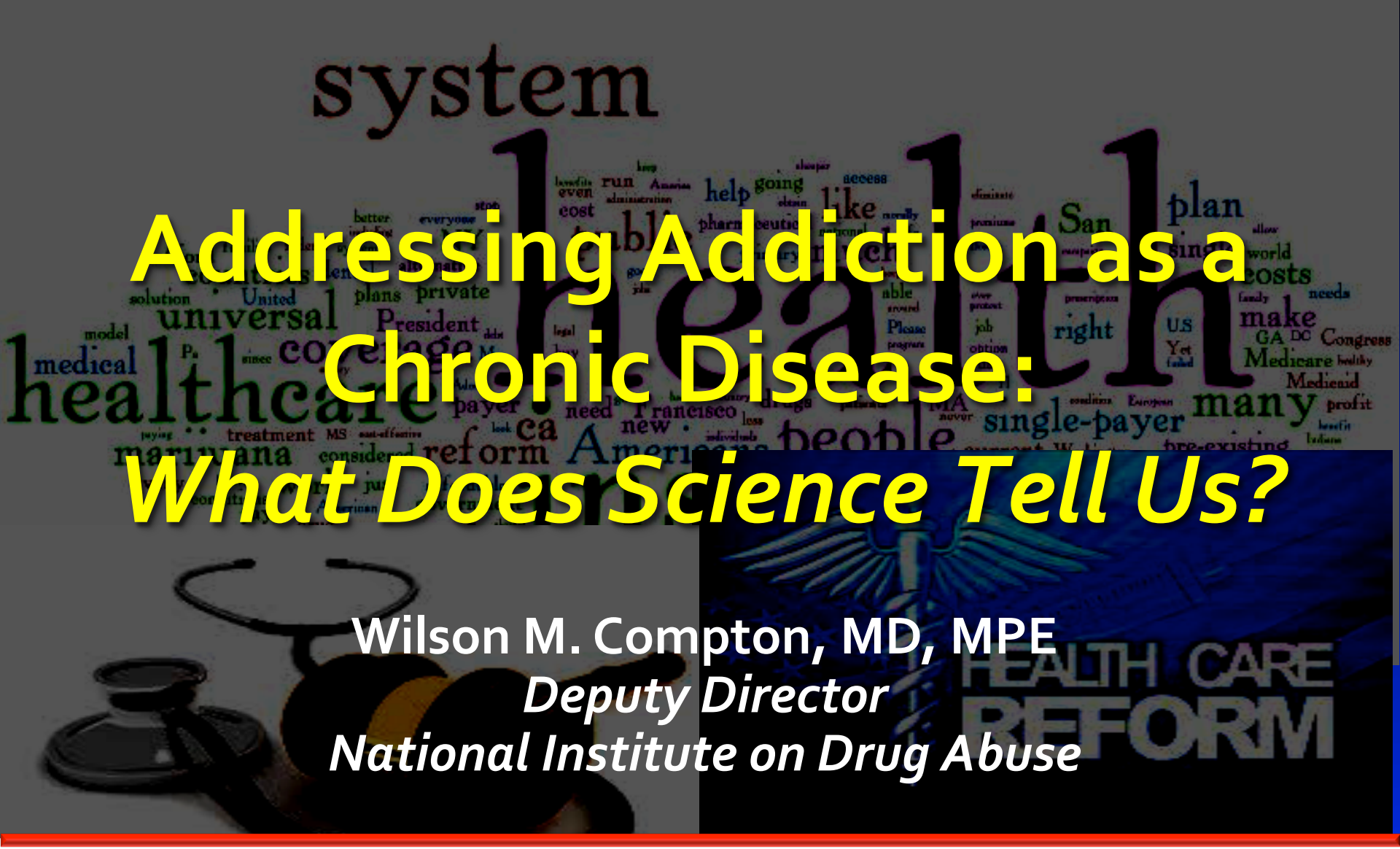


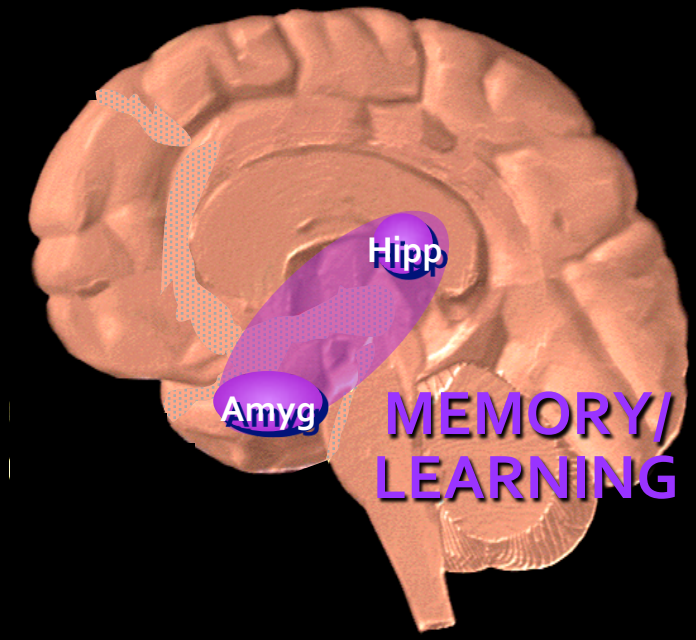
Addressing Addiction as a Chronic Disease: *What Does Science Tell Us?*

Wilson M. Compton, MD, MPE
Deputy Director
National Institute on Drug Abuse

NIH National Institute on Drug Abuse

Science = Solutions

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

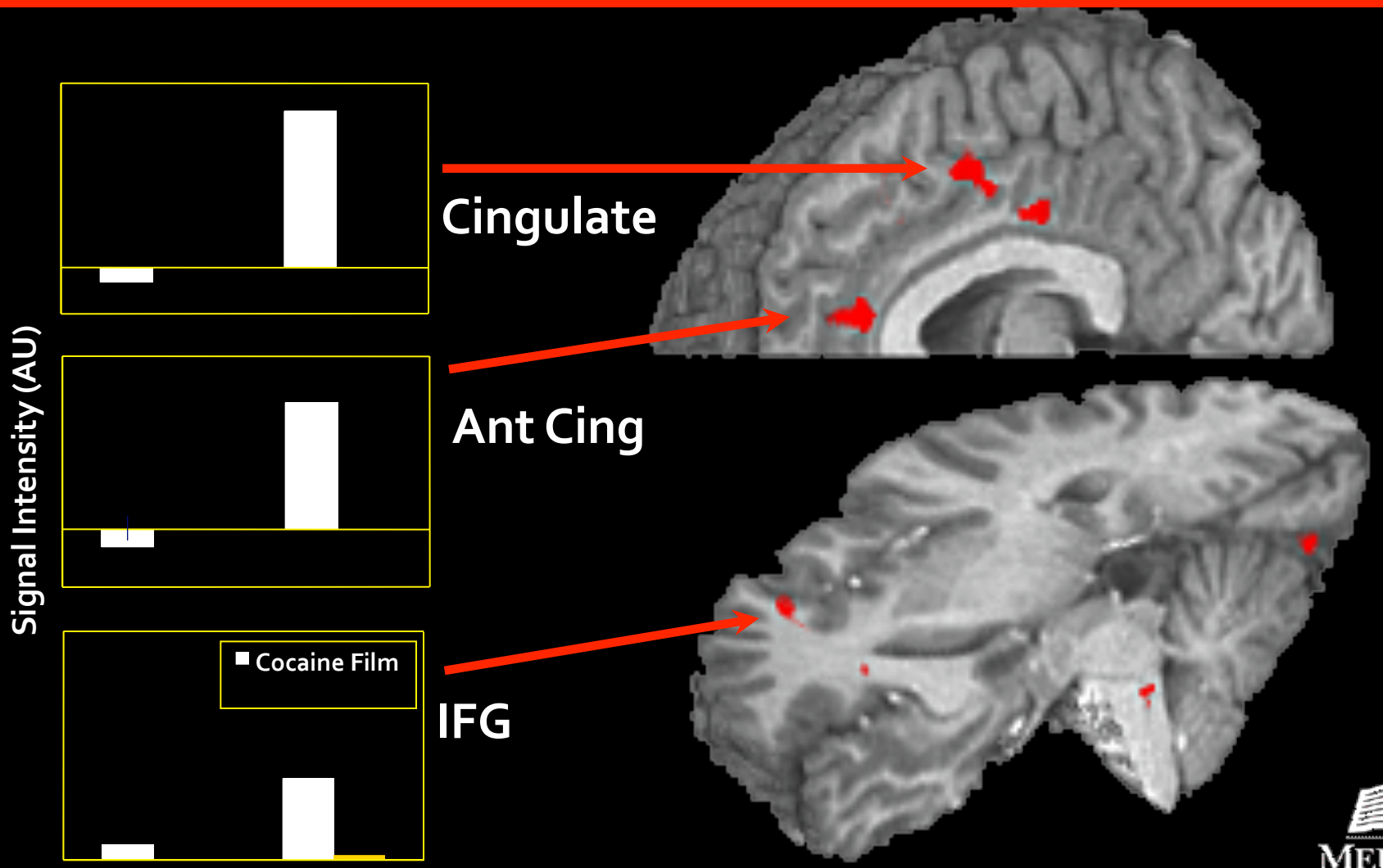


Memories Appear to Be A Critical Part of Addiction

"People, places and things…"

Cocaine Craving:

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

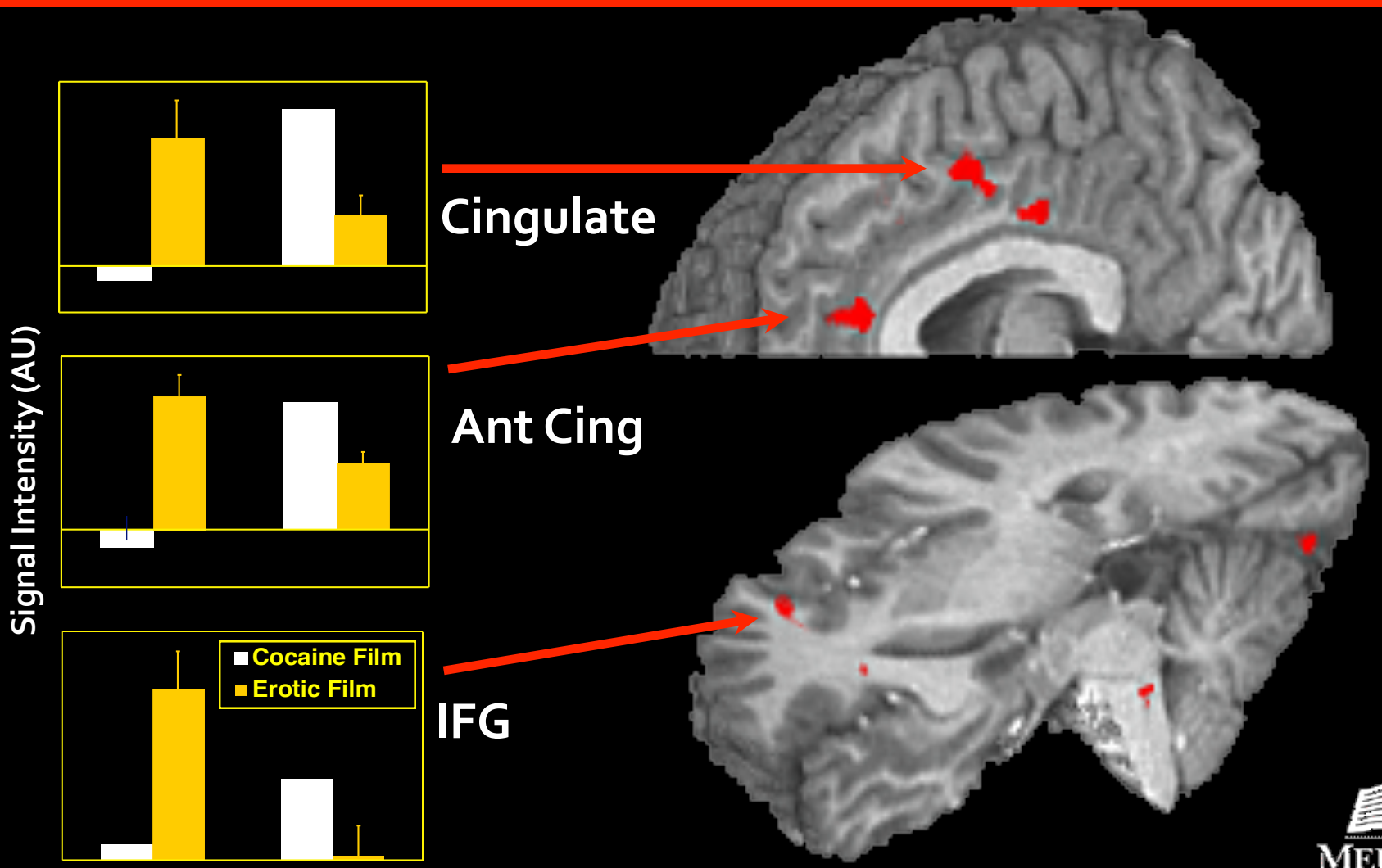


Garavan et al A .J. Psych 2000

MEDICAL COLLEGE OF WISCONSIN

Cocaine Craving:

