Introduction to Medication-Assisted Treatment

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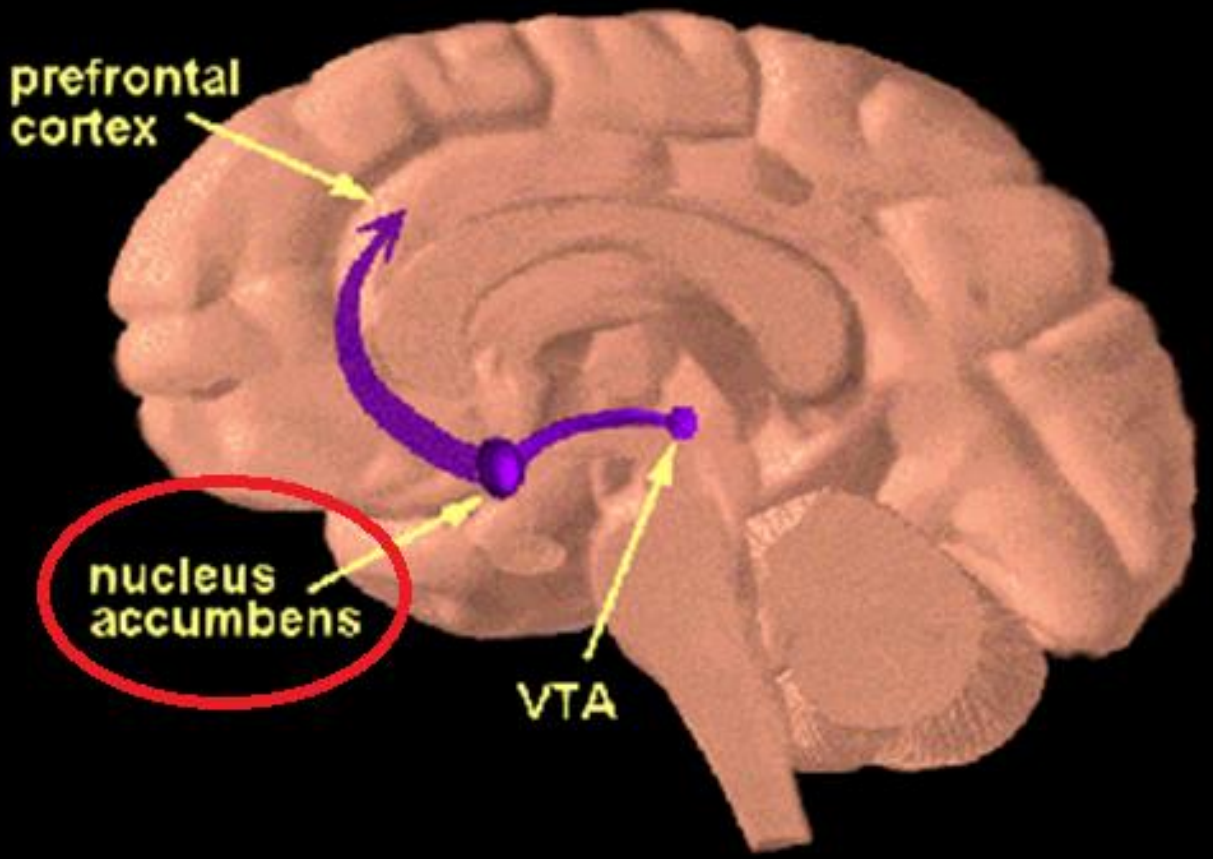
Director, Northern NJ Center of Excellence in MAT

Reward Pathway

- Neurons start in the midbrain → release dopamine in the nucleus accumbens
- Baseline: steady dopamine
- Drugs: burst of dopamine (pleasure/salience/motivation)
- Responsible for “hedonic tone”

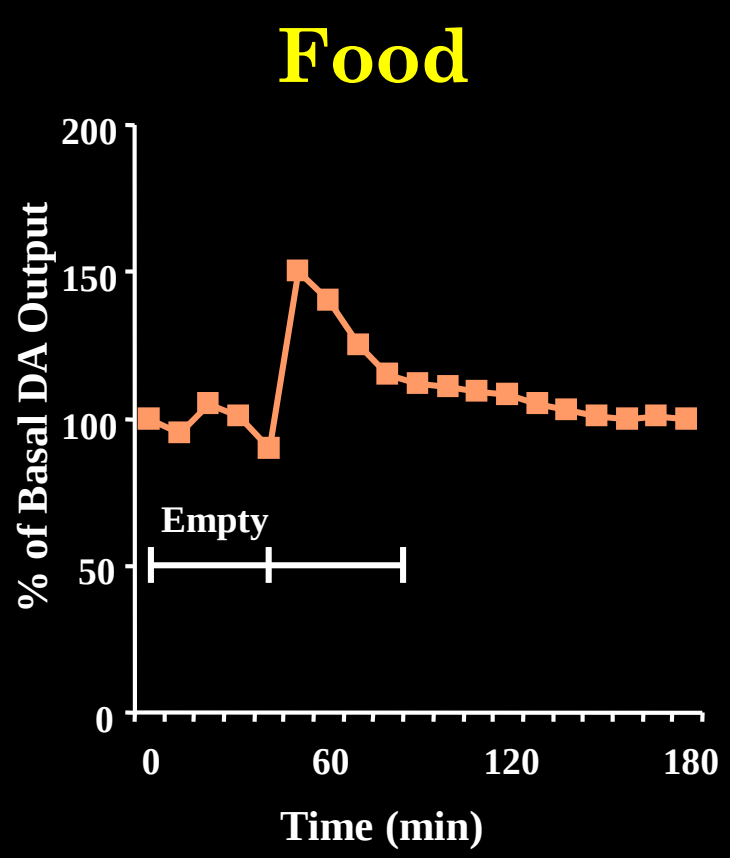


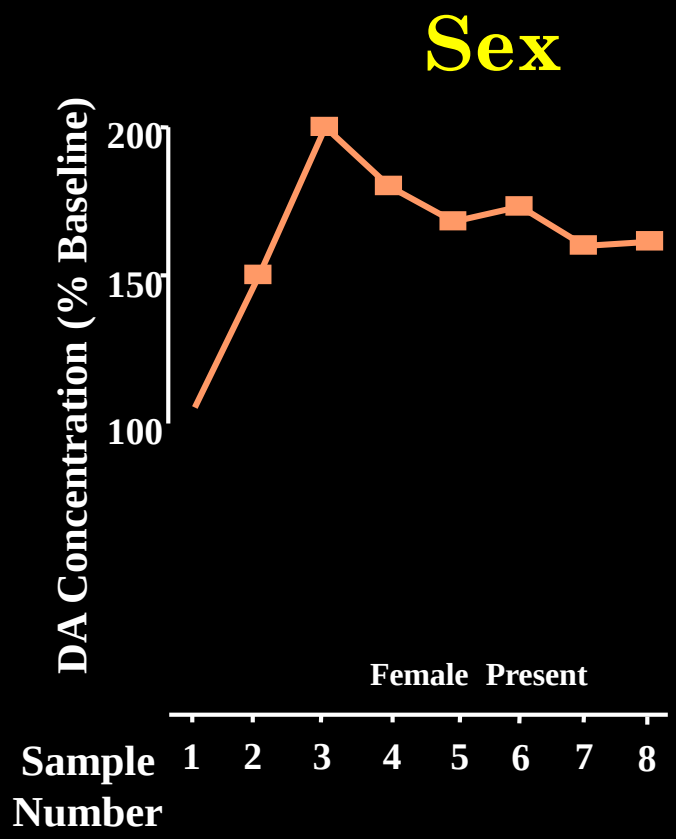
What is Hedonic Tone?

