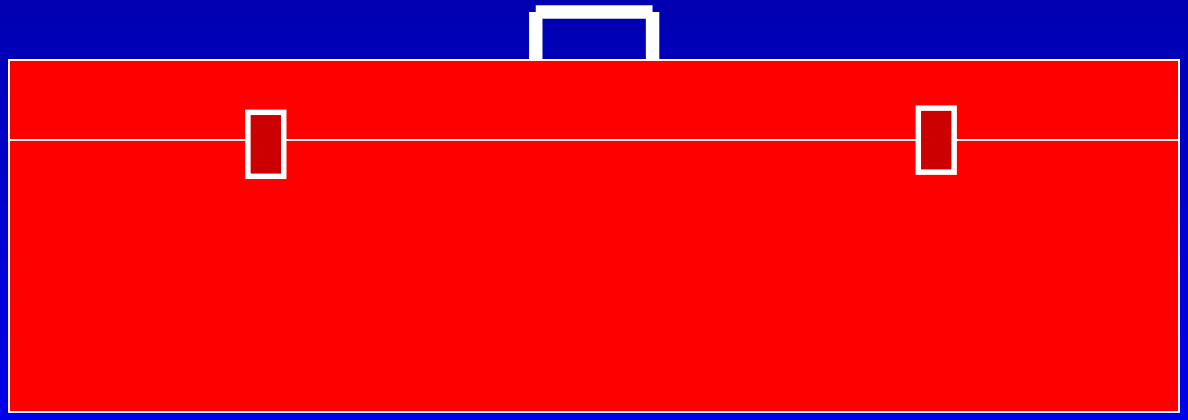
Re-Wired

by ***Drug Use***

The Brains of Addicts Are Different From the Brains of Non-Addicts

…And Those Differences Are An Essential Element of Addiction

We Have a Variety of Effective Treatment Options in the Clinical Toolbox



Available Pharmacotherapies

Opioids

- Methadone
- Naltrexone
- Buprenorphine
- Buprenorphine/ Naloxone

Depot Naltrexone, xt-release (Vivitrol)

Prophine (xt-release bup implant)

Sublocade (xt-release buprenorphine

Lowfexidine (withdrawal)

Nicotine

- ***Bupropion***
- ***NRT***
- ***Varenicline***

Alcohol

- ***Disulfiram***
- ***Oral Naltrexone***
- ***Injectible extended release naltrexone: Vivitrol***
- ***Acamprosate***

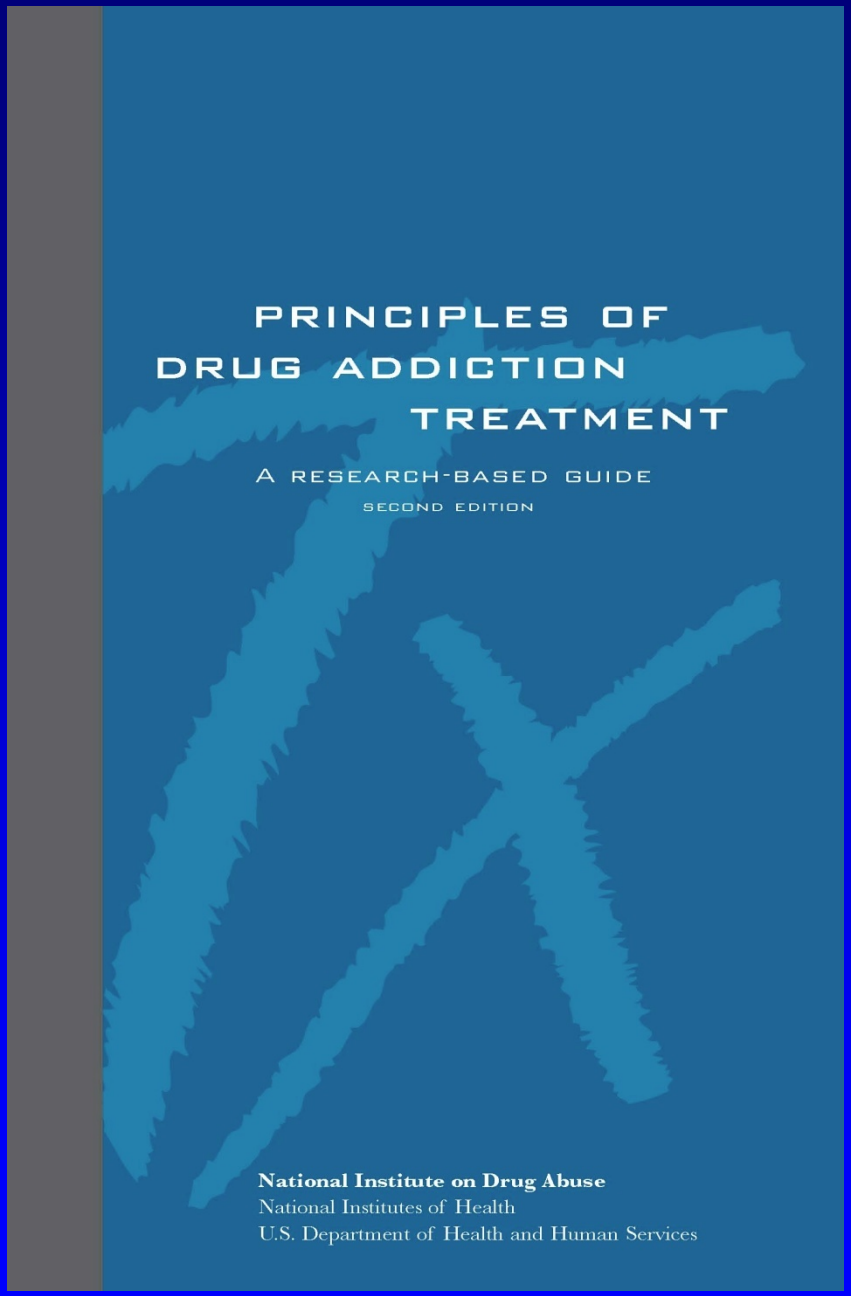
Alcohol Withdrawal

- ***Valium***
- ***Librium***
- ***Tranxene***

Some Efficacious Behavioral Treatments For Drug Dependence

- *Cognitive Behavioral Therapy*
- *Community Reinforcement Approach (CRA) with Vouchers*
- *Contingency Management (Without CRA)*
- *Lower-cost Contingency Management*
- *Brief Strategic Family Therapy*
- *Multidimensional Family Therapy*
- *Behavioral Couples Therapy*
- *Motivational Interviewing / Motivational Enhancement Therapy*
- *Mindfullness*