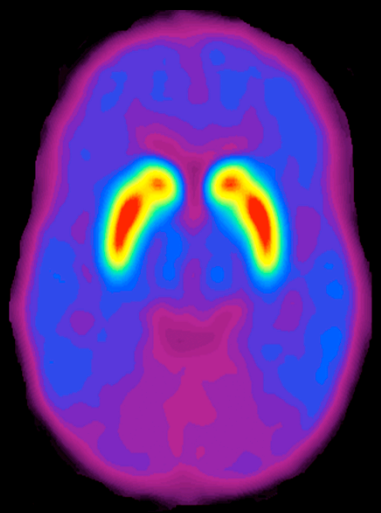
Population (Cocaine Users, Controls) x Film (cocaine, erotic)



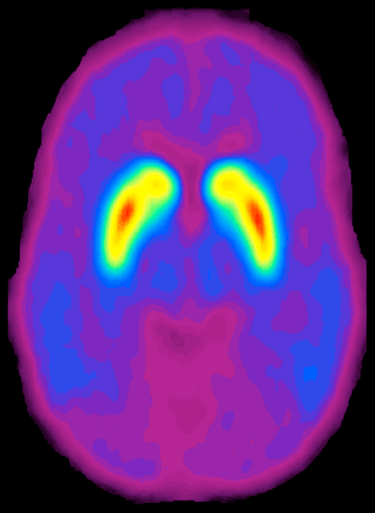
Garavan et al A .J. Psych 2000

MEDICAL COLLEGE OF WISCONSIN

[^{11}C]Raclopride Binding In Cocaine Abusers (n=18) Viewing a Neutral and a Cocaine-Cue Video



Control Video



Cocaine Cue Video

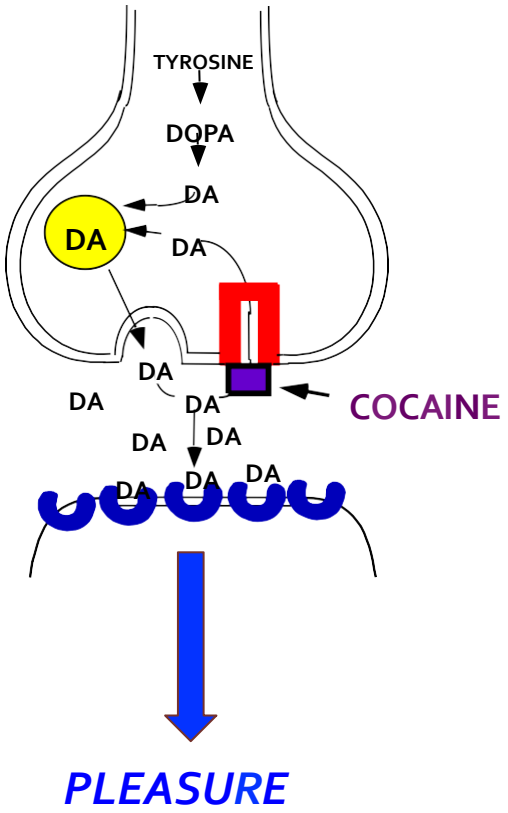
Viewing a video of cocaine scenes decreased specific binding of [11C] raclopride presumably from DA increases

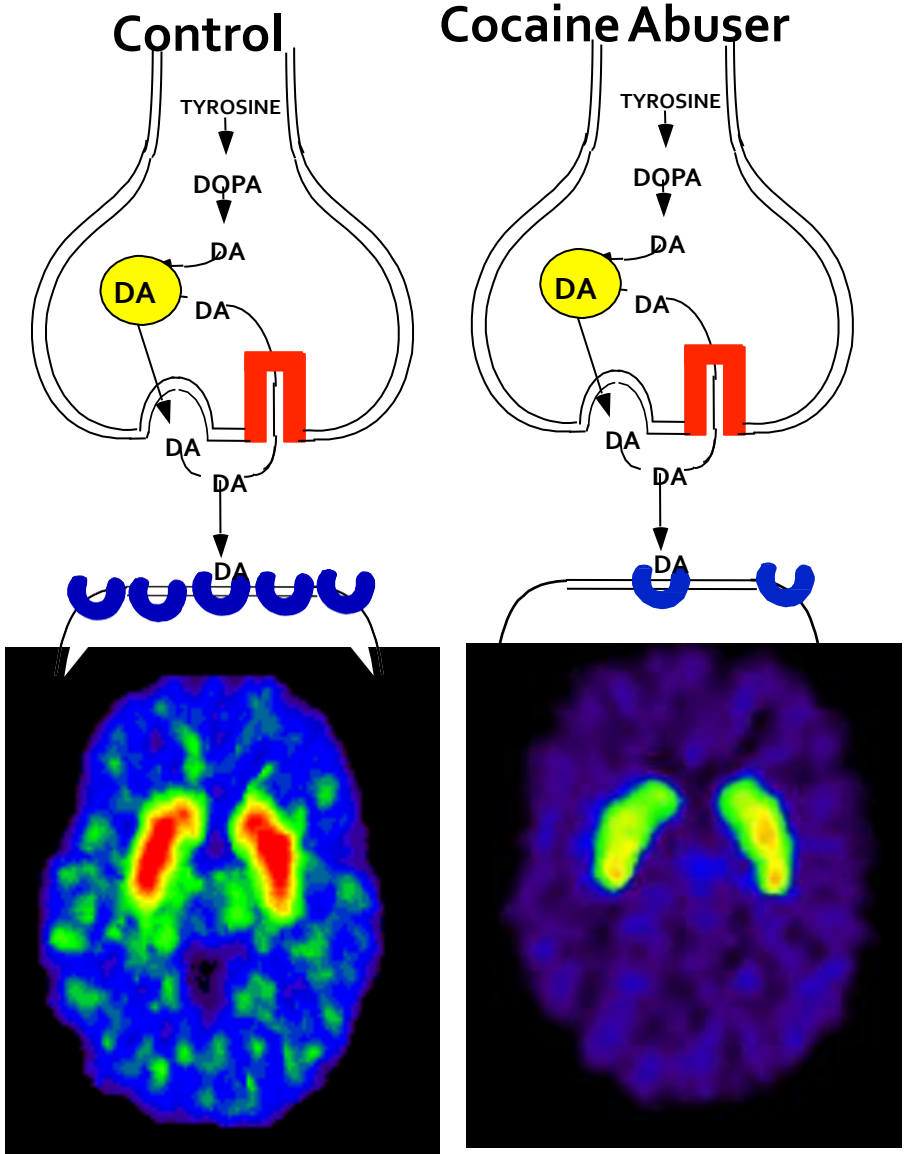
SOURCE: Volkow et al , J Neuroscience, 2006

Even Unconscious Cues Can Elicit Brain Responses

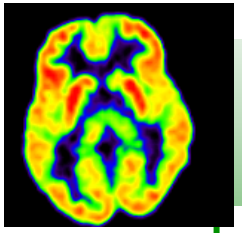
Repeated Drug Use Changes the Brain

Weakens the Brain Dopamine System





Expected Consequences of Reduced Striatal Dopamine Receptor (D2) Signaling in Indirect Pathway



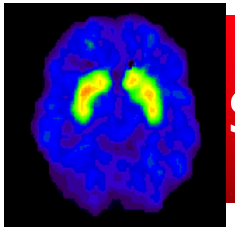
Glucose Metabolism

FRONTAL CORTEX

excitation

Thalamus

LOW D2 Receptors



Striatum

inhibition

GPe

inhibition

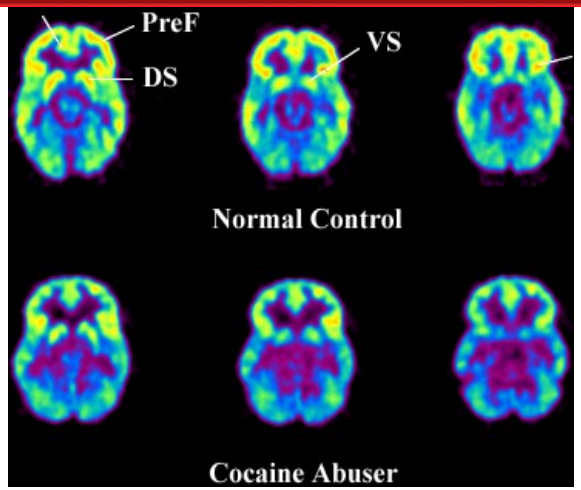
inhibition

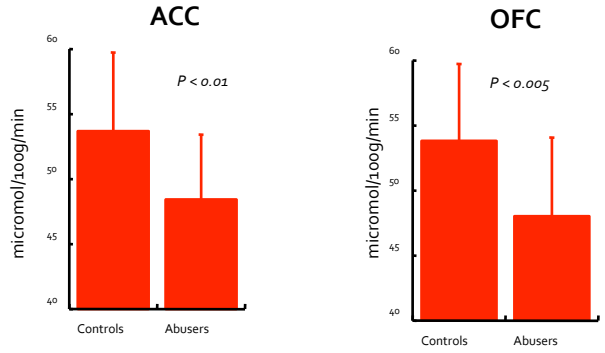
VTA
SN

STN

SNR-
GPi

excitation



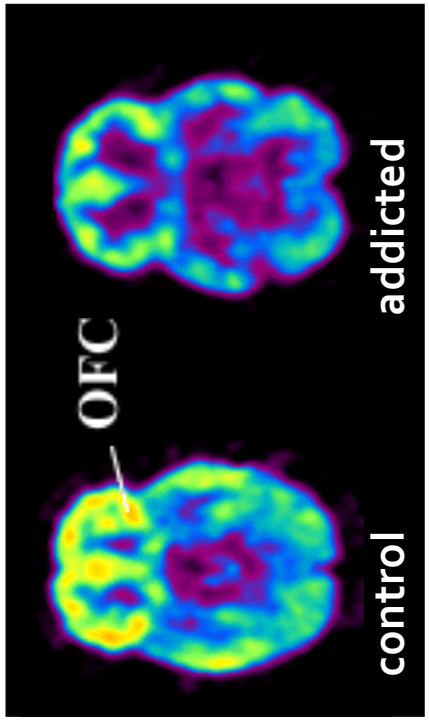


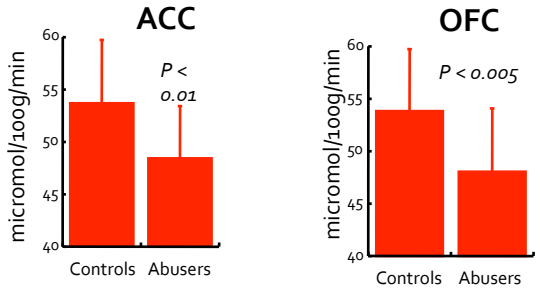
Brain glucose metabolism is reduced in frontal cortex of cocaine abusers

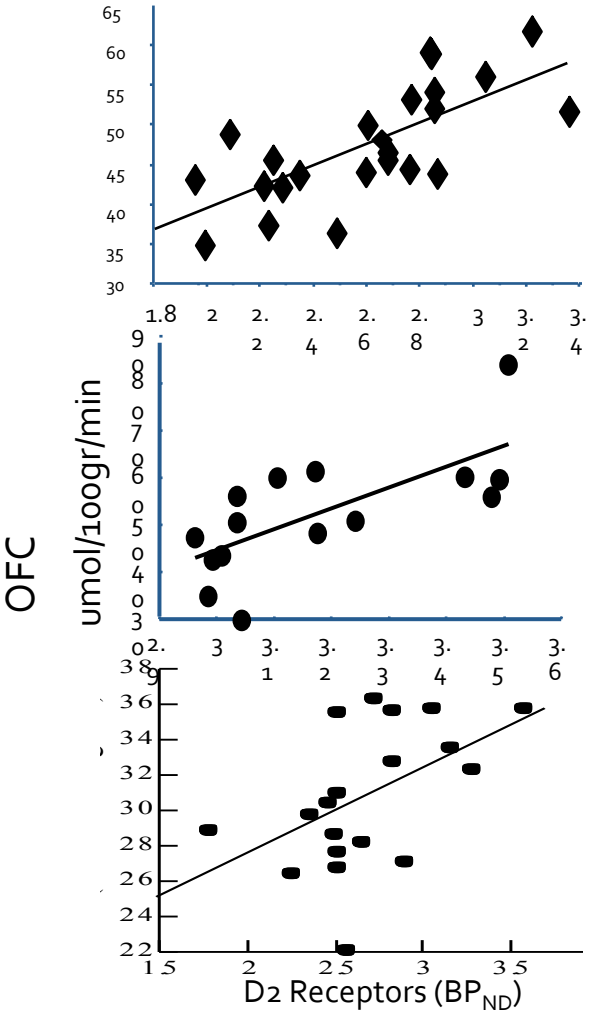
Volkow et al., PNAS 2011.