- Sense of well-being, happiness, pleasure, contentment
- "Set" in the reward pathway
- Range: Euphoria ←→ Dysphoria
- Altered by psychoactive activities/substances
- Reward Deficiency Syndrome?
  - Kenneth Blum: DRD2 allele → lower D2

Slide courtesy of Dr. Ed Salsitz

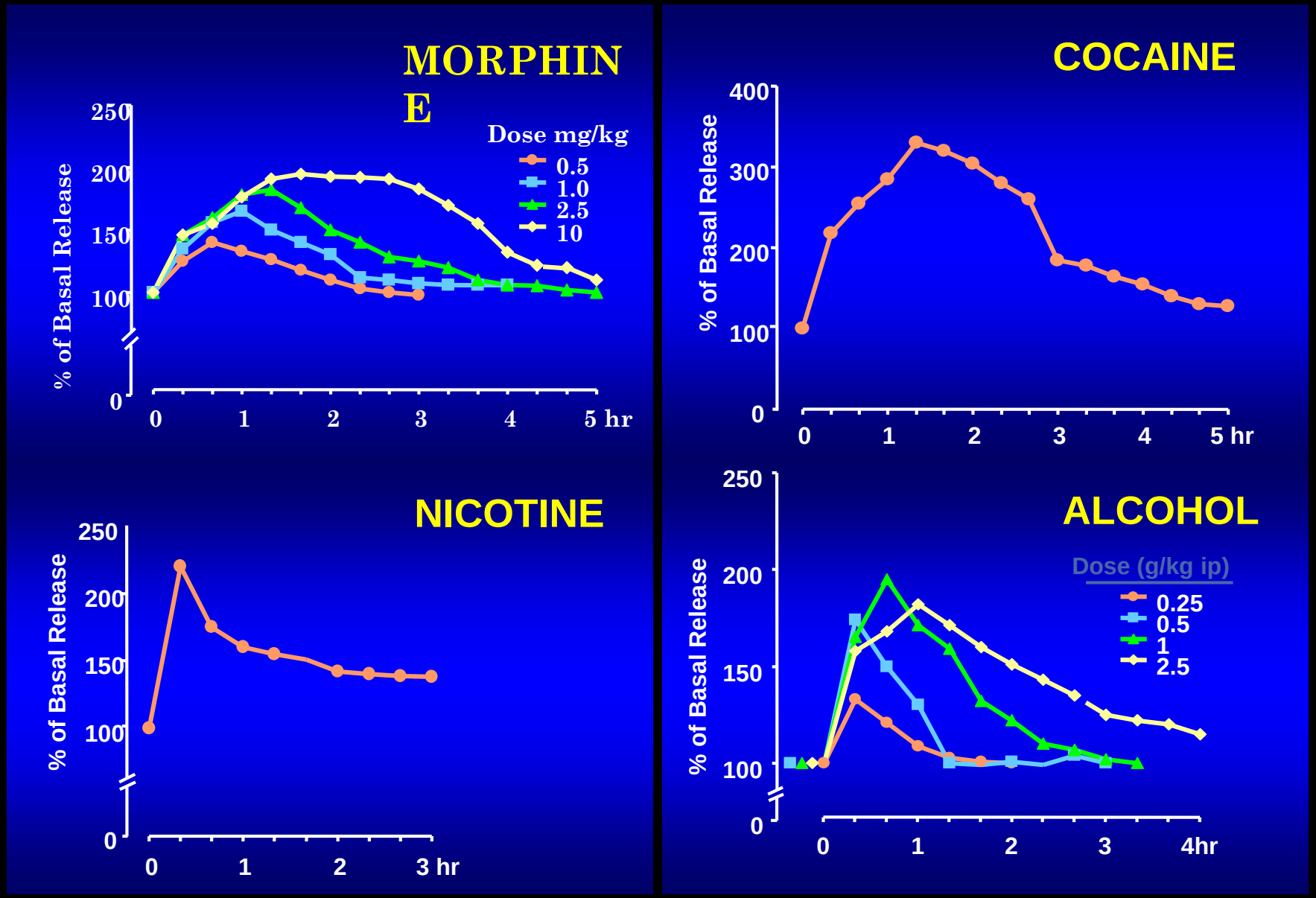
Natural Rewards and Dopamine Levels





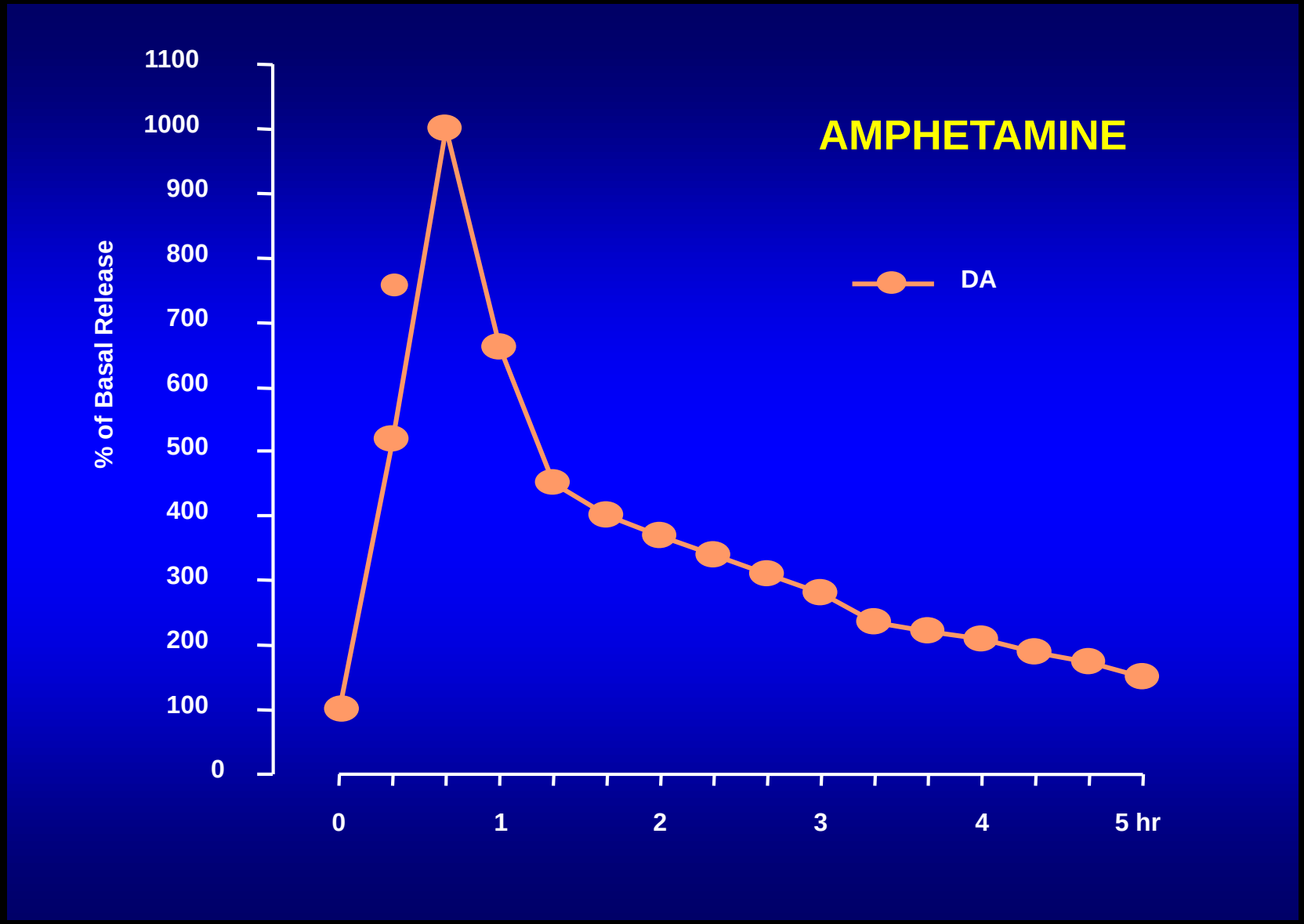
Adapted from: Di Chiara et al, *Neuroscience*, 1999
Adapted from: Fiorino and Phillips, *J Neuroscience*, 1997