Treating a Biobehavioral Disorder Must Go beyond just Fixing the Chemistry

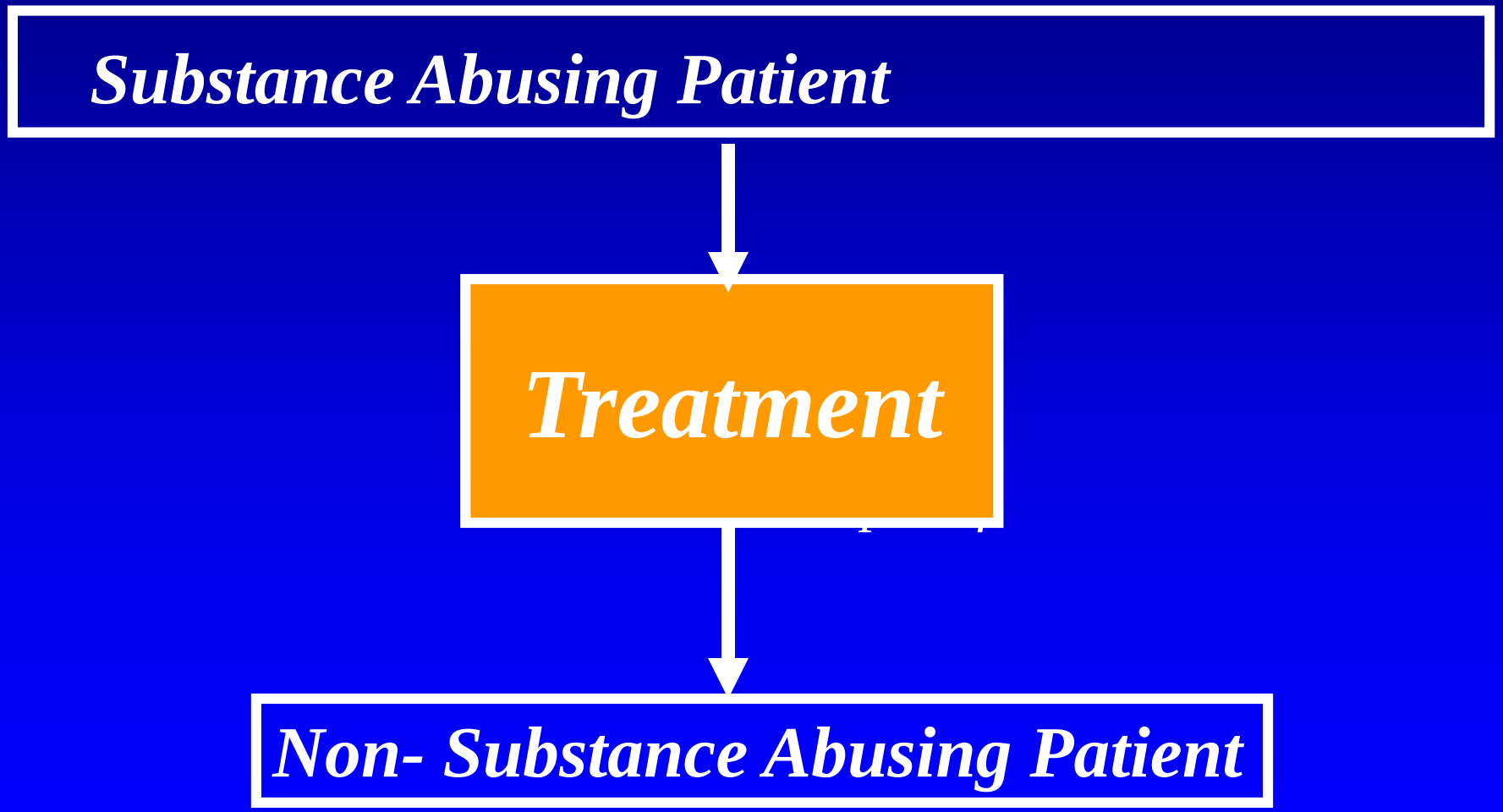

PRINCIPLES OF
DRUG ADDICTION
TREATMENT
A RESEARCH-BASED GUIDE
SECOND EDITION
National Institute on Drug Abuse
National Institutes of Health
U.S. Department of Health and Human Services

We Need to Treat the Whole Person!

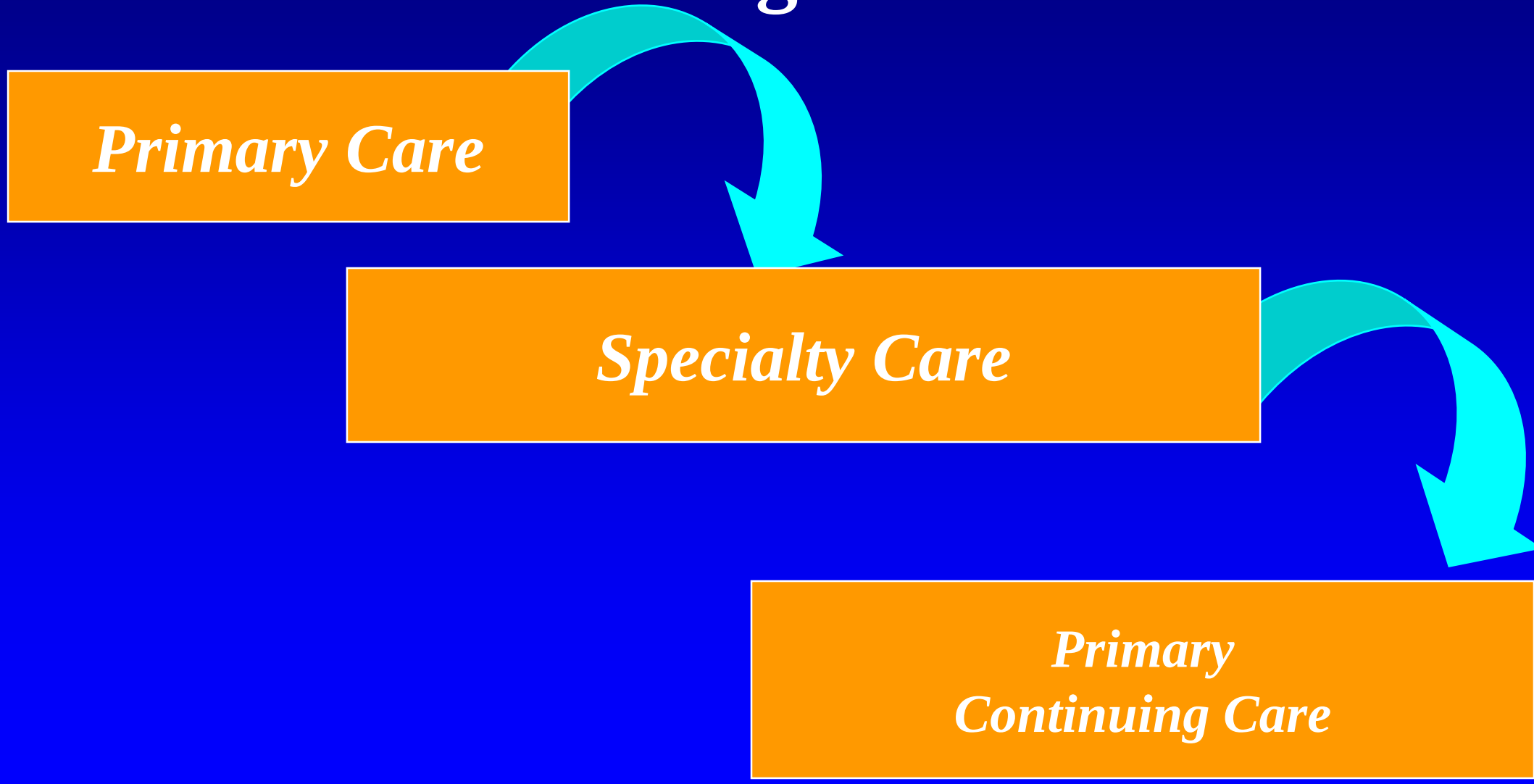
The Most Effective Treatment Strategies Will Attend to all Aspects of Addiction:

- Biology
- Behavior
- Social Context

The Acute Care Treatment Model

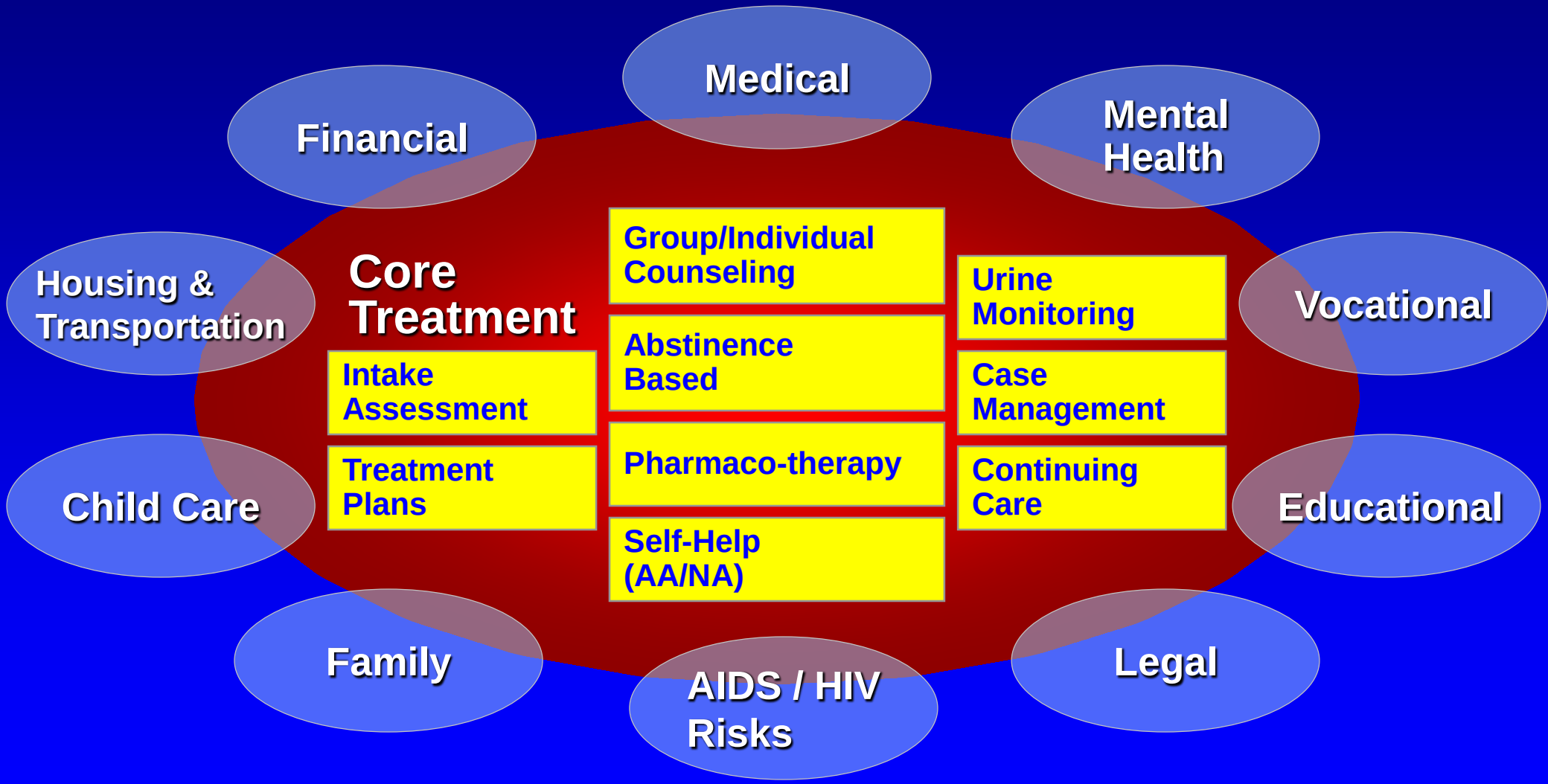


A Continuing Care Model



We Need to View and Treat Addiction as a Chronic, Relapsing Illness

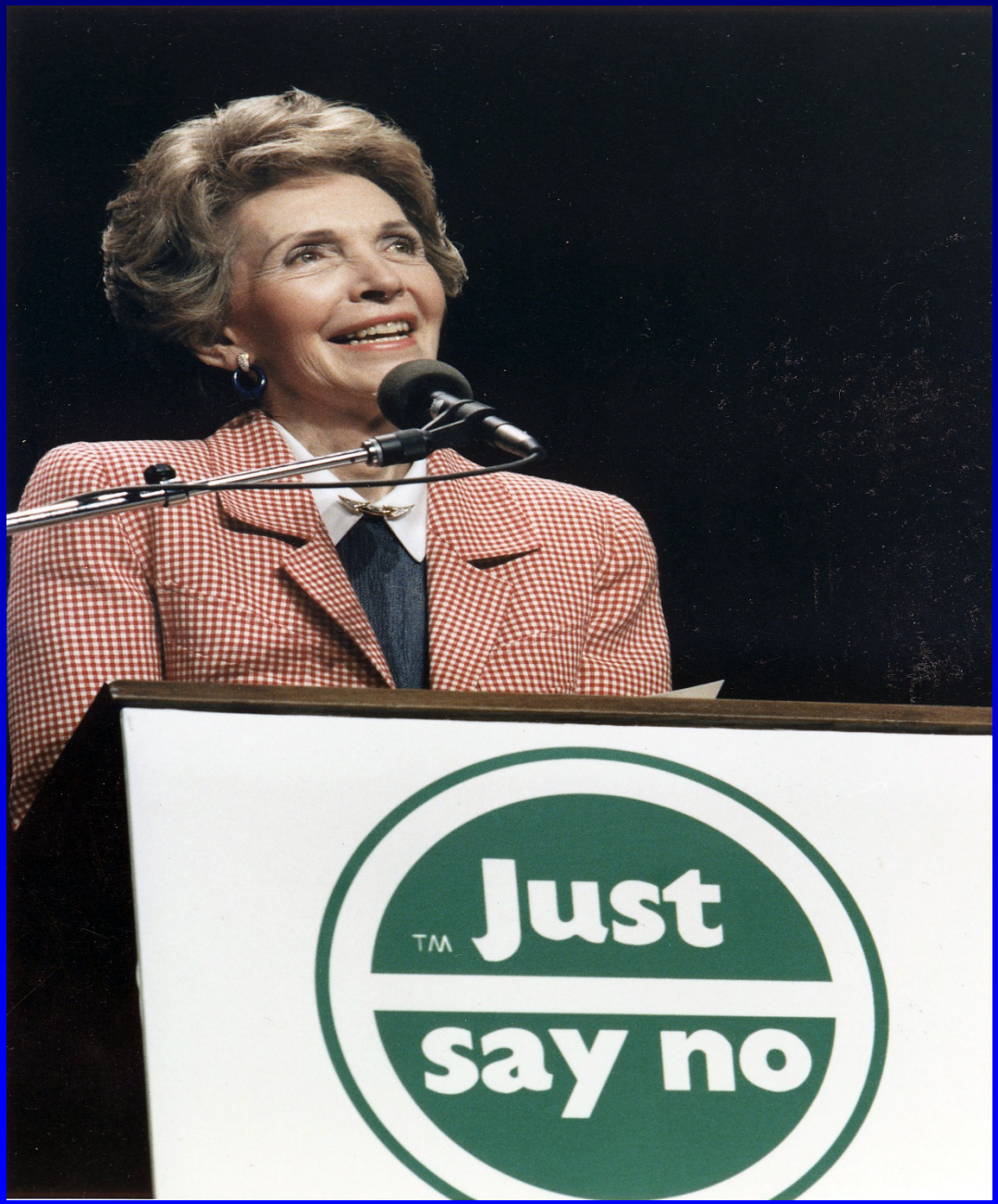
Drug Abuse Treatment Core Components and Comprehensive Services