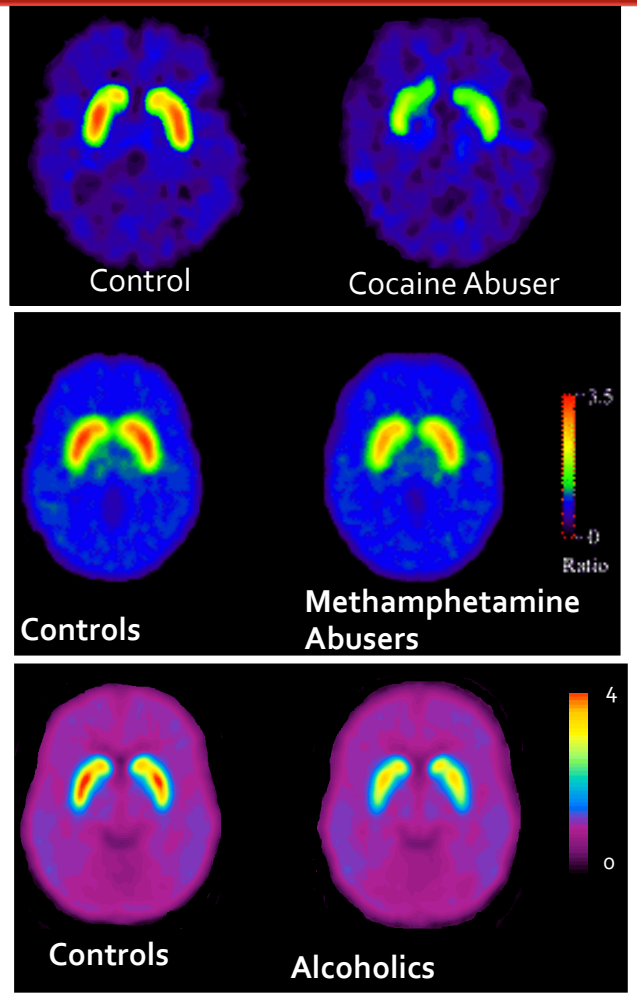
Low Levels of Striatal D2 Receptors Are Associated with Impaired Activity in Frontal Regions

Volkow et al., PNAS 2011.

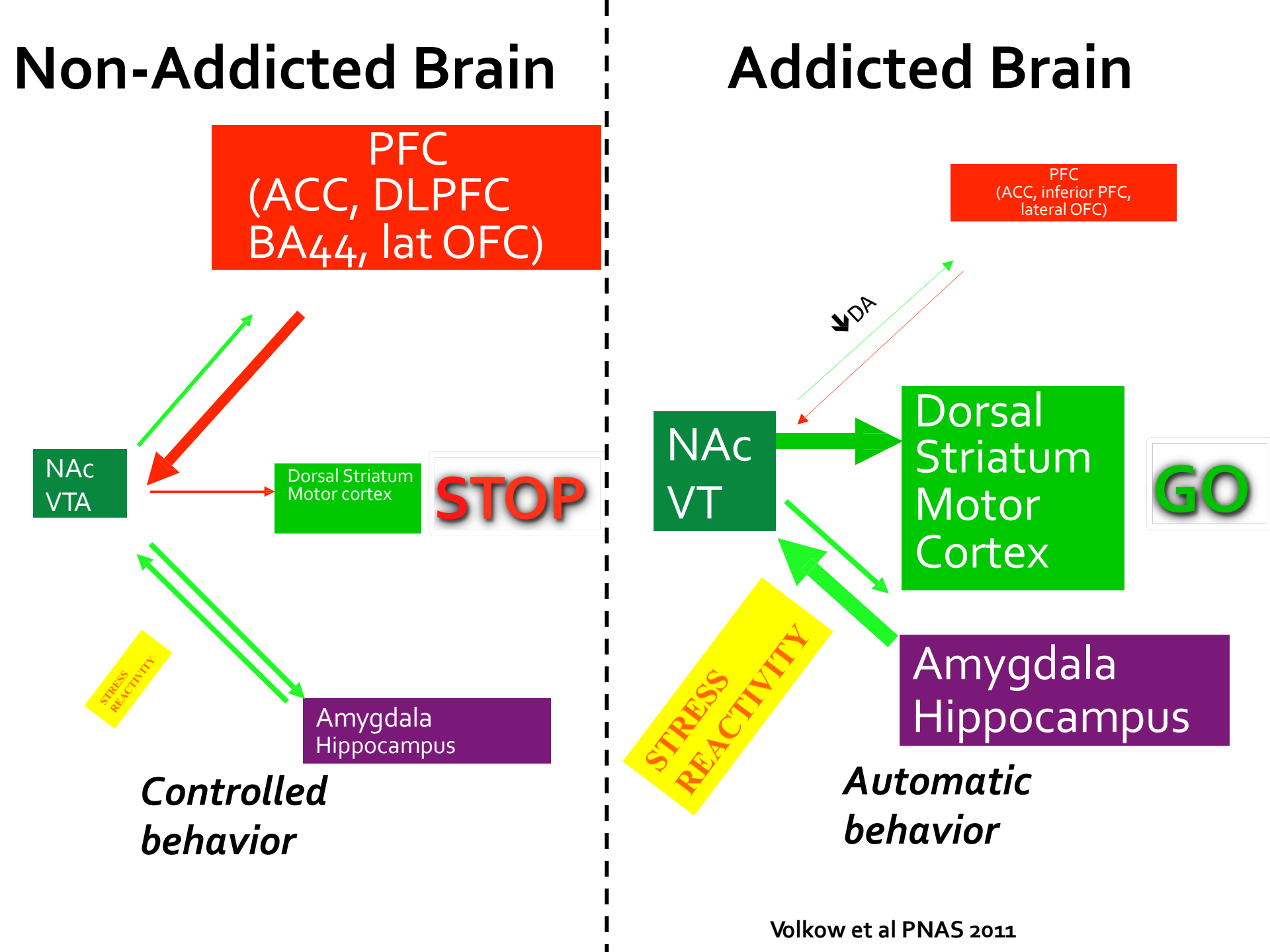




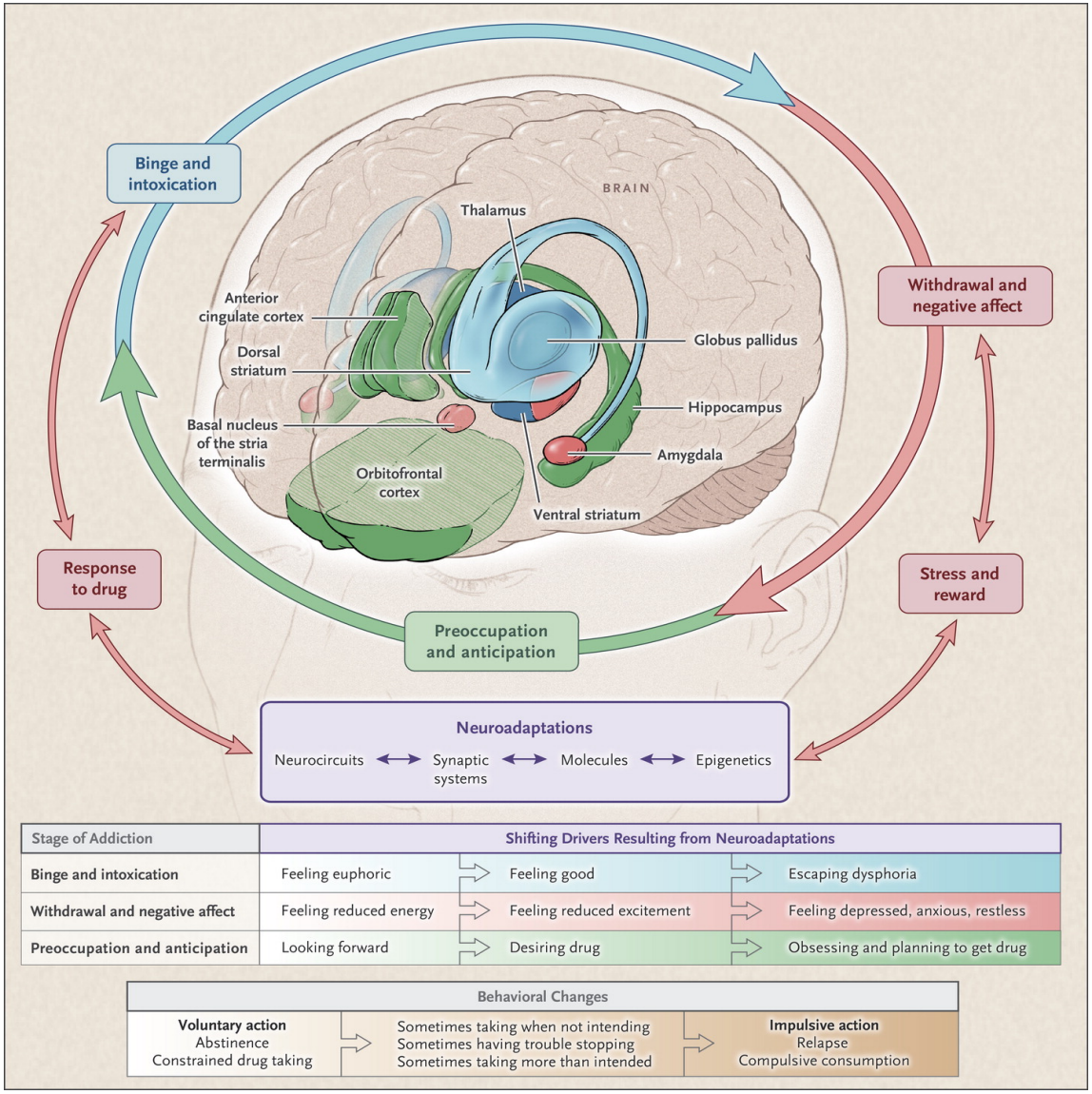




DA D2 receptors


Non-Addicted Brain
PFC
(ACC, DLPFC
BA44, lat OFC)
NAc
VTA
Dorsal Striatum
Motor cortex
STOP
STRESS
REACTIVITY
Amygdala
Hippocampus
Controlled
behavior
Addicted Brain
PFC
(ACC, inferior PFC,
lateral OFC)
DA
NAc
VT
Dorsal
Striatum
Motor
Cortex
GO
STRESS
REACTIVITY
Amygdala
Hippocampus
Automatic
behavior
Volkow et al PNAS 2011

Stages of Addiction



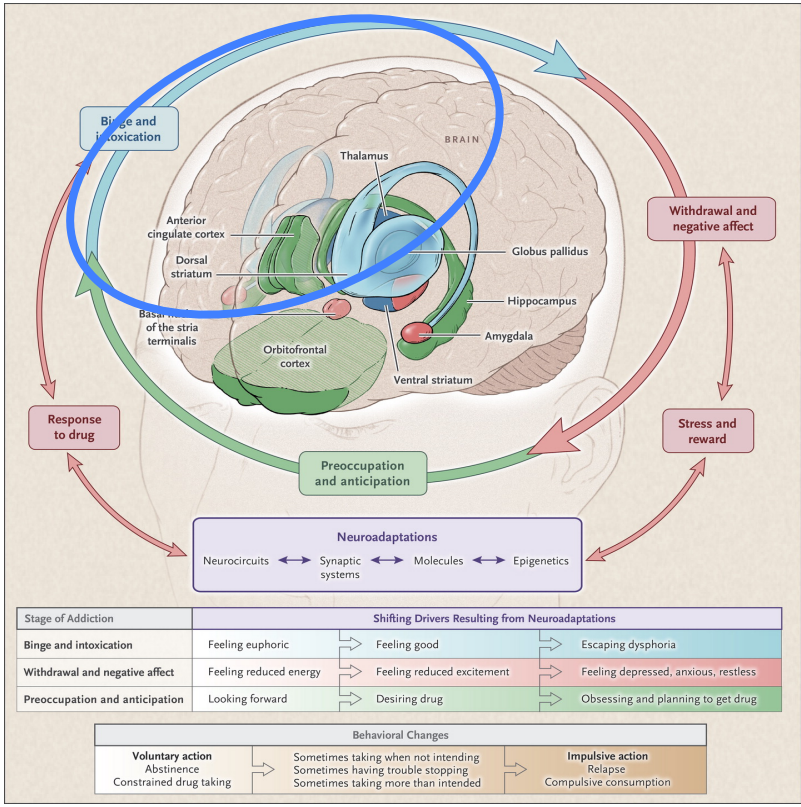
Stage of Addiction	Shifting Drivers Resulting from Neuroadaptations		
Binge and intoxication	Feeling euphoric	Feeling good	Escaping dysphoria
Withdrawal and negative affect	Feeling reduced energy	Feeling reduced excitement	Feeling depressed, anxious, restless
Preoccupation and anticipation	Looking forward	Desiring drug	Obsessing and planning to get drug

Behavioral Changes		
Voluntary action Abstinence Constrained drug taking	Sometimes taking when not intending Sometimes having trouble stopping Sometimes taking more than intended	**Impulsive action** Relapse Compulsive consumption

Volkow, Koob, Mclellan, *Neurobiologic Advances from the Brain Disease Model of Addiction*, NEJM, 2016

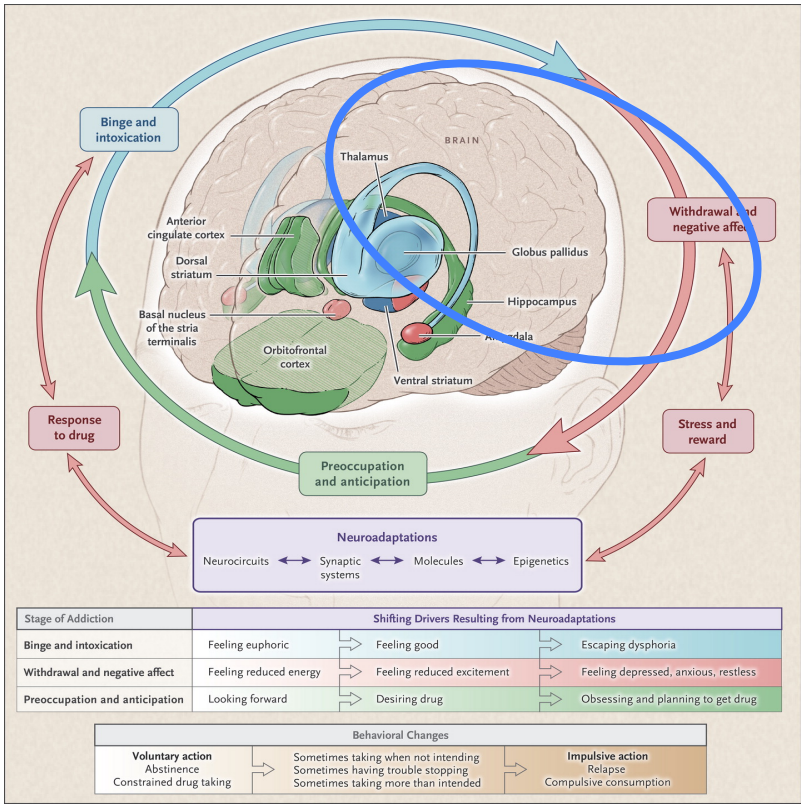
Binge and Intoxification

- All drugs activate dopamine in reward region
- Link to preceding environmental stimuli
- Cue-induced anticipatory dopamine release
- Conditioned response trigger craving (even after drug use stops)