Effects of Drugs on Dopamine Levels



Adapted from: Di Chiara and Imperato, *Proceedings of the National Academy of Sciences USA*, 1988; courtesy of Nora D Volkow, MD

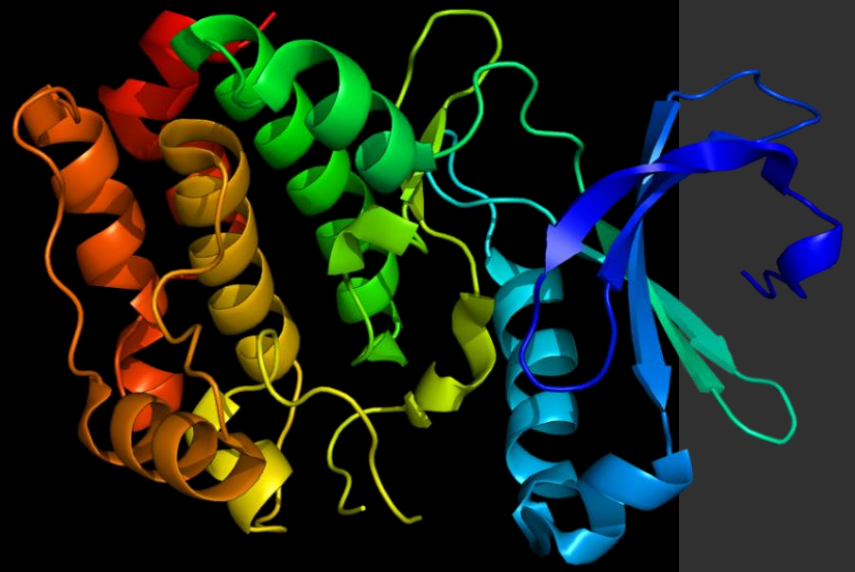
Effects of Drugs on Dopamine Levels



Adapted from: Di Chiara and Imperato, *Proceedings of the National Academy of Sciences USA*, 1988; courtesy of Nora D Volkow, MD

Acute drug effects

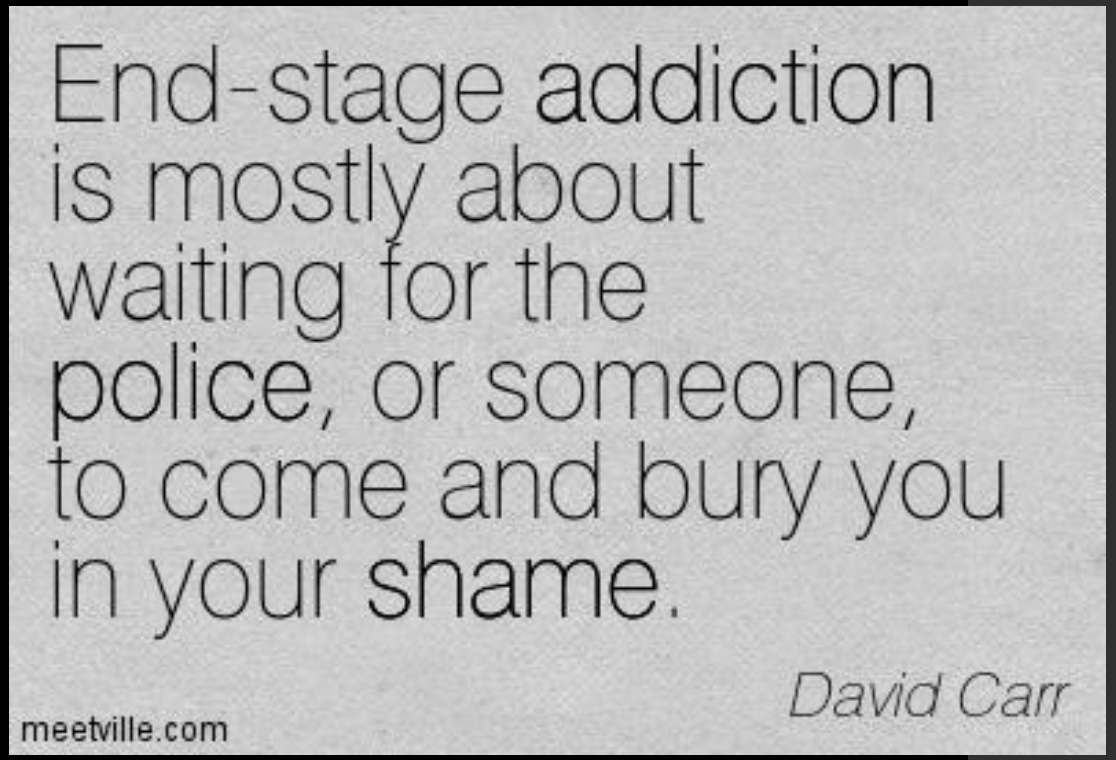
- Extra dopamine release → changes in cell signaling
  - *D1 DA receptor stimulation →*
    cAMP-dependent protein kinase (PKA) →
    phosphorylation of CREB →
    immediate early gene products such as cFos →
    short-term neuroplastic changes for a <u>few hrs/days</u>



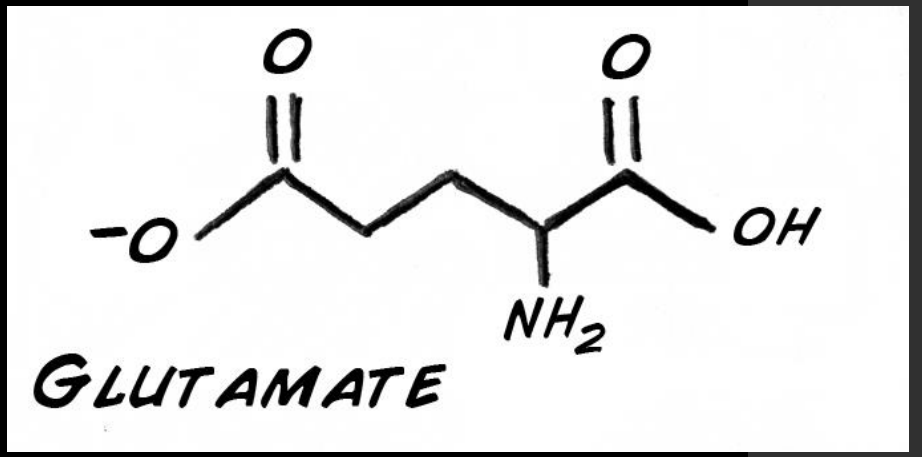
… but none of this explains long-lasting behavioral changes

How to explain end-stage addiction?