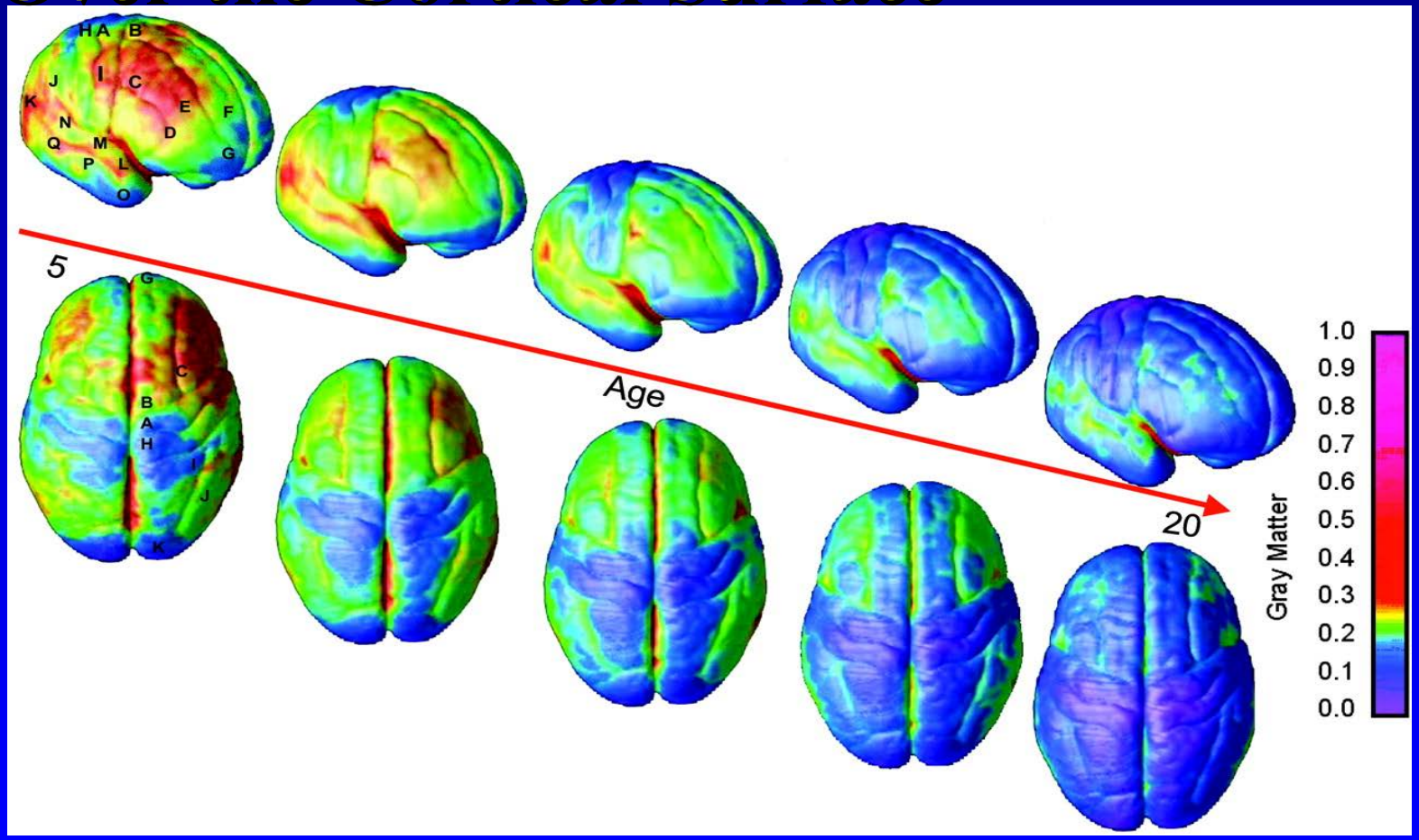
Etheridge, Hubbard, Anderson, Craddock, & Flynn, 1997 (PAB)

Prevention

- What do we know about prevention of substance use disorder?

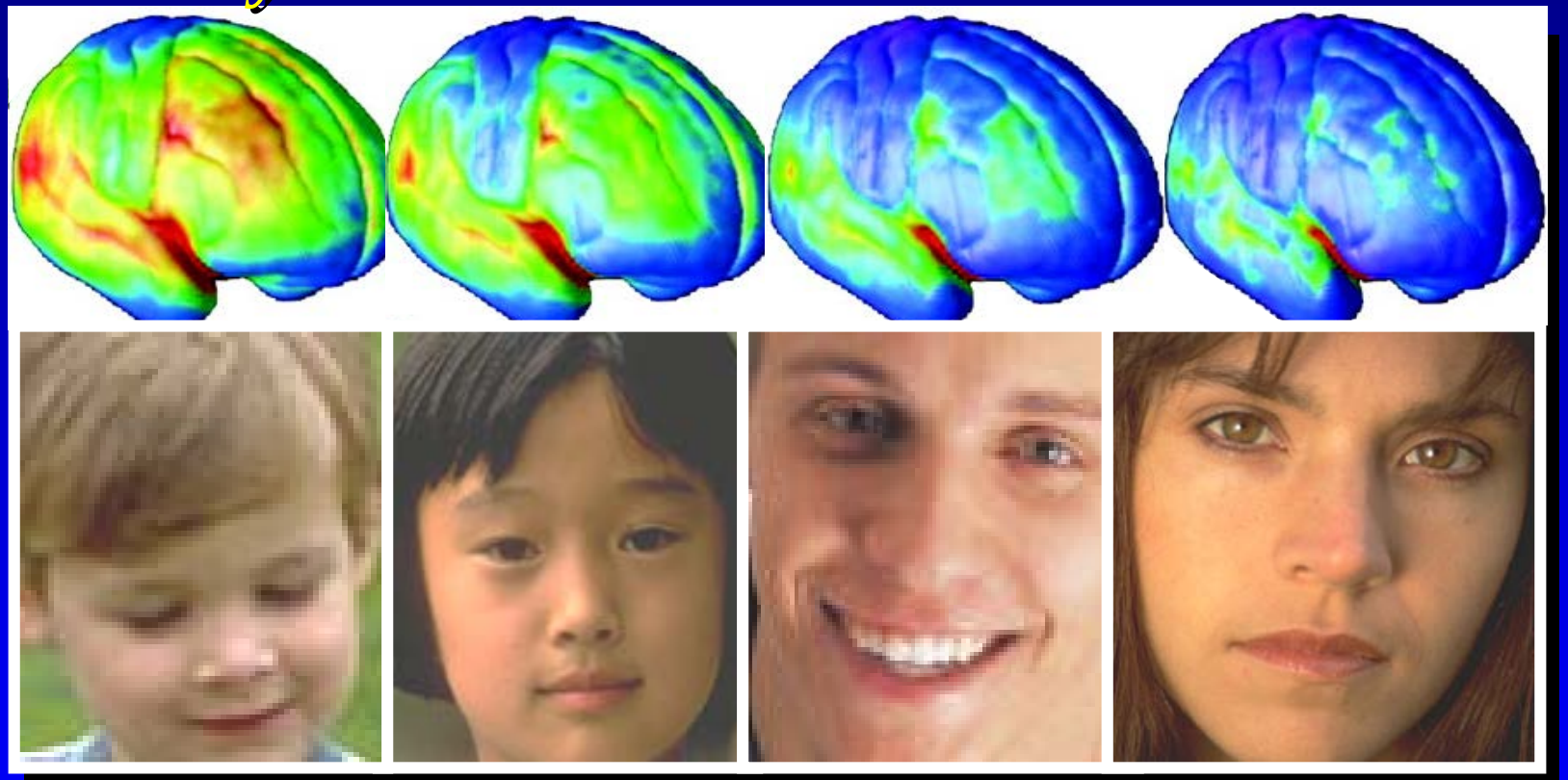

Just
TM
say no

Right Lateral and Top Views of the Dynamic Sequence of GM Maturation Over the Cortical Surface