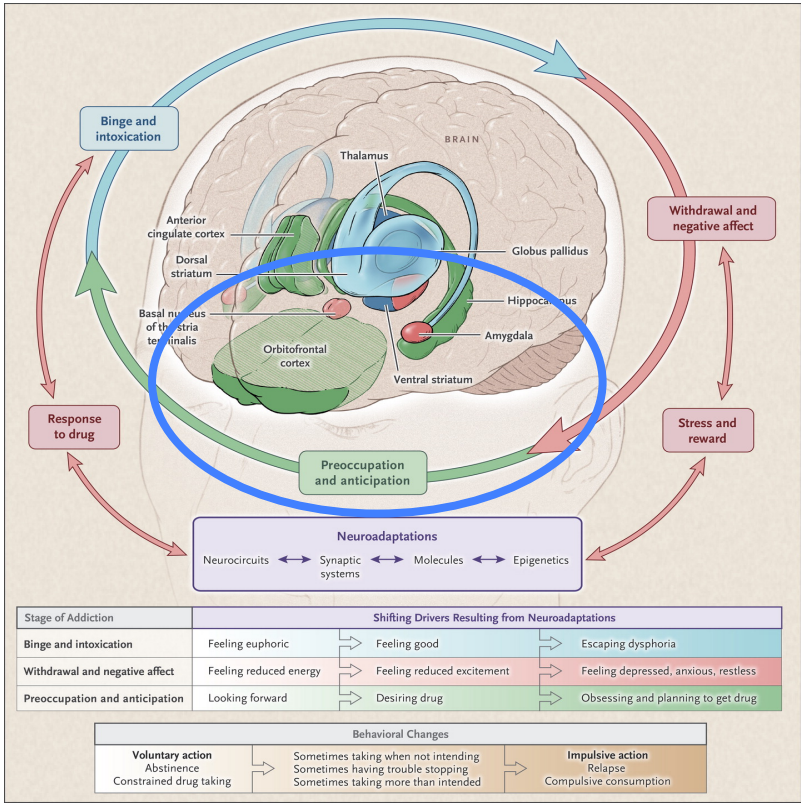
Withdrawal and Negative Effect

- Reduced dopamine levels -> diminished reward system
- Increased stress/ negative emotions (“anti-reward” system)
- Shift from desire for pleasure to avoiding distress



Preoccupation and Anticipation

- Prefrontal changes to executive processes
- Impaired self-regulation, decision making
- Difficulty resisting strong urges
- Impulsiveness



"…altered signaling in prefrontal regulatory circuits, paired with changes in the circuitry involved in reward and emotional response, creates an imbalance that is crucial to both the gradual development of compulsive behavior in the addicted disease state and the associated inability to voluntarily reduce drug-taking behavior, despite the potentially catastrophic consequences."

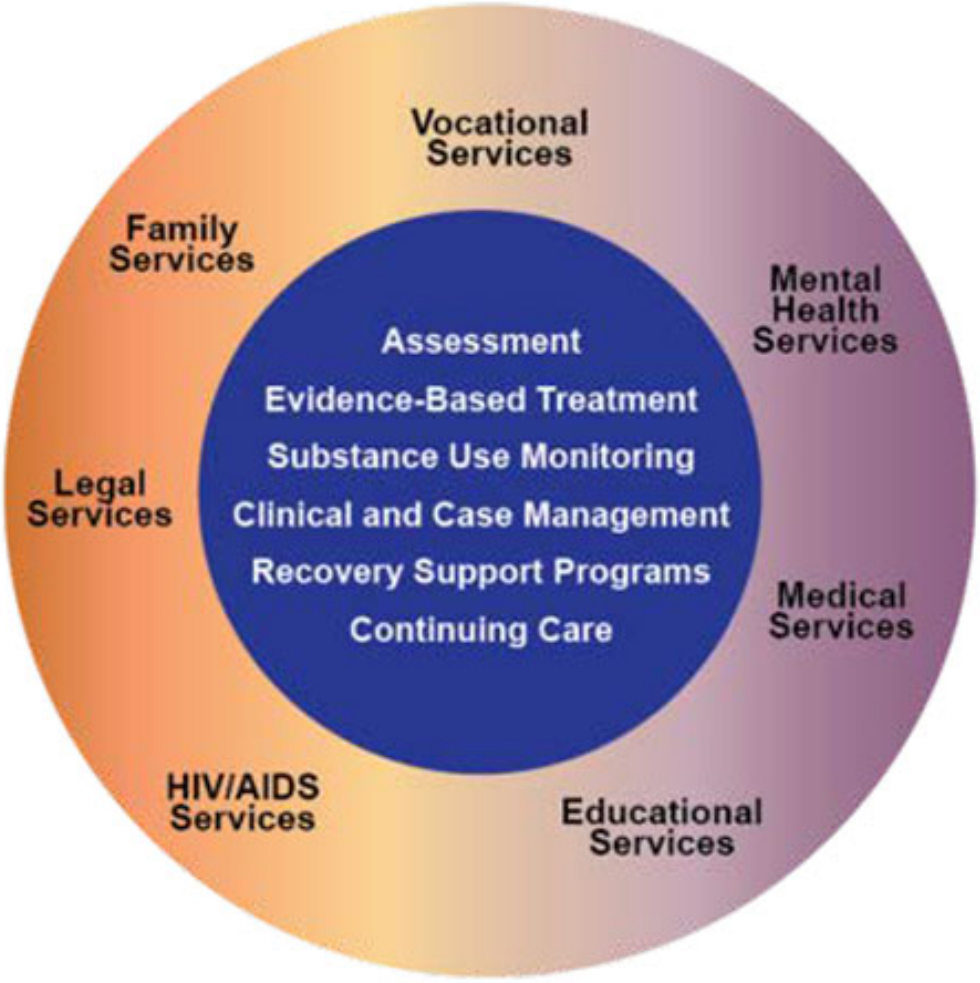
Volkow, Koob, McLellan, NEJM, 2016

Effective Strategies Attend to Multiple Aspects of Addiction:

- Behavior
- Biology
- Social Context

Science =

Components of Comprehensive Drug Addiction Treatment



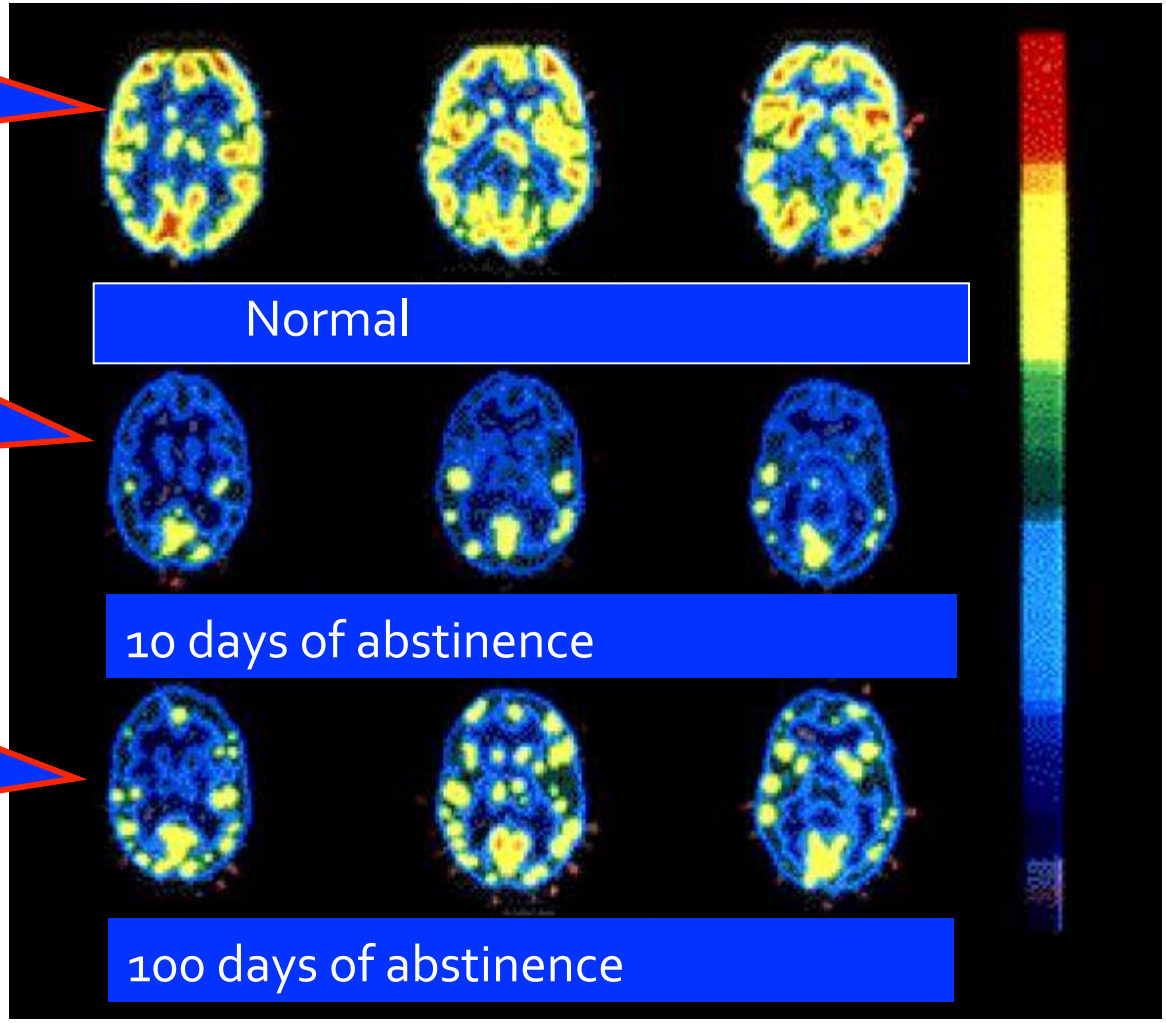
The best treatment programs provide a combination of therapies and other services to meet the needs of the individual patient.

Prolonged Substance Use Injures The Brain: *Healing Takes Time*

Normal levels of brain activity in PET scans show up in yellow to red

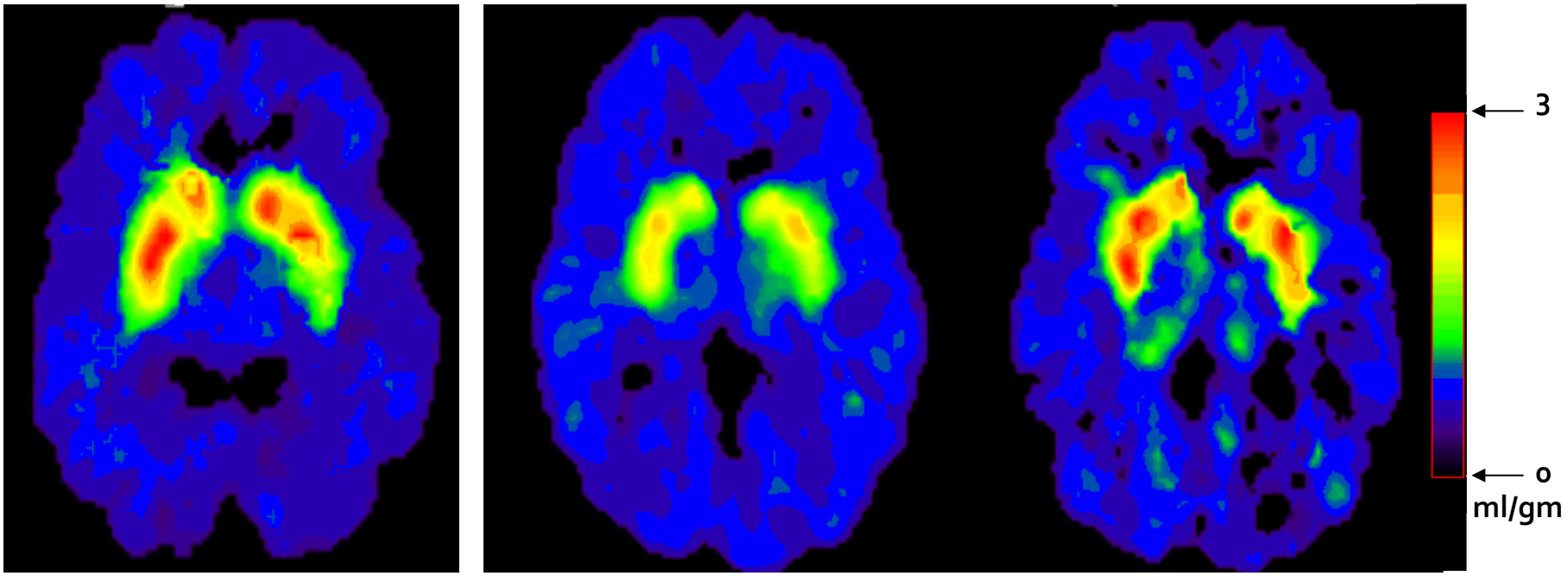
Reduced brain activity after regular use can be seen even after 10 days of abstinence

After 100 days of abstinence, we can see brain activity "starting" to recover



Source: Volkow ND, Hitzemann R, Wang C-I, Fowler IS, Wolf AP, Dewey SL. Long-term frontal brain metabolic changes in cocaine abusers. Synapse 11:184-190, 1992; Volkow ND, Fowler JS, Wang G-J, Hitzemann R, Logan J, Schlyer D, Dewey 5, Wolf AP. Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. Synapse 14:169-177, 1993.