- Overwhelming desire to obtain drug
- Diminished ability to control drug seeking
- Reduced pleasure from biological rewards

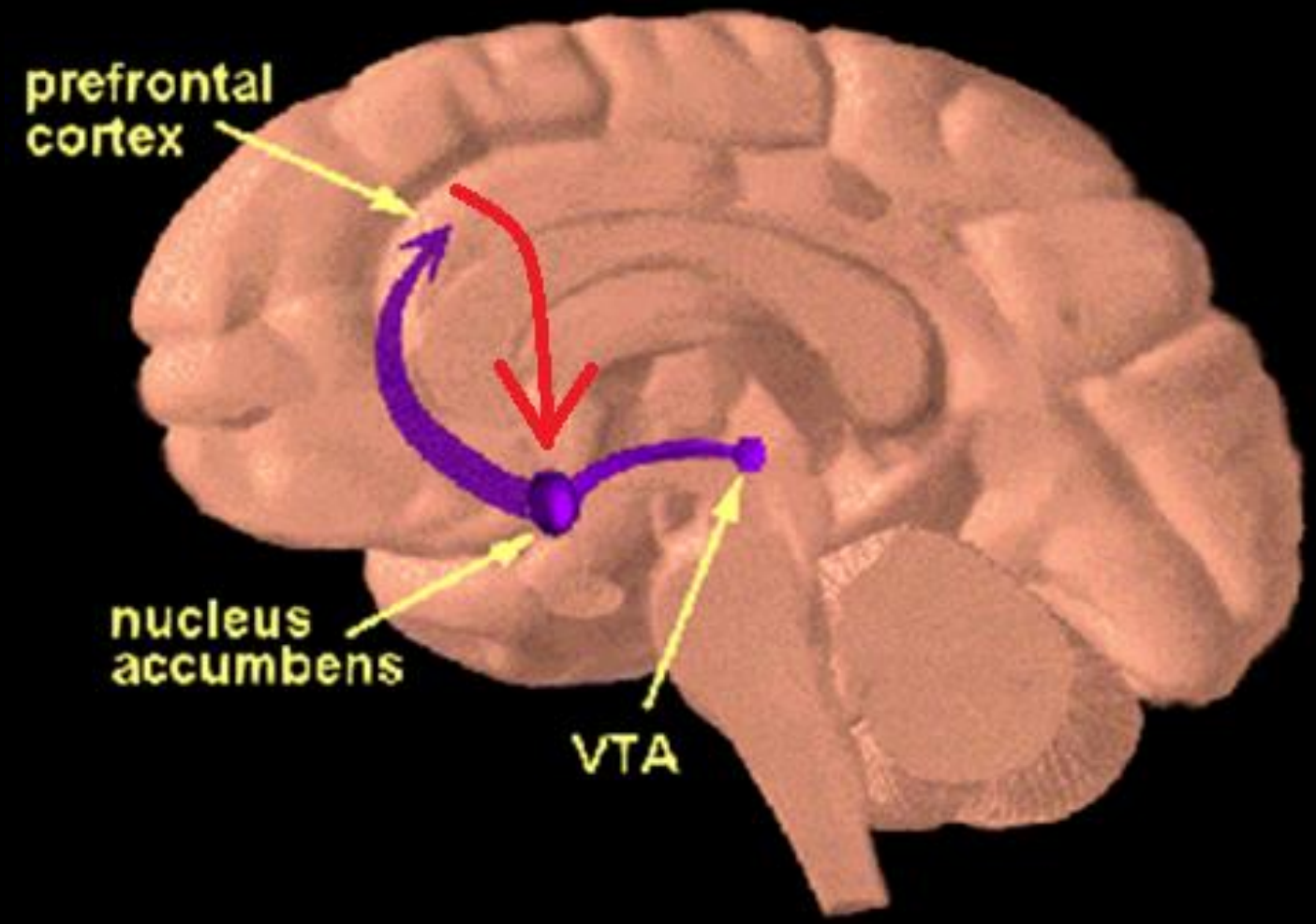


Transition to addiction



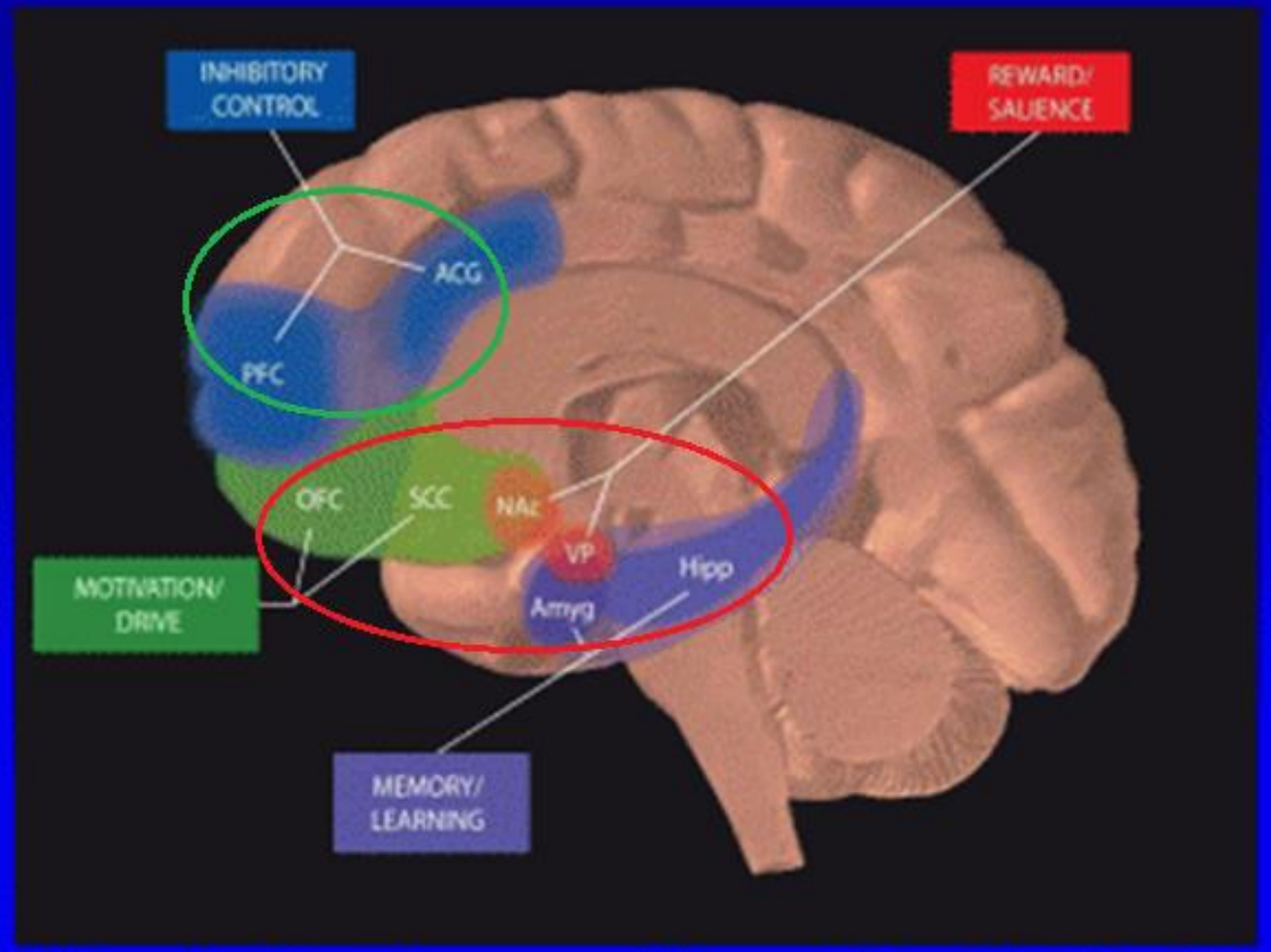
- Repeated use → brain changes that last for days-weeks
  - *Long-acting proteins involved*
    - Δ *FosB = transcriptional regulator,*
      increases AMPA glutamate receptor subunits