Source: Gogtay, Nitin et al. (2004) Proc. Natl. Acad. Sci. USA 101, 8174-8179

- Exposure to drugs of abuse during adolescence could have profound effects on ***Brain Development & Brain Plasticity***



- Understanding drug abuse and addiction from a ***Development Perspective*** has important implications for their **Prevention & Treatment**

Judgment

Amygdala

Emotion

Motivation

Physical coordination, sensory processing

Prefrontal Cortex

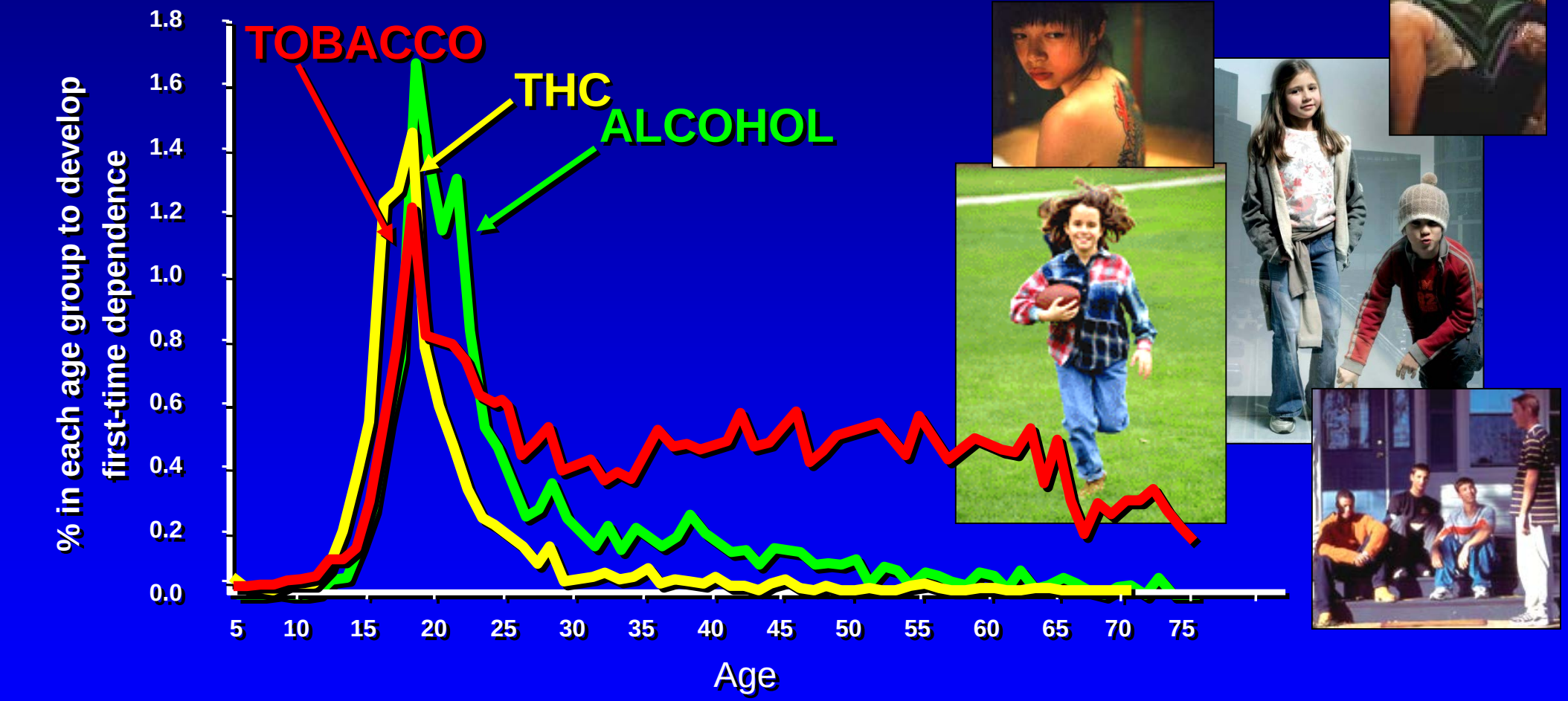
Nucleus Accumbens

Cerebellum

K. Winters

Addiction Is a Developmental Disease

starts in childhood and adolescence



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

National Epidemiologic Survey on Alcohol and Related Conditions, 2003

Principles of Substance Abuse Prevention for

Early Childhood

A Research-Based Guide

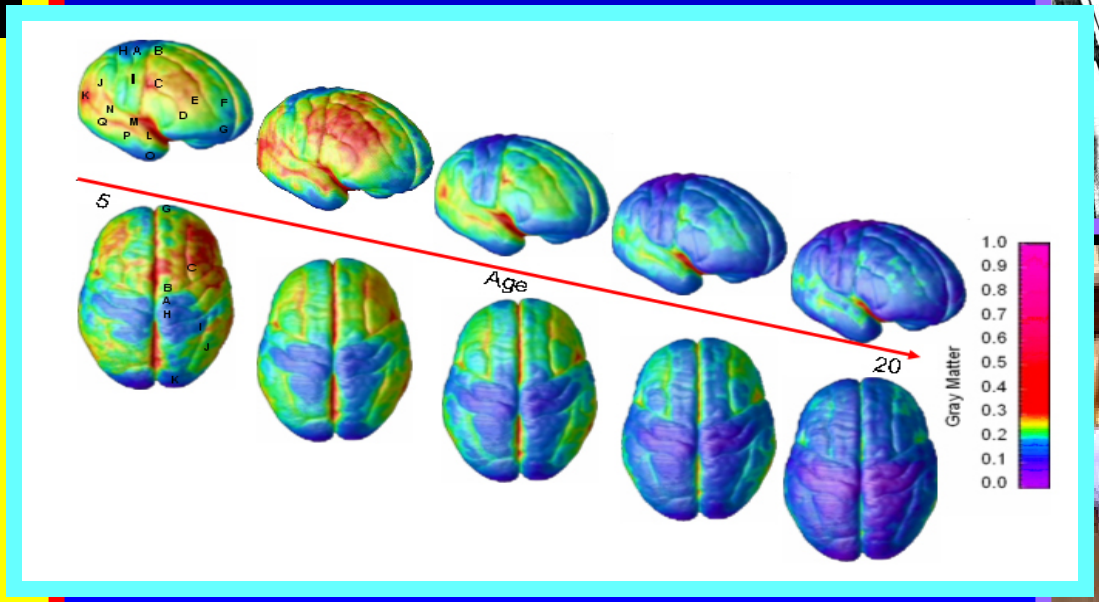
Principles of Substance Abuse Prevention for Early Childhood

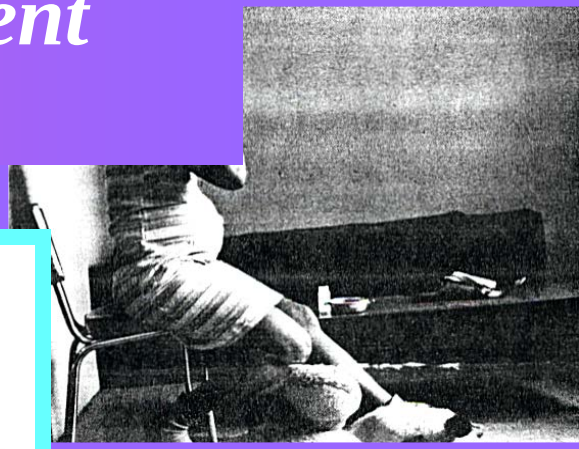
1. Intervening early in childhood can alter the life course trajectory in a positive direction.
2. Intervening early in childhood can both increase protective factors and reduce risk factors.
3. Intervening early in childhood can have positive long-term effects.
4. Intervening in early childhood can have effects on a wide array of behaviors, even behaviors not specifically targeted by the intervention.
5. Early childhood interventions can positively affect children's biological functioning.
6. Early childhood prevention interventions should target the proximal environments of the child.
7. Positively affecting a child's behavior through early intervention can elicit positive behaviors in adult caregivers and in other children, improving the overall social environment.