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



Normal Control

METH Abuser
(1 month detox)

METH Abuser
(14 months detox)

Source: Volkow, ND et al., Journal of Neuroscience 21, 9414-9418, 2001.

Brain Changes During Recovery?

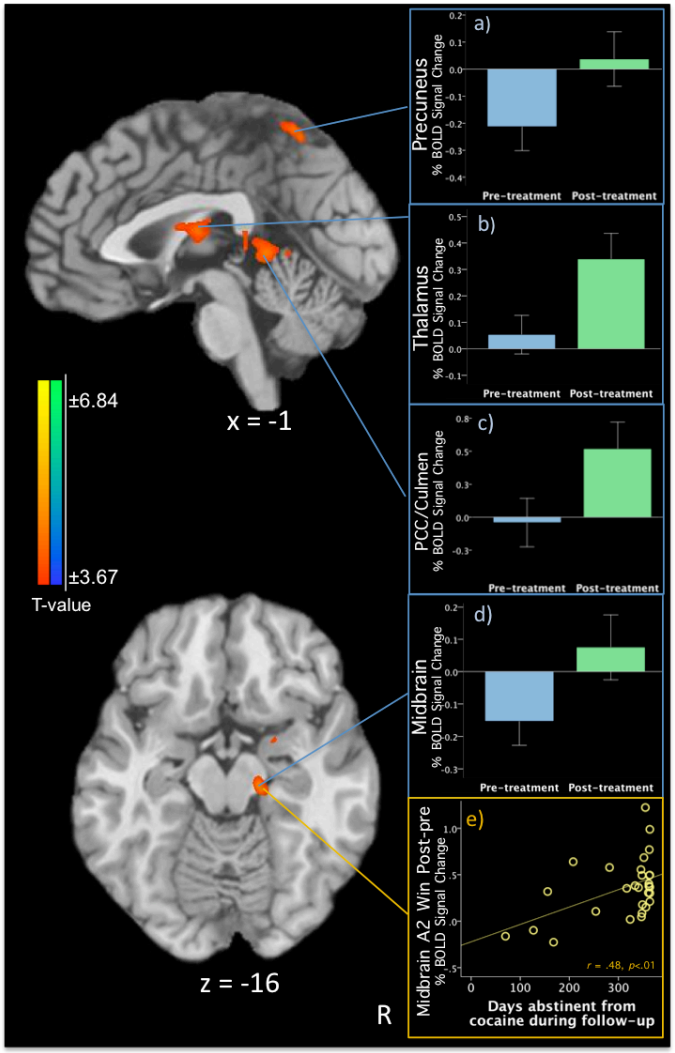
- Relatively few studies have examined brain changes with discontinued use.
- Neurofunctional changes during recovery may provide important insights to treat, prevent relapse, and maintain recovery

Neurofunctional Reward Processing Changes in Cocaine During Recovery

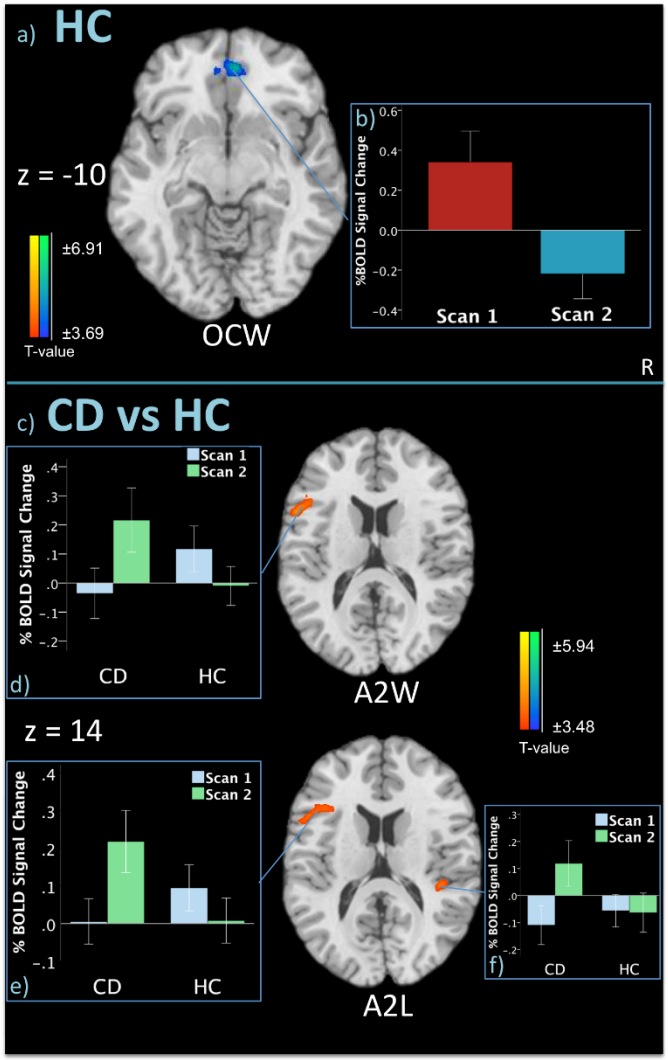
Balodis, et al, Neuropsychopharmacology, January, 2016

- One of first longitudinal pre/post treatment neuroimaging studies
- Design: 29 cocaine dependent patients/12 weeks treatment/1 year follow up
- Results: Enhanced dopamine brain regions during "non-drug anticipatory processing" following treatment
- Conclusion: Neural data may clarify impact on long-term recovery

Changes in Reward Processing Detected with Treatment (1-year Follow Up)



Cocaine Dependent (CD) participants demonstrated increased anticipatory reward activity in the midbrain, thalamus, and precuneus). Increased midbrain activity correlated with cocaine abstinence during the 1-year follow-up.



Source: Balodis IM, Kober H, Worhunsky PD, Stevens MC, Pearlson GD, Carroll KM, Potenza MN. Neorofunctional reward processing changes in cocaine dependence during recovery. *Neuropsychopharmacology* 2016, 1-10 [epub ahead of print]

Recovery Research

- Neurological effects during stages of recovery
- Data on individuals in recovery
- Effectiveness of the emerging range of recovery support services
- Culturally-specific adaptations of long-existent services
- Understanding and improving recovery systems of care.

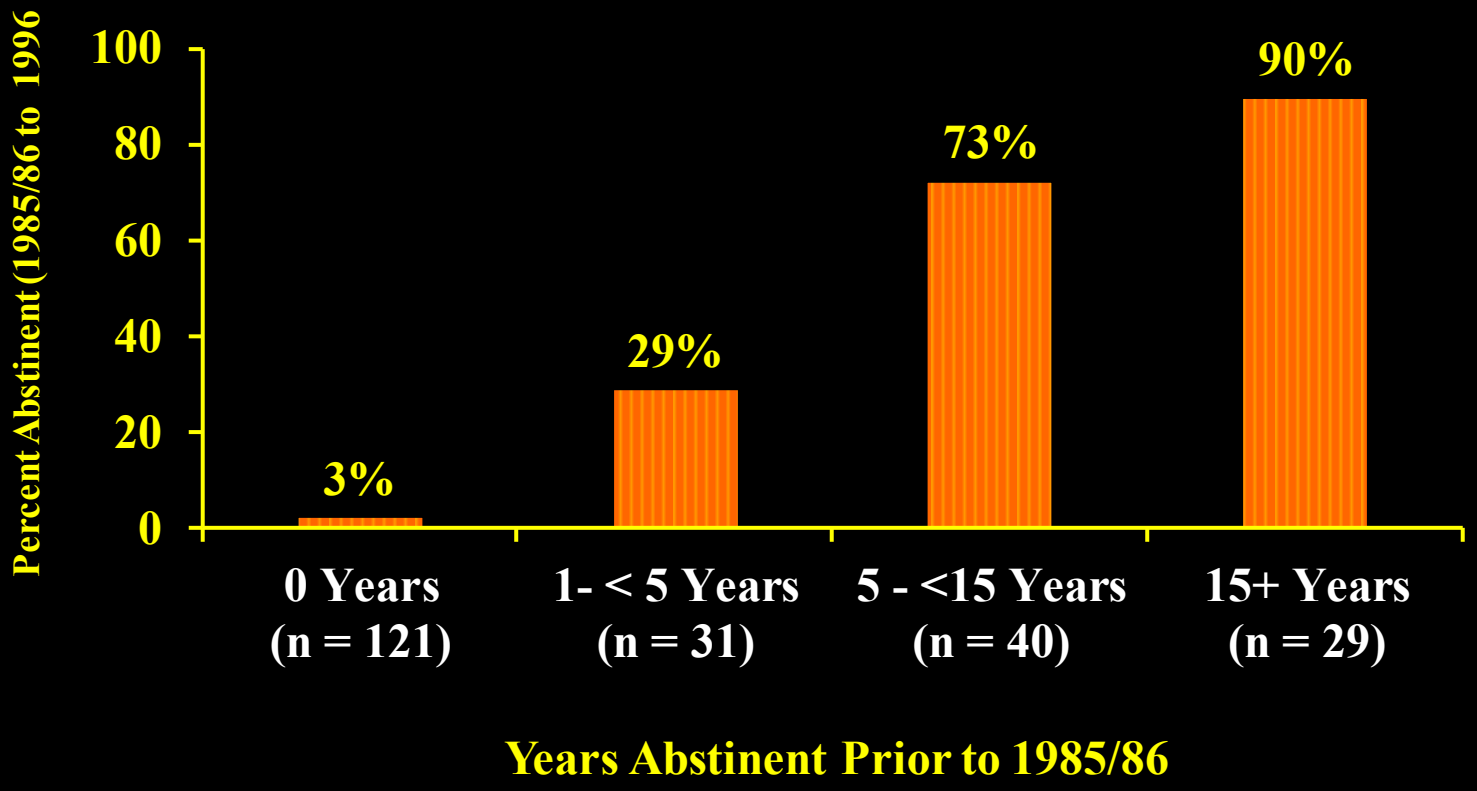
Longitudinal Research

UCLA/CALDAR Key Findings

Opioid addiction is a chronic relapsing condition

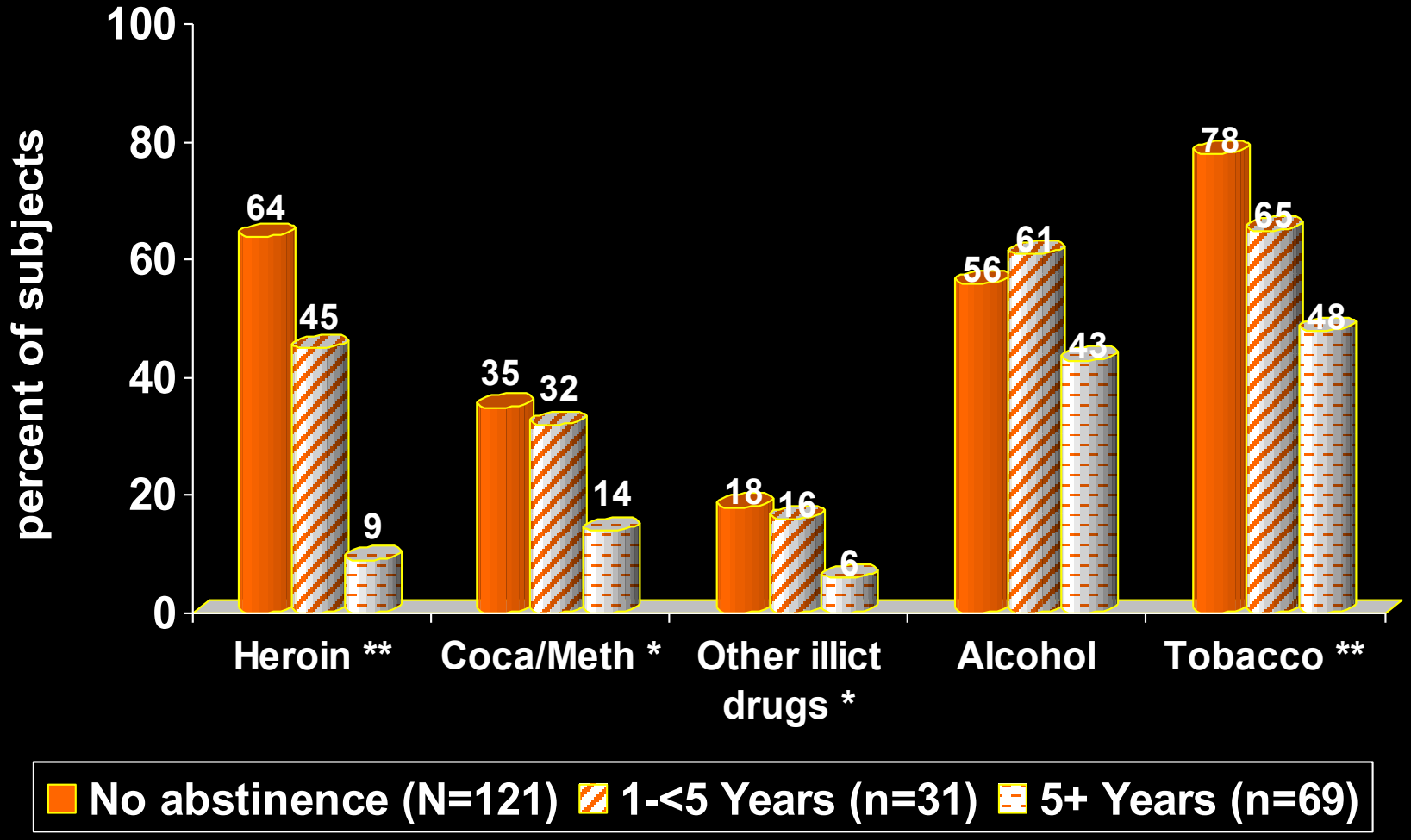
Is stable long-term recovery possible?