Create new circuits based on glutamate, not dopamine



New circuits created from prefrontal cortex (glutamate)

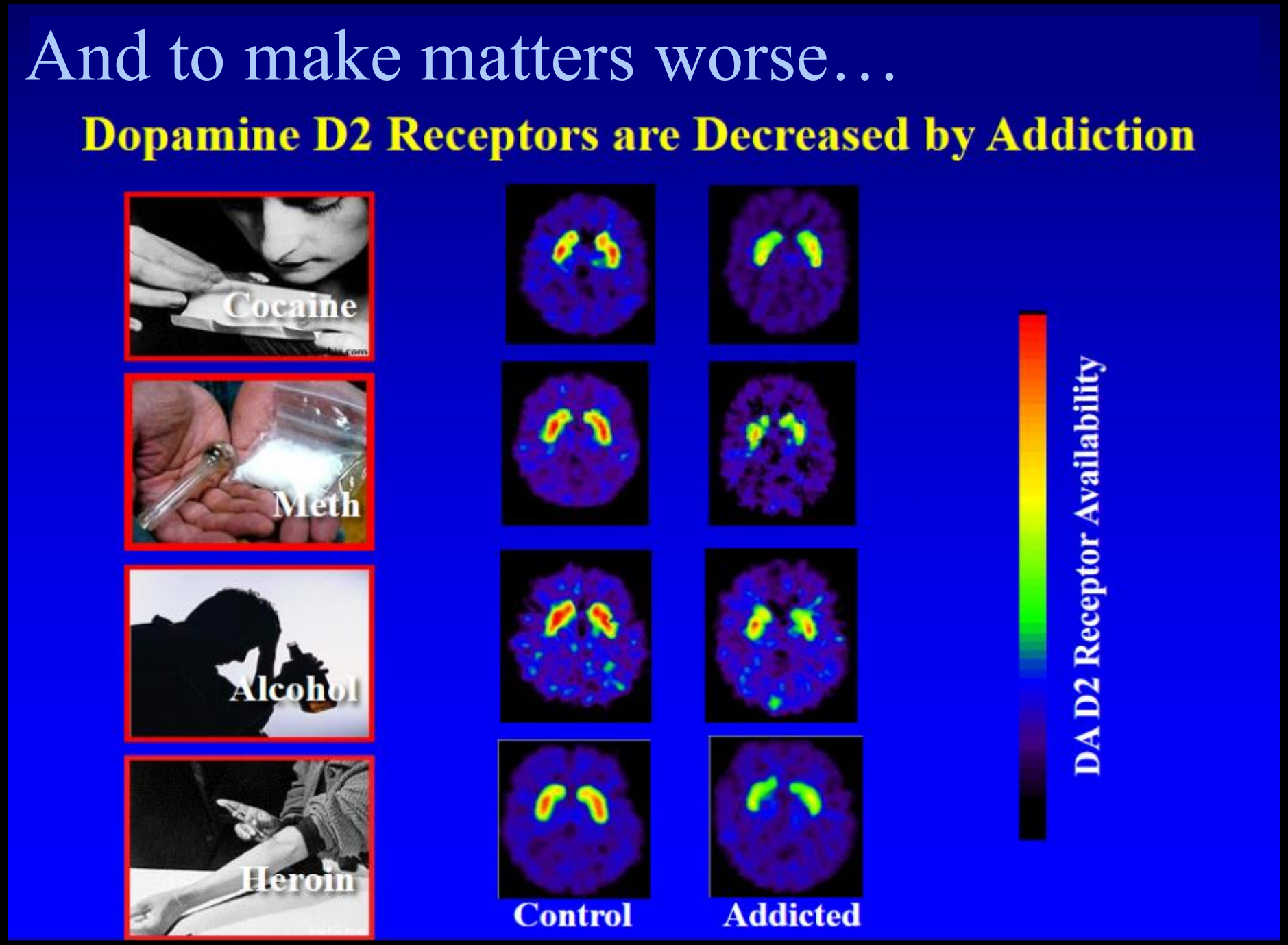
Circuits Involved In Drug Abuse and Addiction



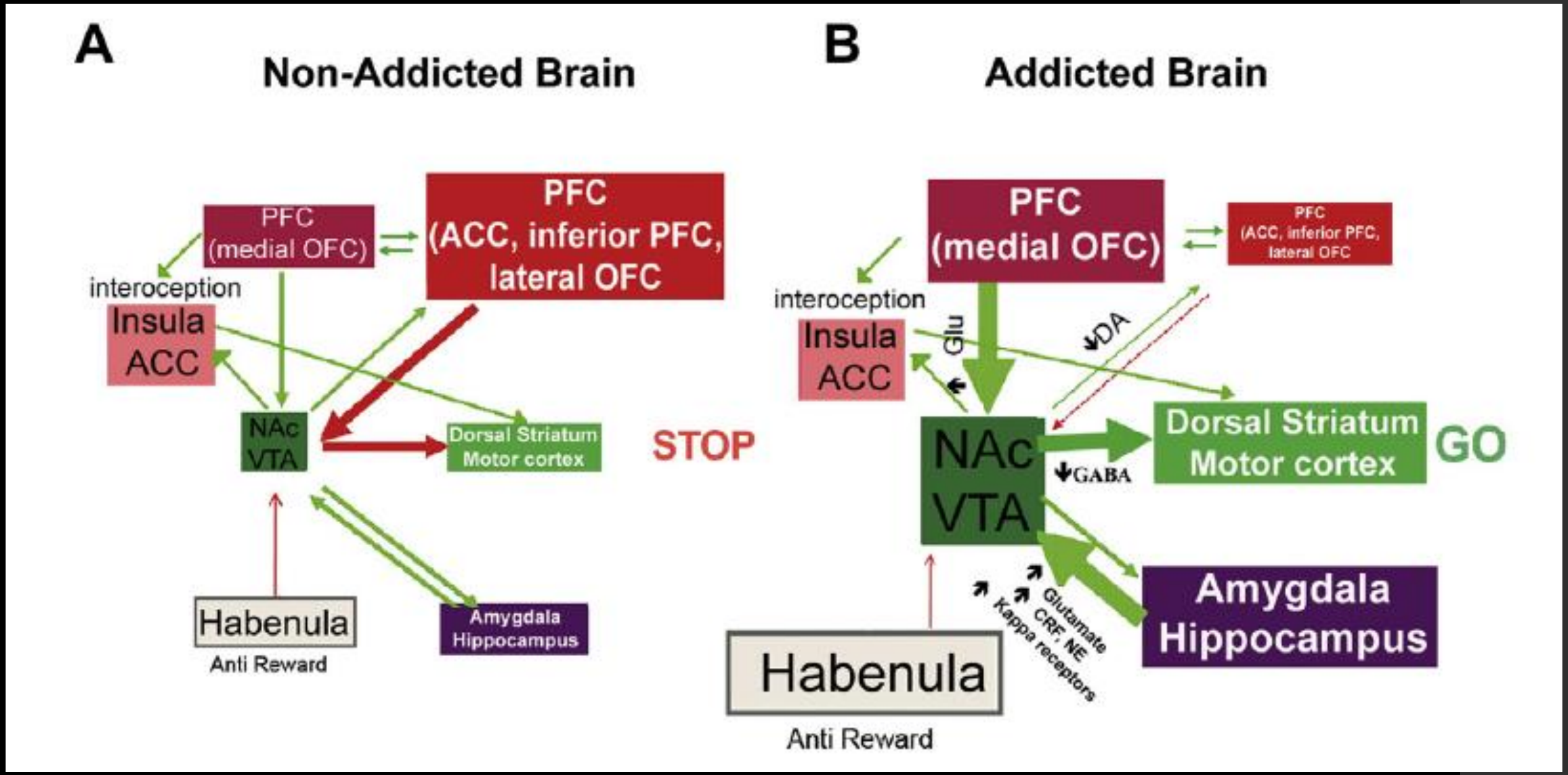
All of these brain regions must be considered in developing strategies to effectively treat addiction