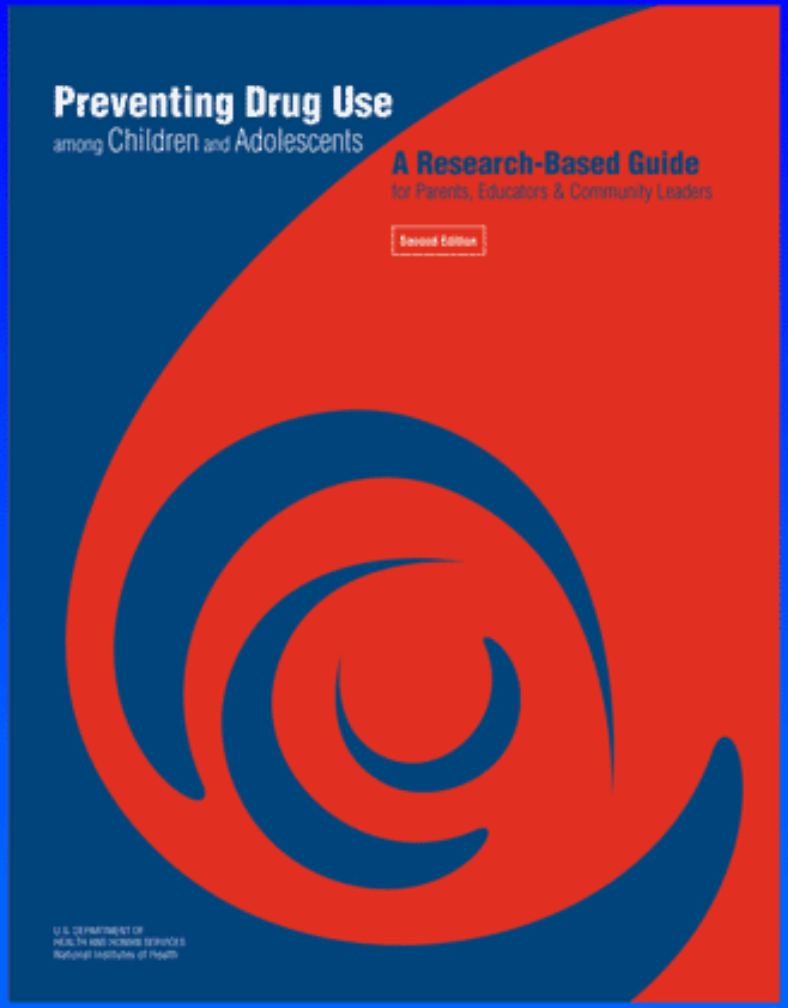
For more information visit: www.drugabuse.gov/earlychildhood

NIH National Institute on Drug Abuse

Genes, Environment and Development






Preventing Drug Use
among Children and Adolescents
A Research-Based Guide
for Parents, Educators & Community Leaders
Second Edition