Longer Time in Abstinence Highly Associated with Abstinence in the Next Ten Years



Hser, Y. (2007). *Journal of Addictive Diseases, 26*(1), 51-60

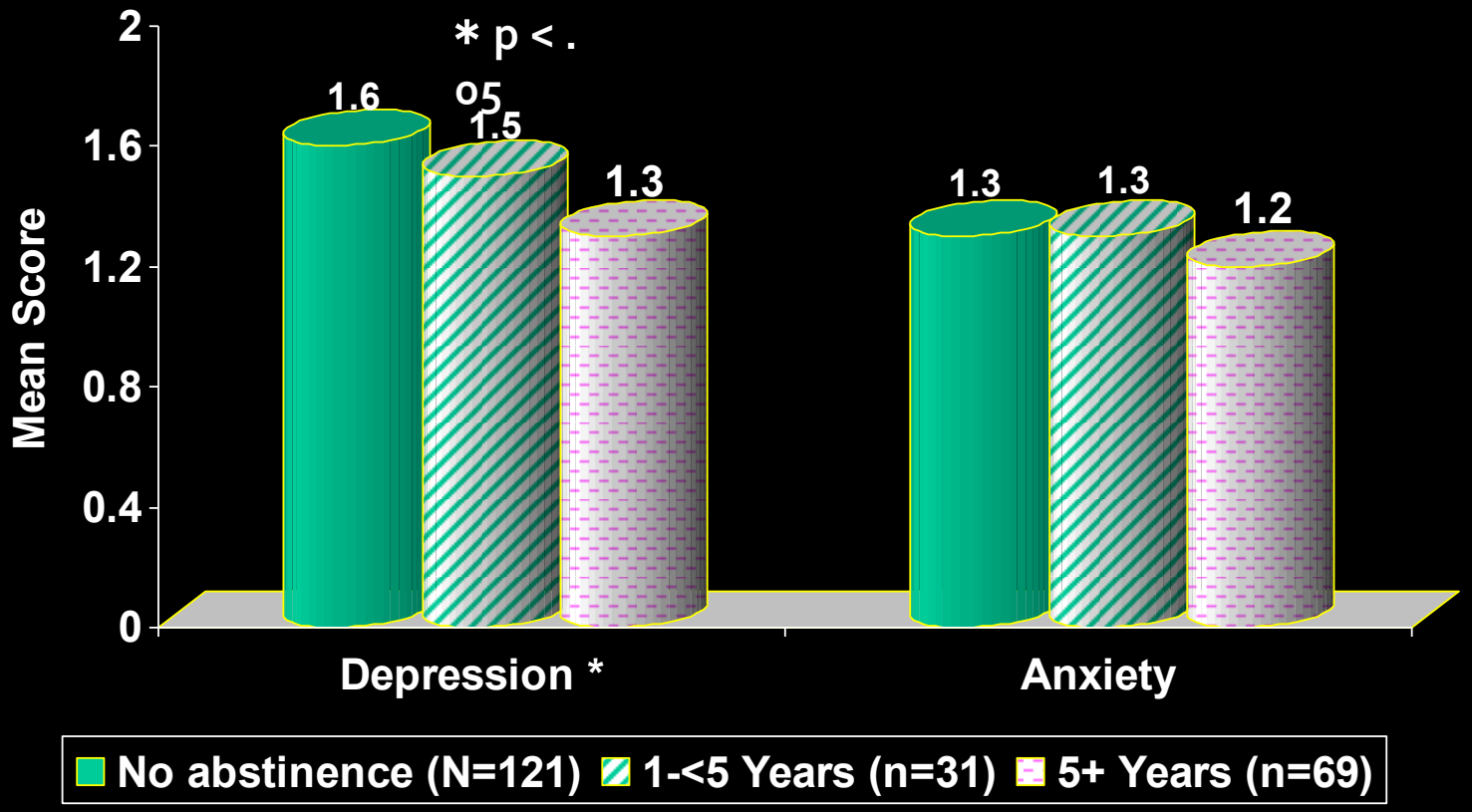
Alcohol, Tobacco and Illicit Drug Use at the 33-year Follow-up



* p<.05; **p < .01

Hser, Y. (2007). *Journal of Addictive Diseases, 26*(1), 51-60

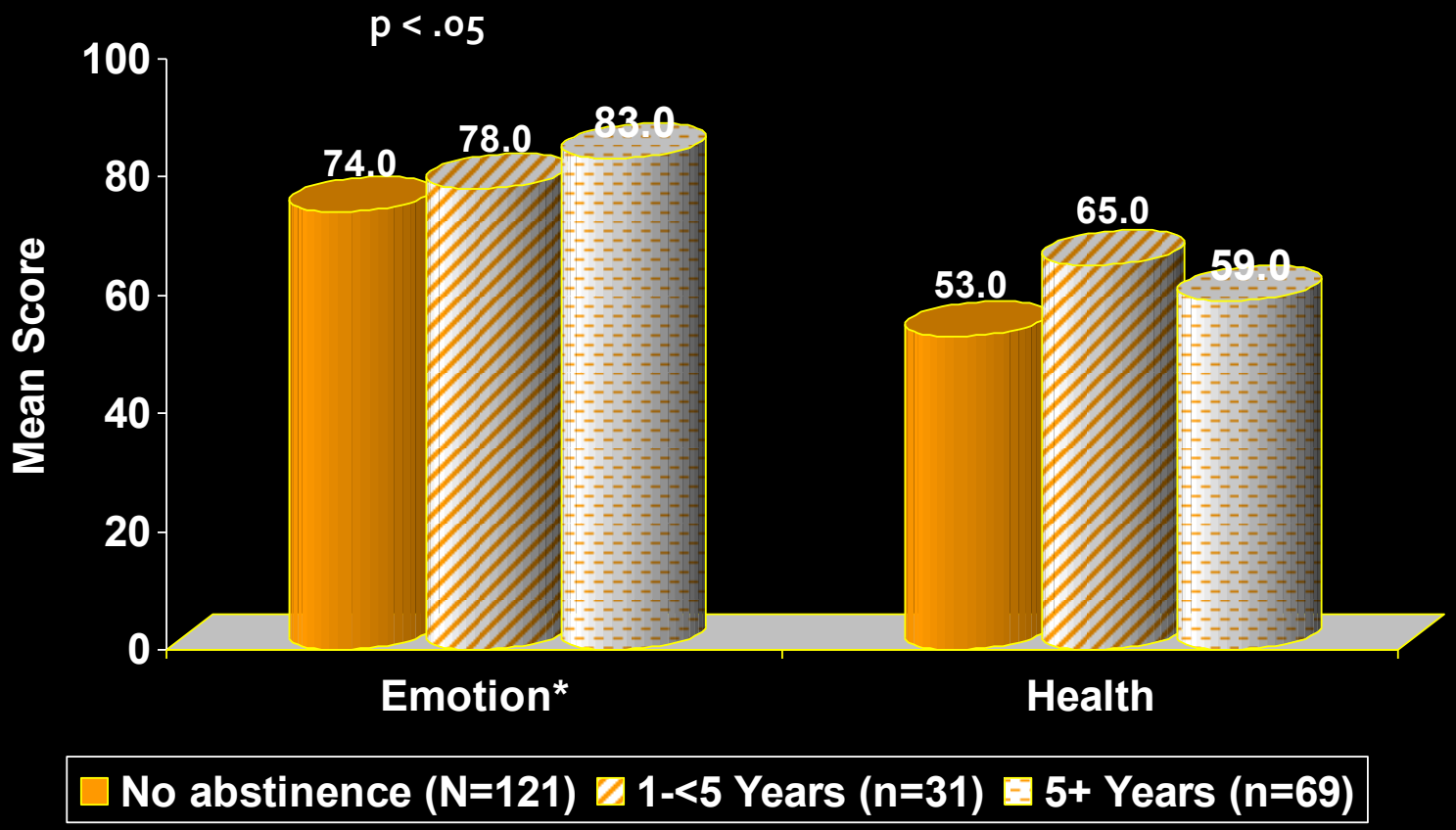
More than 5 Years of Abstinence: Predicting lower depression



SCL58 Scale (1- 4) at the 33-year follow-up: higher scores indicate greater symptom severity.

Hser, Y. (2007). *Journal of Addictive Diseases, 26*(1), 51-60

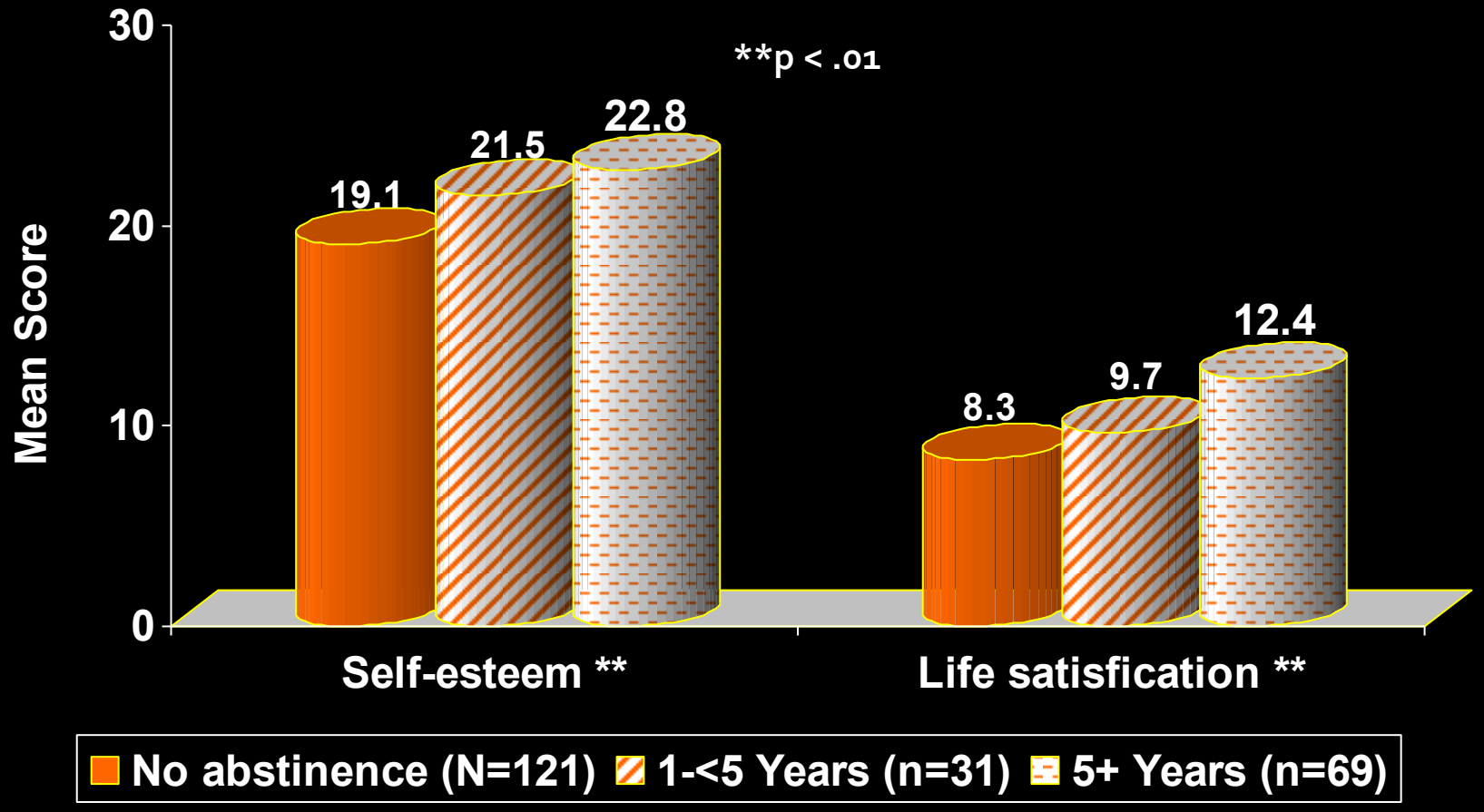
More than 5 Years of Abstinence: Predicting better emotional well-being



SF36 Scale (0-100) at the 33-year Follow-up: higher scores indicate better a status