NIDA

And to make matters worse…



NIDA



Volkow ND, Baler RD. Addiction science: Uncovering neurobiological complexity. *Neuropharmacology* 2014;76:235-49.

Blue =
mature state

Time

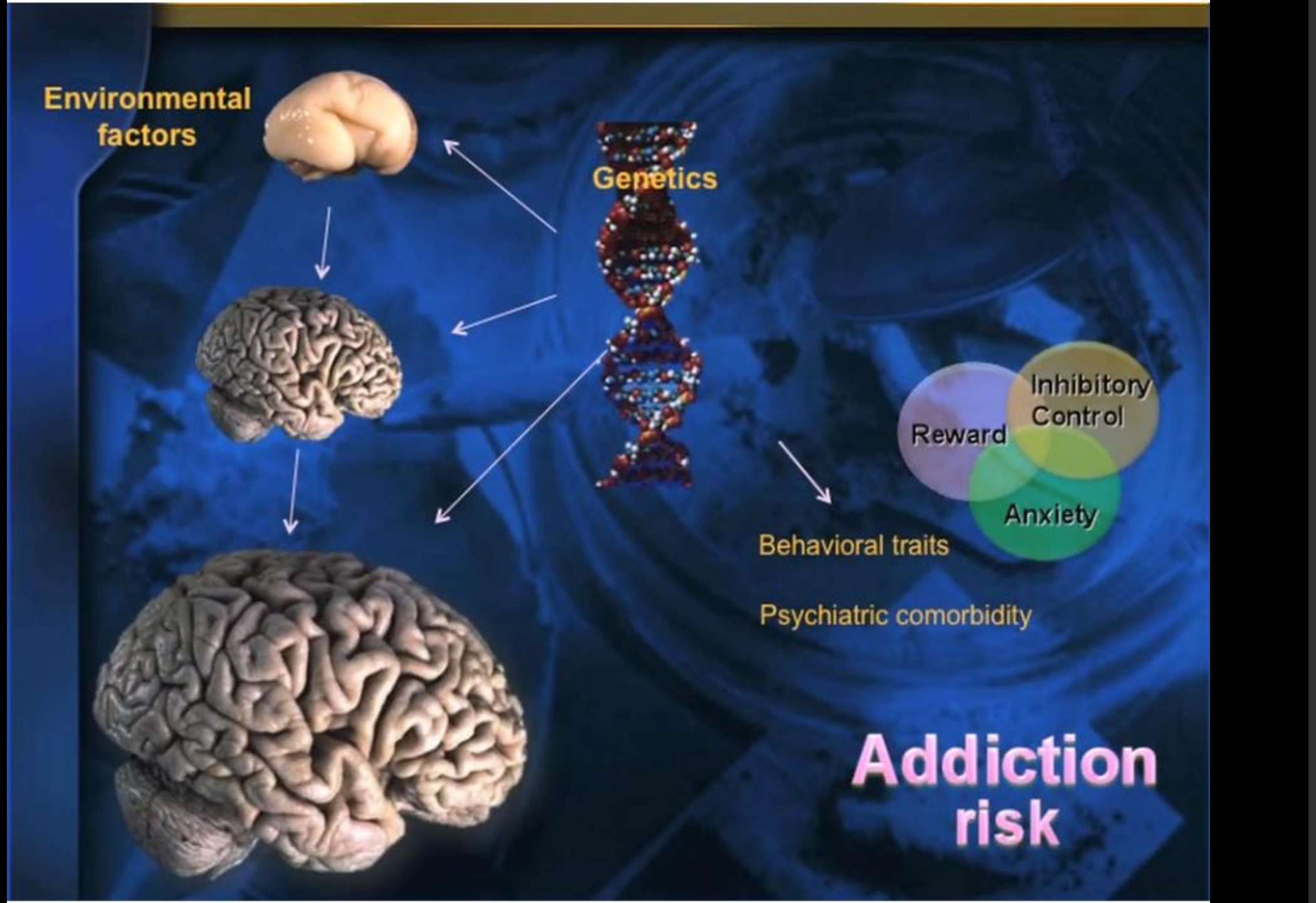
5

1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0

Gray Matter

Copyright

Acad. Sci., 2004


Environmental factors
Genetics
Inhibitory Control
Reward
Anxiety
Behavioral traits
Psychiatric comorbidity
Addiction risk

What environmental factors make us vulnerable to addiction?

dopamine D2 receptor — the DRD2 gene). Concomitantly, environmental factors such as stress (high stress combined with polymorphisms in dopaminergic genes, as well as other neurotransmitter genetic variants), and social defeat also alter brain-reward mechanisms in such a manner as to impart vulnerability to addiction [7]. Thus, elevated stress levels,

stress & social defeat
(interacting with our genes)

Blum K, Gardner E, Oscar-Berman M, et al. "Liking" and "Wanting" Linked to Reward Deficiency Syndrome (RSD). *Curr Pharm Des* 2012.

Transformative Spiritual Experience

“We’ve been doing this for over 40 years since Nixon… The drugs are more available, purer quality, and cheaper than they’ve ever been before… and we’ve destroyed more lives than drugs have by incarcerating people, hanging felony convictions on them, denying them education, denying them jobs… And we don’t even have one drug-free prison in America.”

- Retired police captain Peter Christ

LAW ENFORCEMENT ACTION PARTNERSHIP
ADVANCING JUSTICE AND PUBLIC SAFETY SOLUTIONS

InSite in Vancouver: An overdose prevention center (i.e., a safe injection site)

BEFORE DCR

Make money.
Buy street heroin.
Hide from the police.
Find or share needle.
Use puddle water.
Rush to inject while keeping a look out.
Throw drug paraphernalia on the ground.
Repeat.