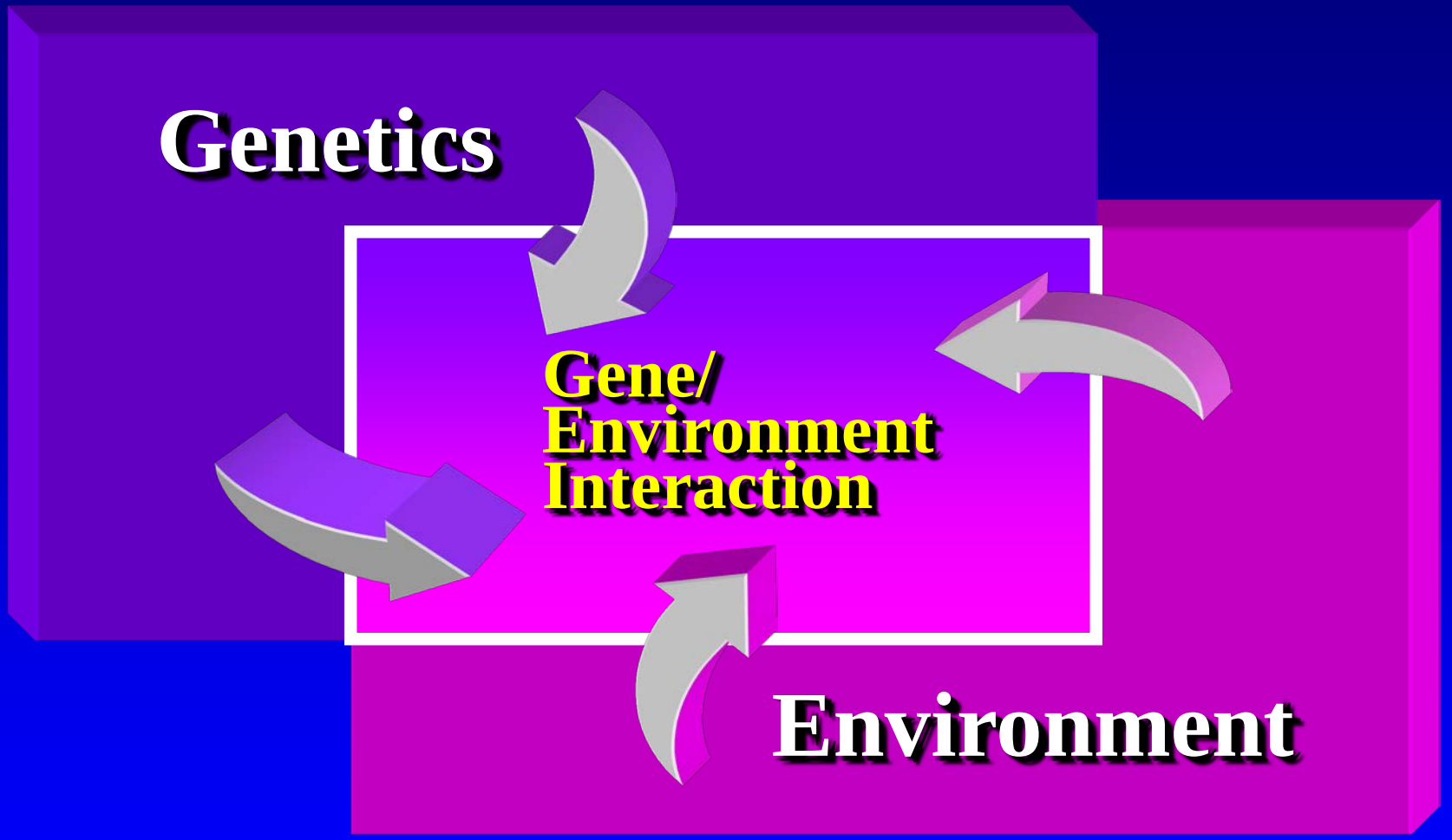
Prevention Programs

- Promotion
- Universal
- Selective
- Indicated

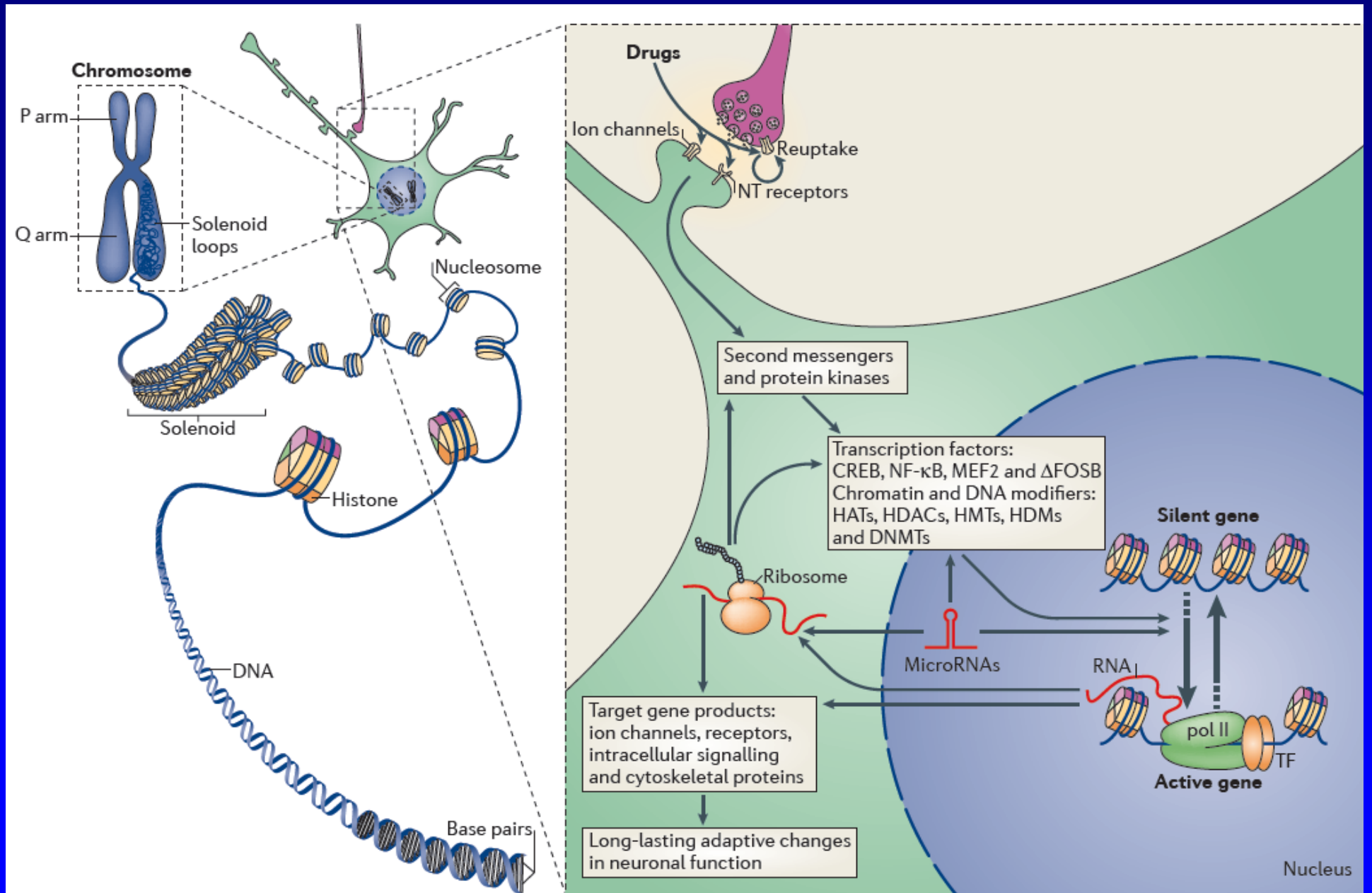
- What's important in all of these approaches?

ACEs

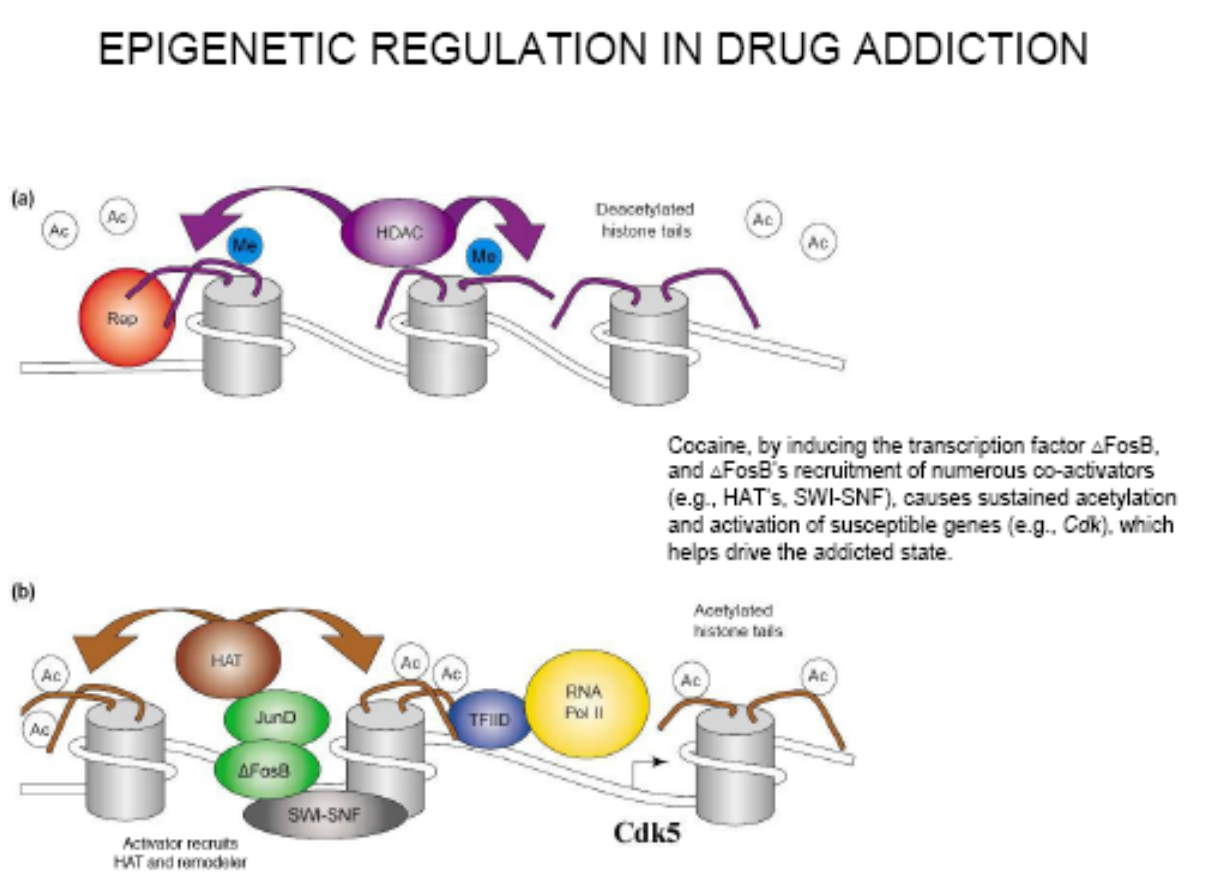
Adverse Childhood Events


Genetics
Gene/
Environment
Interaction
Environment

Epigenetic effects of drugs



Epigenetic Mechanisms Regulate How Genetic Information Is Expressed Across Development, Tissue, Environment and Disease States



- **DNA Methylation – silences gene**
- **Histone Modification – methylation, acetylation, or phosphorylation**
- **Non coding RNA**