Hser, Y. (2007). *Journal of Addictive Diseases, 26*(1), 51-60

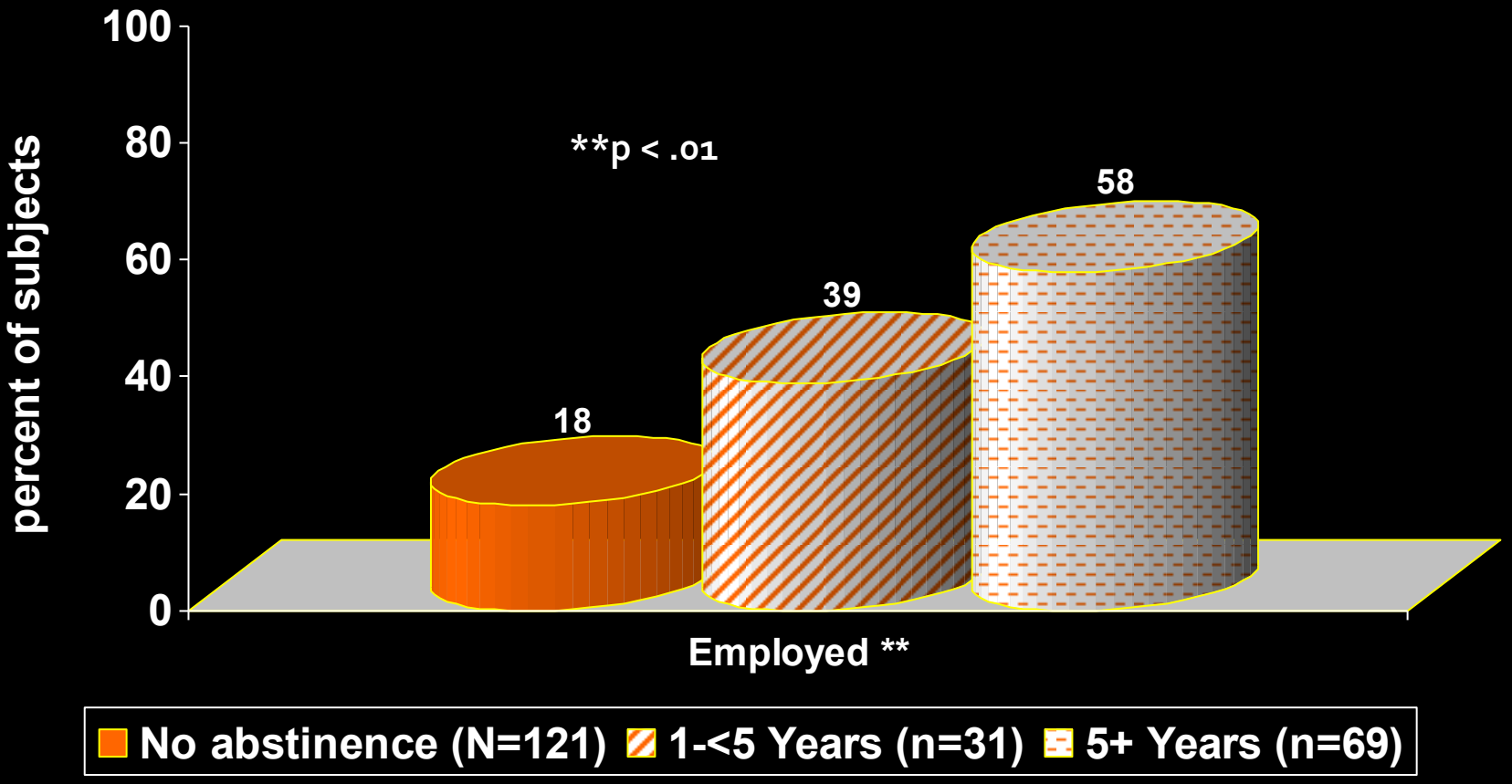
More than 5 Years of Abstinence: Higher self-esteem and life satisfaction



Self-Esteem (0-30) and Life Satisfaction (0-18) Scales at 33-year: Higher scores indicate better status

Hser, Y. (2007). *Journal of Addictive Diseases, 26*(1), 51-60

More than 5 Years of Abstinence: Employment at the 33-year Follow-up



Hser, Y. (2007). *Journal of Addictive Diseases, 26*(1), 51-60

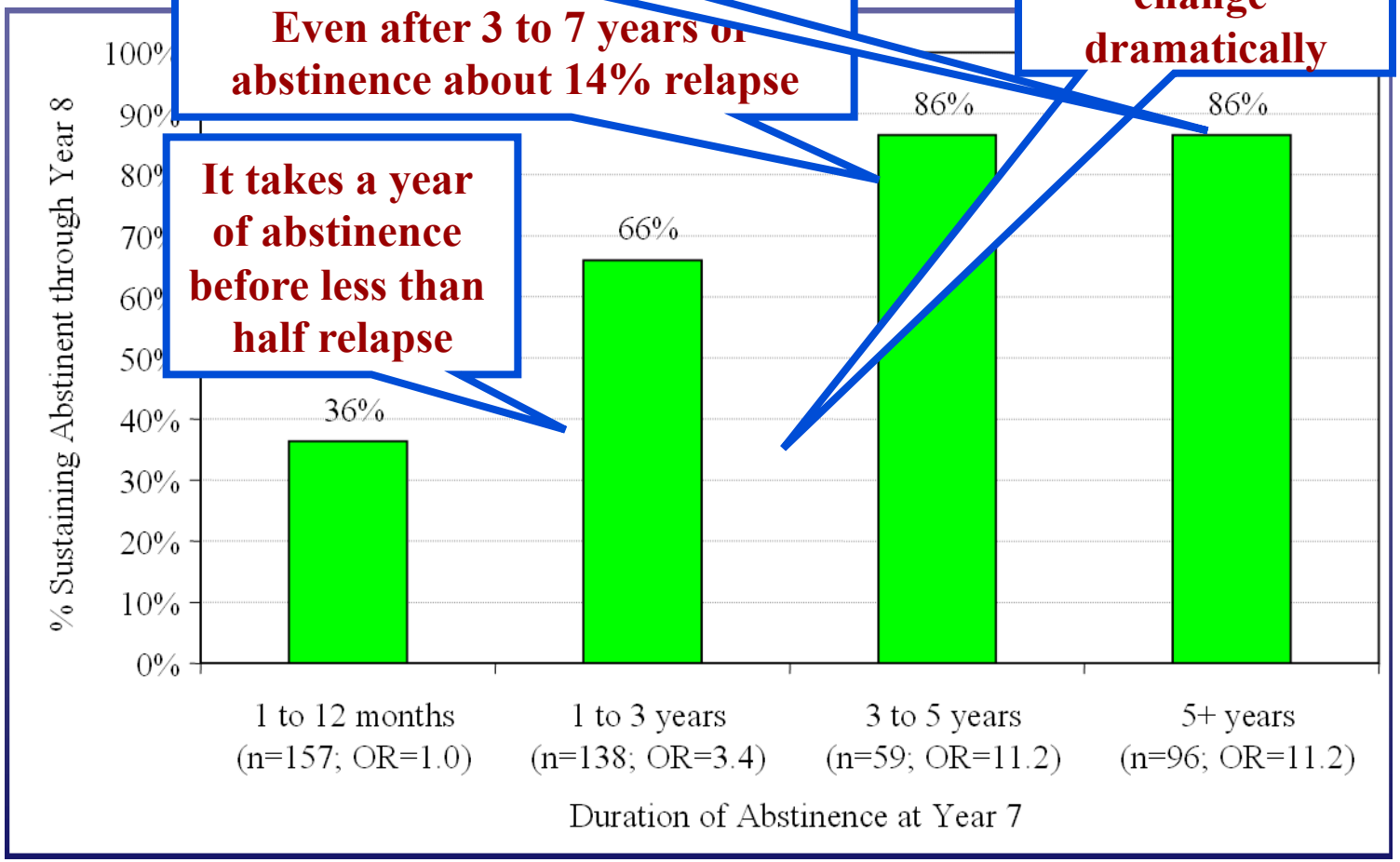
Longitudinal Trends in Recovery

After 5 years – if you are sober, you probably will stay that way.

Even after 3 to 7 years of abstinence about 14% relapse

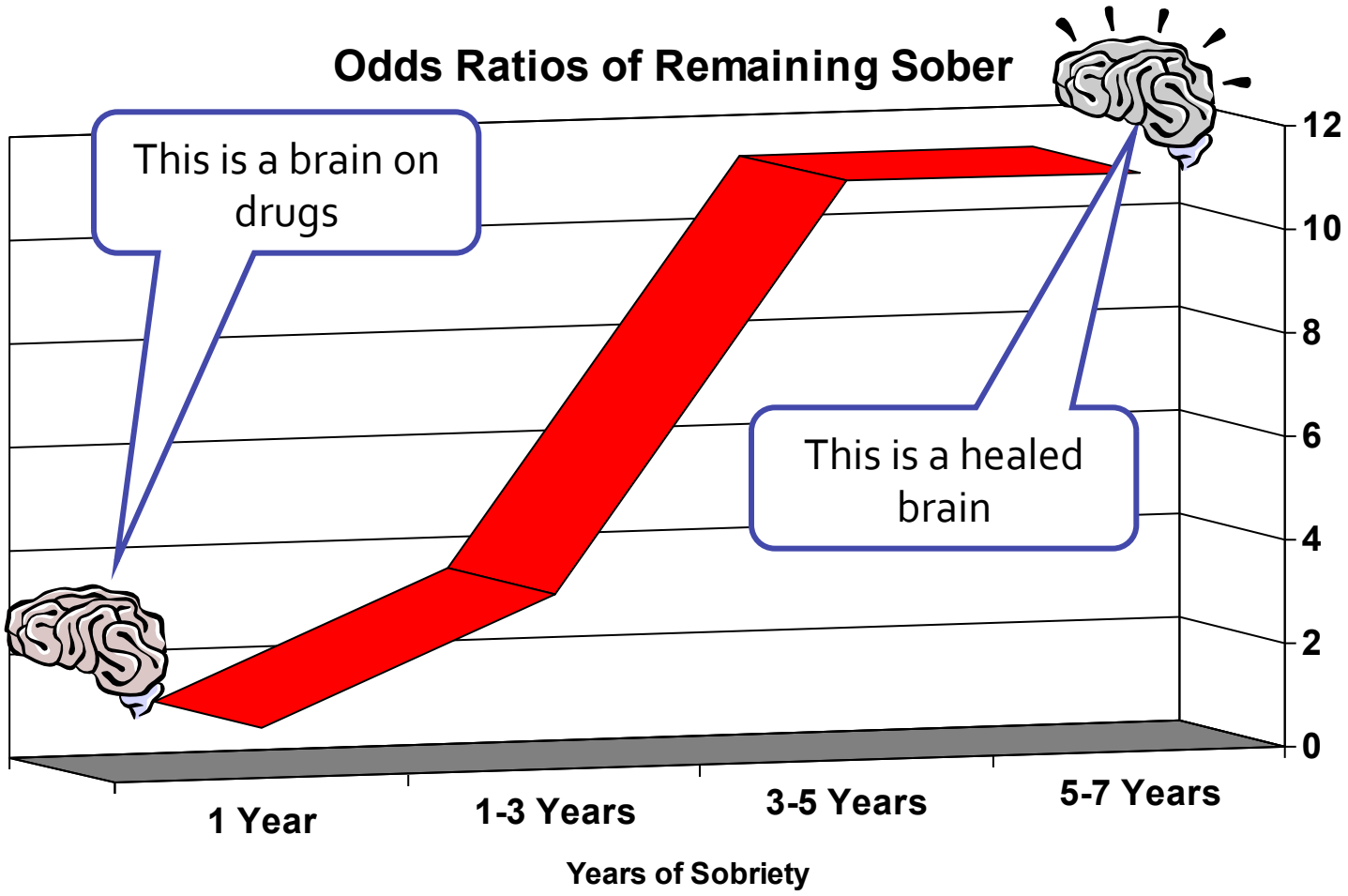
3+ years of abstinence the odds of relapse change dramatically