AFTER DCR

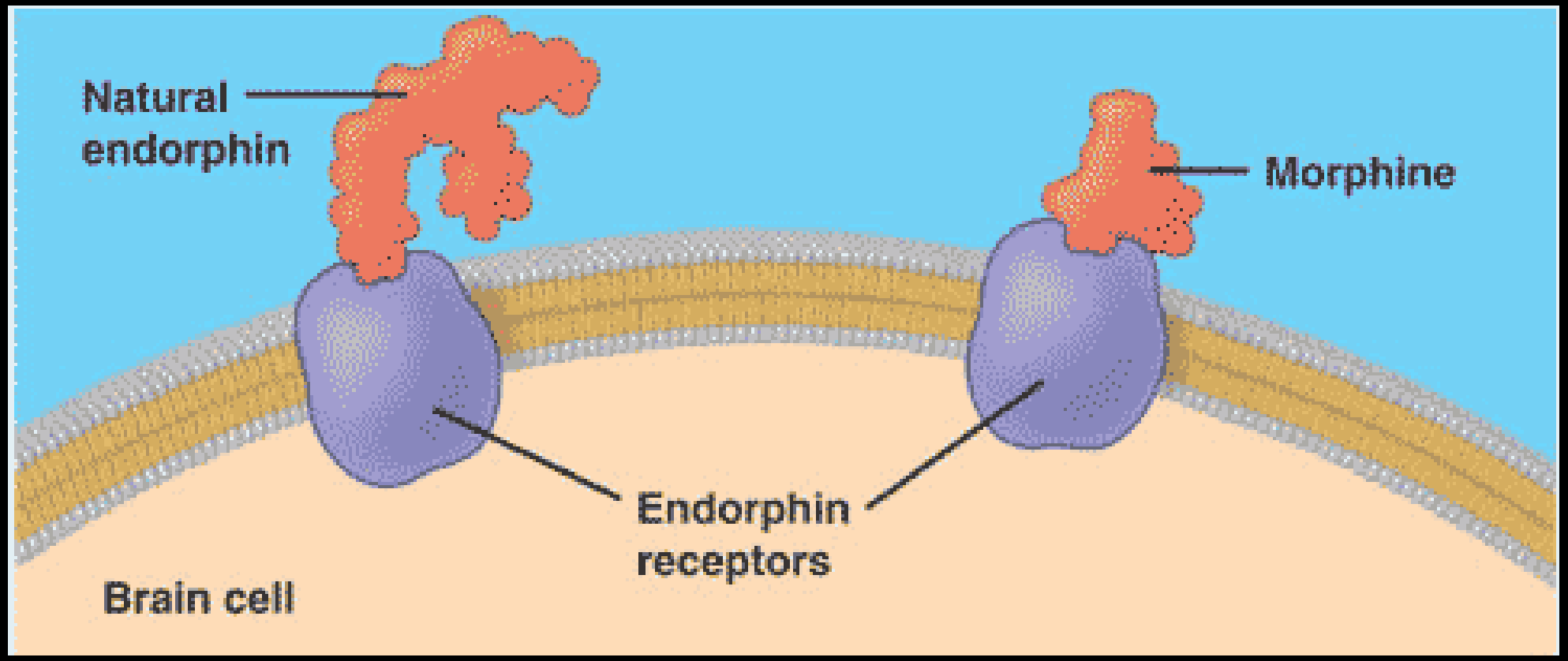
Make money.
Buy street heroin .
Visit DCR.
Receive hygienic paraphernalia (syringe, cookers, filter, alcohol pad) .
Use under supervision of trained professional first aid.
Properly dispose of drug paraphernalia in biohazard containers.
Relax, take a shower, change clothes, talk to a social worker & organise the rest of my day.

Life of people who use drugs before and after the opening of DCR's

Courtesy of InSite

Opioids

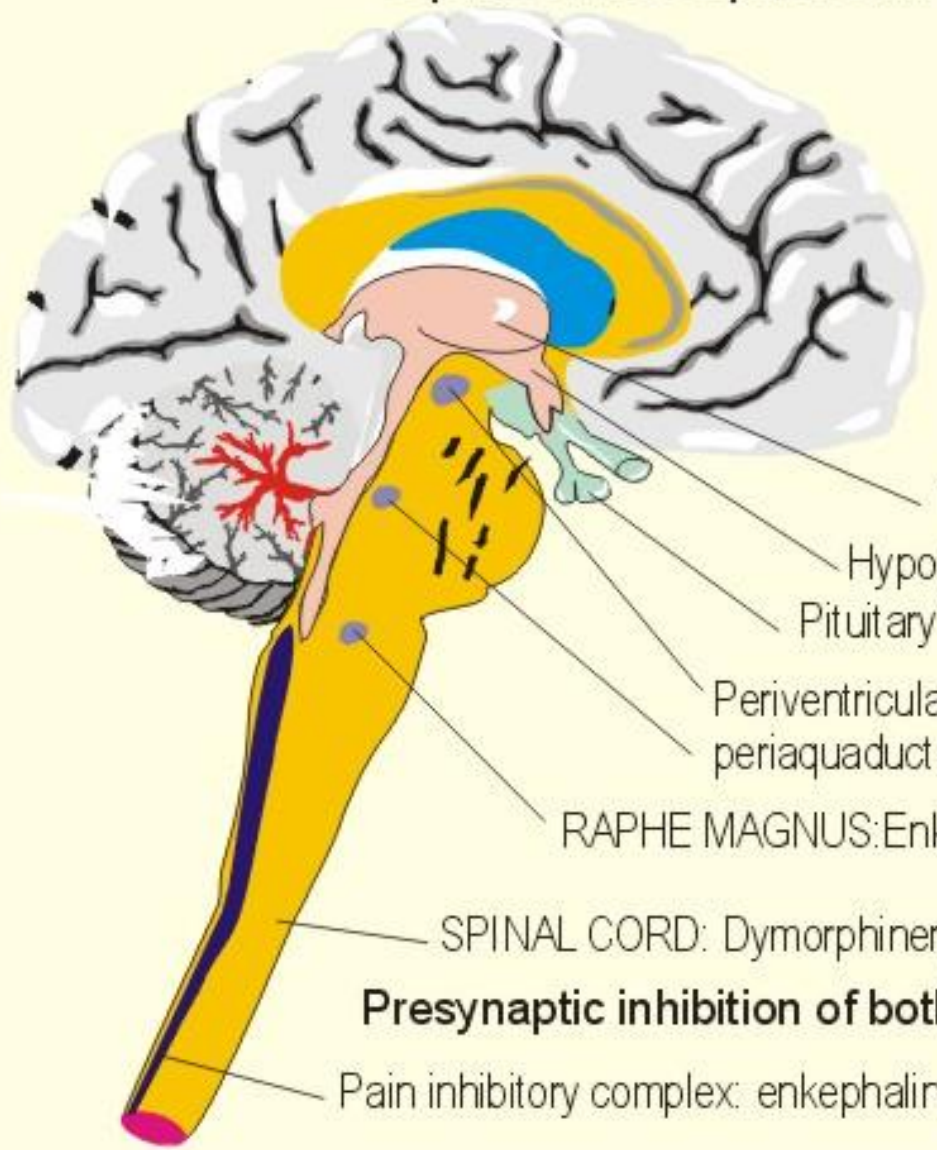
Endogenous vs. Exogenous Opioids



Classification of Opioids

Traditional	*Origin*	*Function*
Strong morphine fentanyl remifentanil **Intermediate** buprenorphine pentazocine butorphanol **Weak** codeine	**Naturally occurring** morphine, codeine, thebaine **Semisynthetic** oxycodone, hydrocodone, hydromorphone, buprenorphine **Synthetic** fentanyl methadone tramadol	**Pure agonists** morphine, fentanyl, remifentanil **Partial agonist** buprenorphine **Agonists-antagonists** pentazocine nalbuphine **Pure antagonists** naloxone naltrexone

Opiate Receptors In The CNS



Thalamus

Hypothalamus

Pituitary glands

} β - endorphin (μ- & δ)