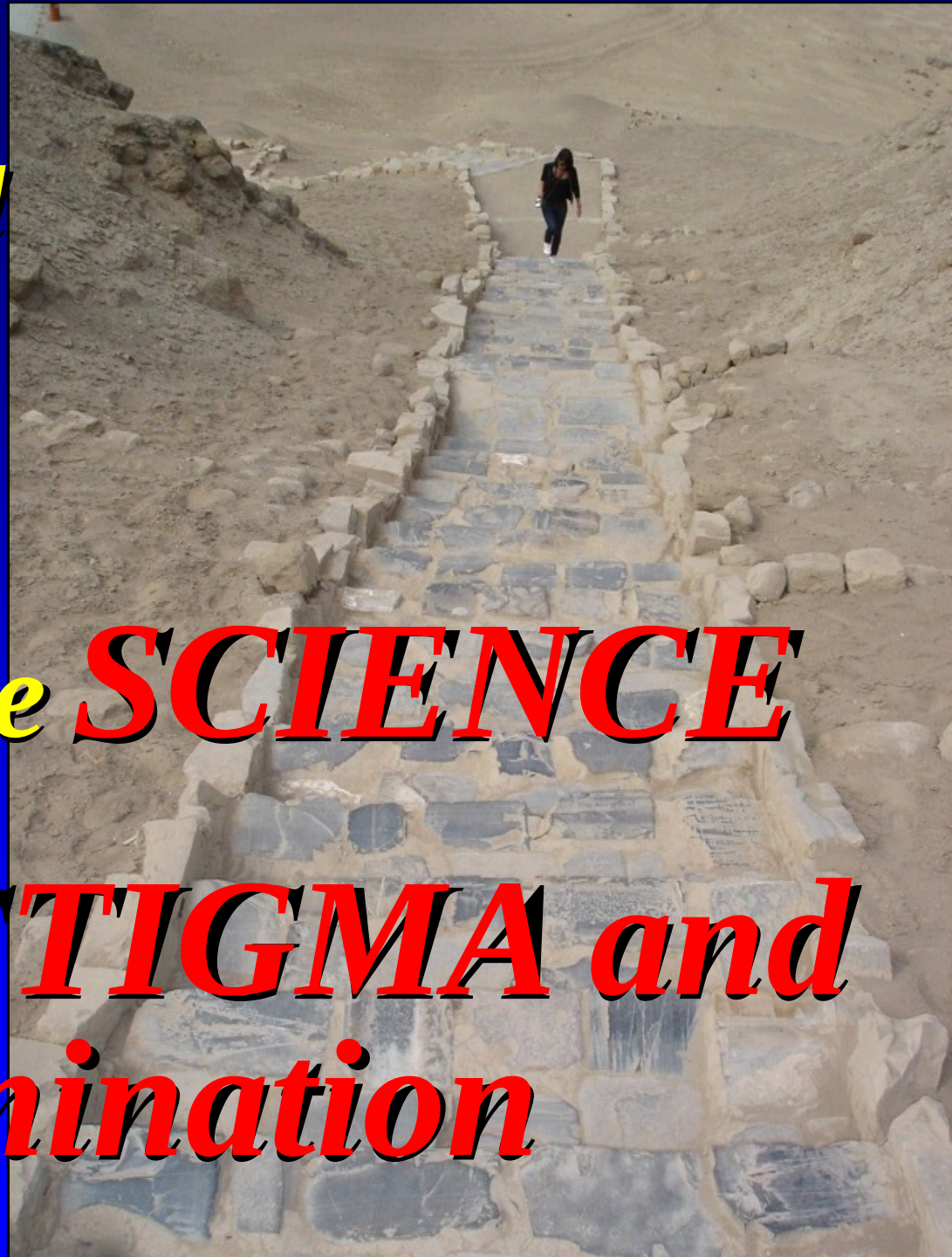
Where Do We Need to Go From Here?

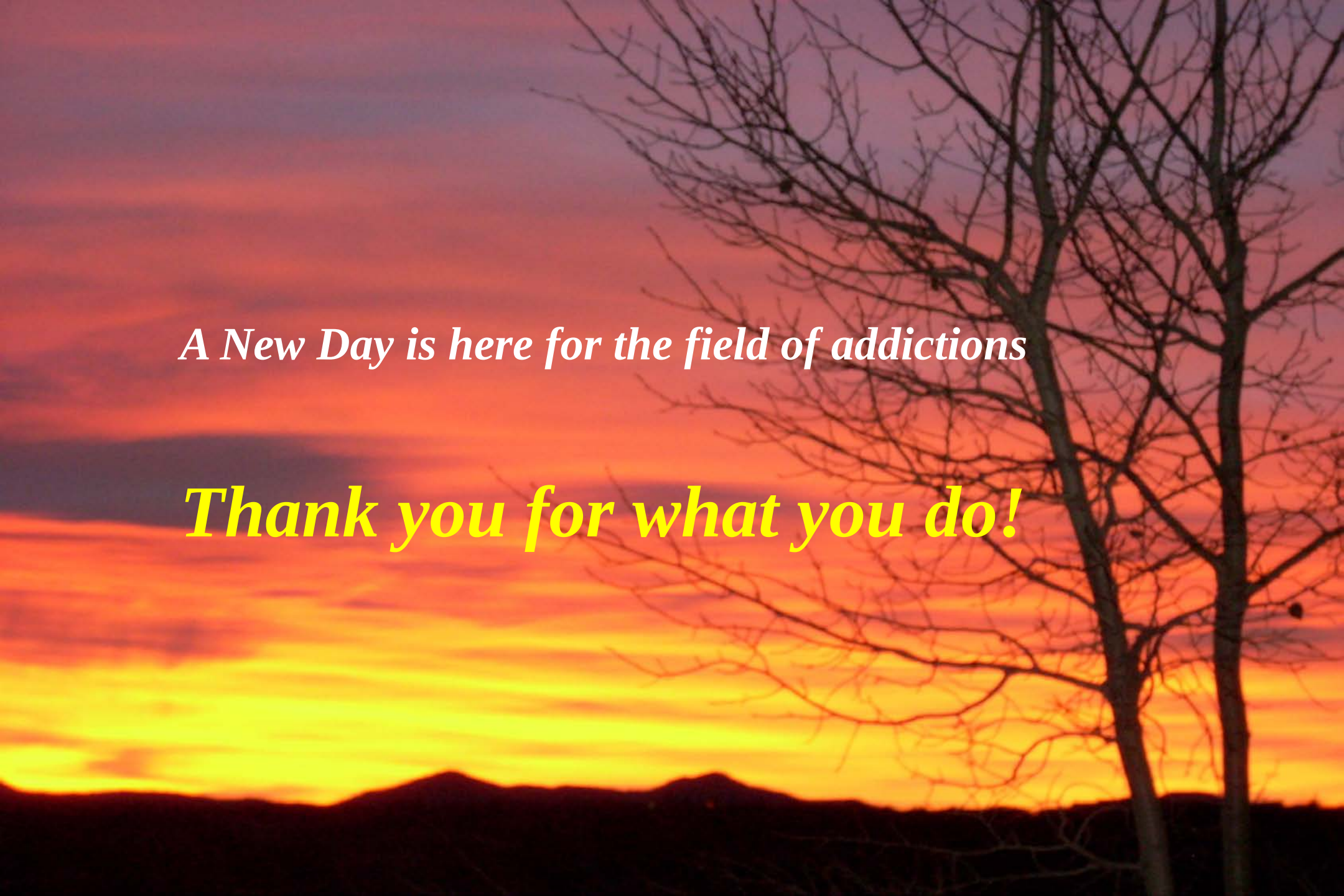
We Need to…

Advance the SCIENCE

and to…

End the STIGMA and Discrimination




A New Day is here for the field of addictions
Thank you for what you do!

Thank You

Tcondon@unm.edu

Center on Alcoholism, Substance Abuse & Addictions