It takes a year of abstinence before less than half relapse



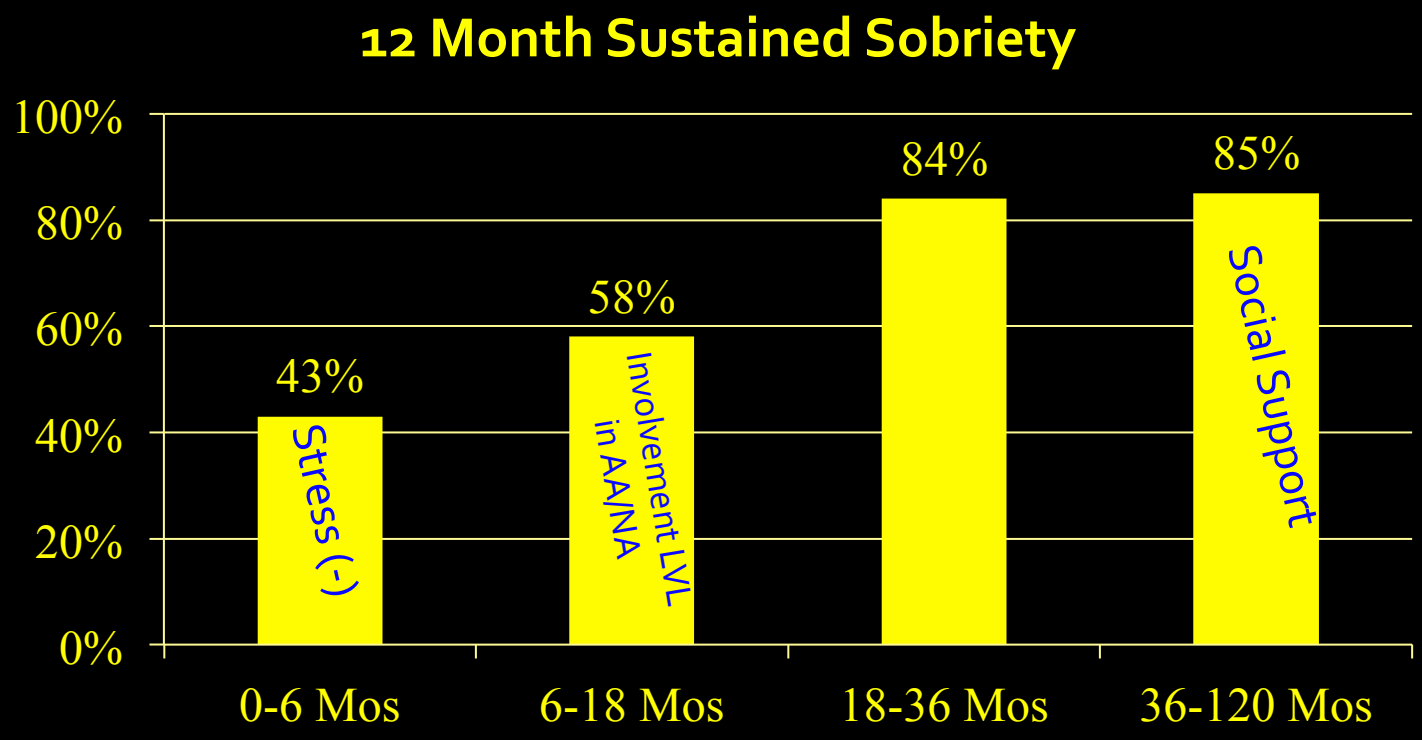
Source: Dennis, Foss & Scott (2007), *Eval. Rev.*

Protective Factors Accrue With Abstinence



Recovery Capital Differentially Predicts Sobriety at Different Stages

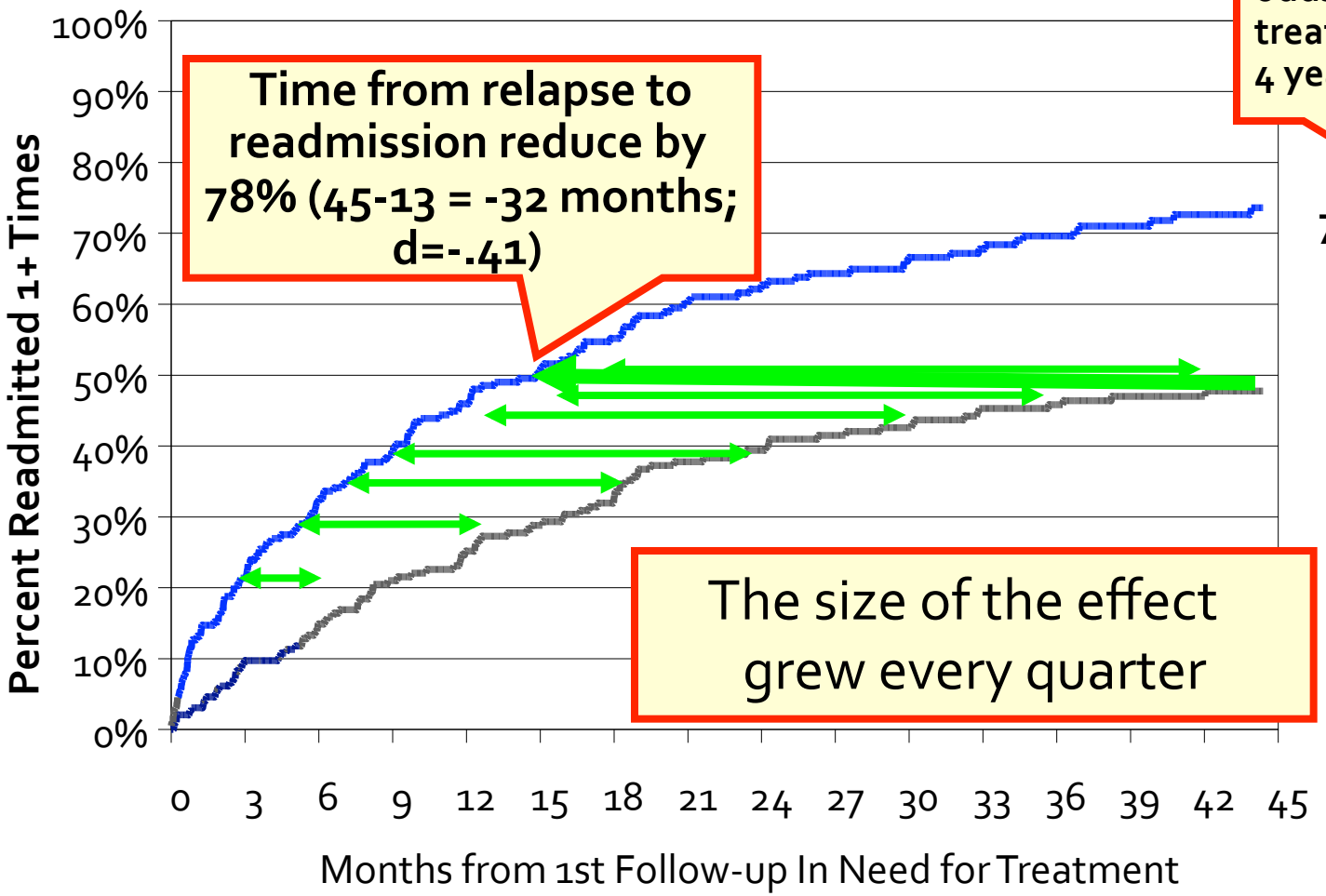
Study of 312 crack & heroin addicts sober at least 30 days at time of enrollment tracked over a 12-month period. Different RC factors predicted sobriety for 3 of 4 groups.*



Laudet, A.B., & White, W.L. (2008). Recovery capital as prospective predictor of sustained recovery, life satisfaction, and stress among former poly-substance users. *Substance Use & Misuse,* 43:27-54.

* Logit Classification 71% of total sample, X^2 40.97 p<.001

ERI-2 Time to Treatment Re-Entry at Year 4



Time from relapse to readmission reduce by 78% (45-13 = -32 months; d=-.41)

RMC increases the odds of re-entering treatment over 4 years by 3.1

74% ERI-2 RMC* (n=198)

48% ERI-2 OM (n=195)

The size of the effect grew every quarter

Wilcoxon-Gehen statistic (df=1) = 28.60, p<.001

OR=3.1, p<.05

RMC associated with: **More abstinence, fewer subsequent drug problems**

Source: Dennis & Scott *Drug and Alcohol Dependence* 2012;121:10-17

THE FIVE-YEAR RECOVERY STANDARD FOR MEDICATION-ASSISTED TREATMENT

Robert L. DuPont, MD, President
Institute for Behavior and Health, Inc.
www.ibhinc.org

WELL-KNOWN OBSTACLES TO ALL ADDICTION TREATMENT

- Most people with substance use disorders (SUDs) do not think that they have a disorder and they do not want treatment
- Most patients referred to treatment do not enter treatment
- Many patients who enter treatment drop out before completion
- Relapse after treatment is the usual outcome of treatment

TODAY'S TREATMENT PARADIGM

- Addiction is a lifelong, potentially life-threatening disorder, while treatment is typically stand-alone, short-term episodes of care
- Even medication-assisted treatment (MAT) which is considered *for life*, faces reality that virtually all patients leave treatment: About half of buprenorphine patients leave in 3-6 months and about half of methadone patients leave in 6-9 months
- Almost all patients leaving MAT relapse to opioid use
- Many patients continue to use alcohol and other drugs while in treatment

3 MISSING ELEMENTS FOR A NEW STANDARD OF FIVE-YEAR RECOVERY

1. Definition of long-term recovery as the goal of all treatment and post-treatment interventions

2. Provision of sustained post-treatment monitoring plus professional and peer support

3. Insistence by others around the patients on sustained abstinence is crucial

WHAT IS MEANT BY RECOVERY?

- Recovery defined as a voluntarily maintained lifestyle characterized by sobriety, personal health, and citizenship

  - 2007 Betty Ford Institute Consensus Panel

- The use of medications as prescribed is absolutely consistent with recovery

Recovery Resources Influence Sobriety – *PHP Gold Standard of Care*

- Survey physician health programs (PHP) for SUD in 49 states*
- Study of PHP outcomes for 904 MDs in 16 state programs**
  - Addiction education
  - Careful screening & needs-based Tx referrals
  - 90-day inpatient followed by intensive abstinence-oriented day Tx
  - Mandatory AA/NA/Oth mutual aid support groups
  - Testing & workplace surveillance over 5-yr period
- 3 levels of relapse
  1. Missing therapy or deception – increase Tx intensity, alert coworkers and family, & increase testing
  2. Use of drugs or alcohol outside medical practice – halt practice, reevaluate, Tx
  3. Use of drugs/alcohol in practice context - halt practice, reevaluate, Tx, repeat lose license
- Results for both studies showed 71% still sober & licensed after 5 years

+Dupont, R.L., McLellan, A.T., Carr, G. Gendel, M., & Skipper, G.E. (2009). How are addicted physicans treated? A national survey of physician health programs. *JSAT,* 37, 1-7.
**Dupont, R.L., McLellan, A.T., White, W.L., Merlo, L.J., & Gold, G.S. (2009). Setting the standard for recovery: Physicians' Health Programs. *JSAT*, 36, 159-171.

THE PHYSICIAN HEALTH PROGRAM (PHP) EXPERIENCE WITH OPIOID DEPENDENCE

DRUG TEST RESULTS

- Physicians with opioid use disorders had the same low rate of positive drug tests as their peers with alcohol use disorders or other non-opioid use disorders

Any Positive Test	Alcohol Only (n=204)	Any Opioids (n=339)	Non-Opioids (n=159)
Yes	40 (20%)	77 (23%)	39 (25%)
No	162 (80%)	259 (77%)	118 (75%)

FOLLOW-UP STATUS

- Physicians with opioid use disorders were as successful completing their monitoring contract and returning to work in medicine as their peers

Status at Follow-Up	Alcohol Only (n=204)	Any Opioids (n=339)	Non-Opioids (n=159)
Completer	119 (58.3%)	220 (64.9%)	101 (63.5%)
Extender	34 (16.7%)	57 (16.8%)	30 (18.9%)
Failed to complete	51 (25.0%)	62 (18.3%)	28 (17.6%)

TAKE-AWAY FINDINGS

- Regardless of the substance(s) physicians previously used, more than three-quarters of PHP participants remained abstinent throughout their monitoring period and beyond

- Physicians with opioid use disorders were able to remain abstinent from alcohol and all other drugs, without buprenorphine or methadone*

*1 physician was treated with methadone for chronic pain

NOW IS THE TIME FOR A NEW STANDARD

- ACA & Parity will lead to shifts in SUD treatment from acute, limited programmatic care to personalized sustained care of chronic illness
- More benefits for SUD treatment
- Adoption of chronic care model through proactive team treatment, multiple interventions and regular monitoring will lead to:
  - Long-term accountability for health care system
  - Stable, long-term recovery for patients

THE CHALLENGE FOR ADDICTION TREATMENT

- Find ways to extend the PHP model for the treatment of opioid use disorders, with and without the use of medications
- The Hazelden-Betty Ford Foundation is leading the abstinence treatment field by integrating medications into the treatment of patients with opioid use disorders
- Integrate elements of the model into routine health care, as is increasingly done for all serious chronic disorders with focus on prevention, intervention, treatment and lifetime monitoring to prevent and detect relapses

ADDRESSING THE ISSUE OF LEVERAGE

- Five-year recovery is possible with strong support of people who care about those with SUDs
- Families are at the top of the list of who can provide the necessary leverage
- There are roles for health care, the criminal justice system and employers
- While nearly all physicians initially object to PHP care management, when they are in recovery they recognize that the PHPs saved their lives

REFERENCES + RESOURCES

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Research Targets for Recovery

(Betty Ford Institute Consensus Research Conference on Extending the Continuum of Care)

- **Optimal ways to monitor recov y progress**
- **Ways to int grate co uit are wi h Tx for seamless re y s**
- **Way**
- **Ways to e.g., fri**
- **Staffing ve KSAS**
- **Plan ns cessful patients**

All of this change requires reengineering how we delivery treatment and recovery support services.

McKay. J.R., Carise, D., Dennis, M.L., DuPont, R., Humphreys, K., Kemp, J., Reynolds, D., While, W., Armstrong, R., Chalk, M.., Haberle, B., McLellan, T., O'Connor, G., Pakull, B., Schwartzlose, J. (2009). Exttending the benefits of addiction treatment: Practical strategies for continuing care and recovery. *JSAT, 36(2) 127-130.*

Three Distinctions Among Collaborative Models[1]

- **Coordinated: Routine screening for behavioral health problems in primary care settings, but delivery of services may occur in different settings.**

- **Co-located: Medical services and behavioral health services located in the same facility.**

- **Integrated: Medical services and behavioral health services located either in the same facility or in separate locations.**

[1] Collins, C. Hewson, D., L., Munger, R., & Wade, T. (2010). Evolving Models of Behavioral Health Integration in Primary Care. Milbank Memorial Fund .

Summary

- Neuroscience suggests that established memories and other CNS differences require a long-term perspective
- Five year duration appears to be a good benchmark regarding further abstinence, criminal behavior and overall functioning
- Treatment systems need to address these long-term needs

***Science* =**

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Science = Solutions

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