Periventricular nuclei
periaquaductal grey

} Morphine
Dynorphin (μ)

RAPHE MAGNUS:Enkephalin (δ)

SPINAL CORD: Dymorphinergic neuron with κ-receptors

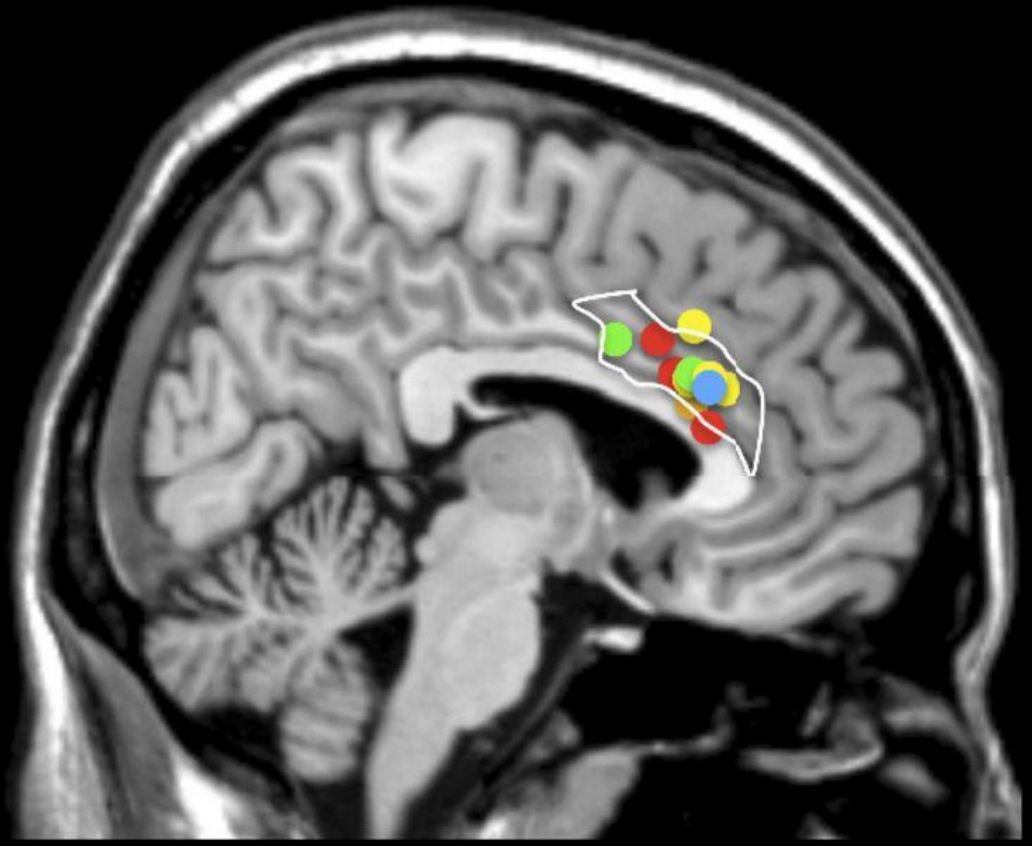
Presynaptic inhibition of both III and IV fibres by enkephalins

Pain inhibitory complex: enkephalin (δ)

Fig. 3-10

KMc

Distress and Pain:
Dorsal Anterior Cingulate Cortex



- Pain
- Social rejection
- Hunger
- Thirst
- Breathlessness

Opioid Intoxication

- Euphoria experienced as a “rush” of intensely pleasurable feelings

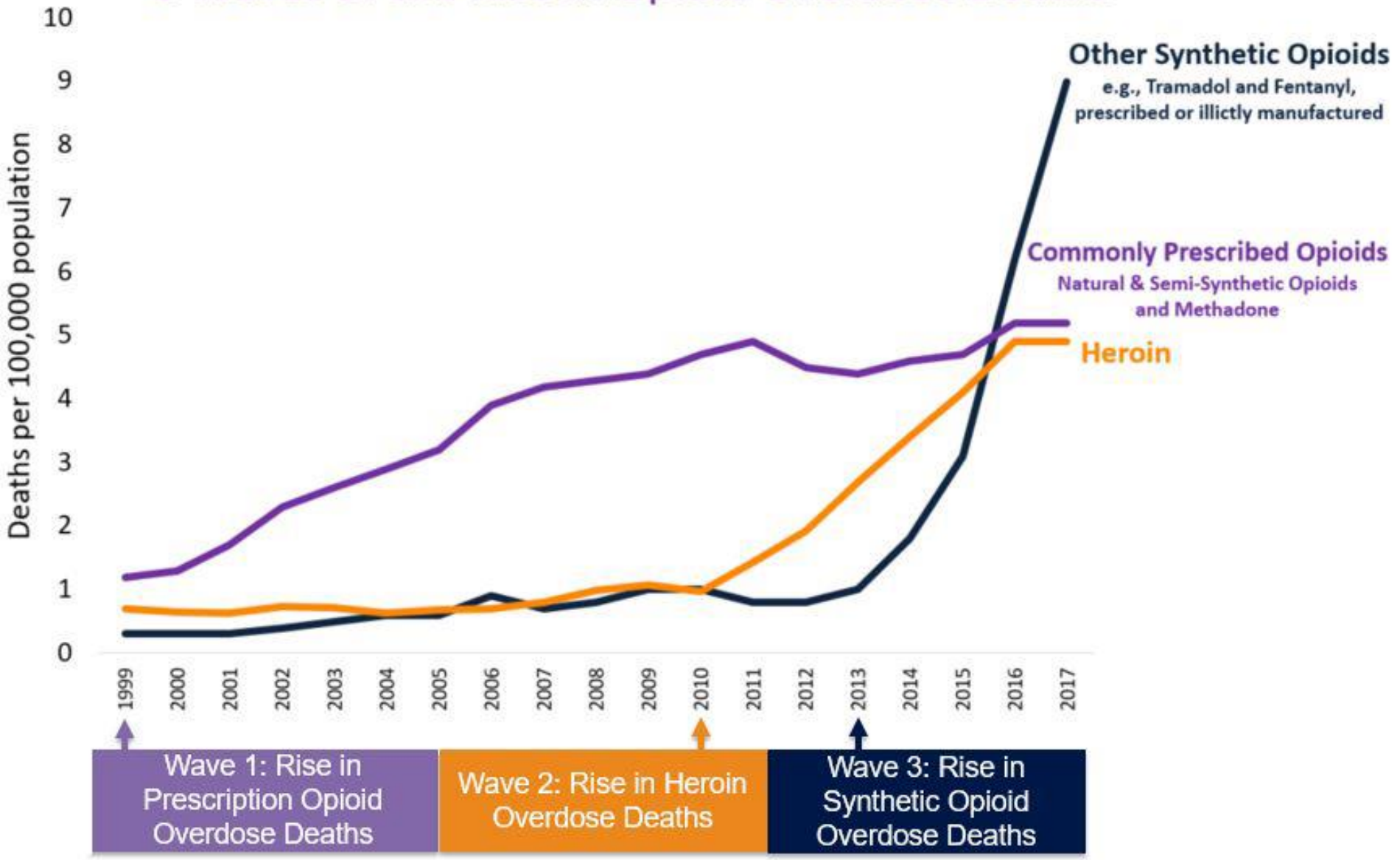
- Reduced psychological pain:
  - Anxiety, depression, anger, paranoid ideation/psychosis

- GI: nausea, vomiting, constipation
- Miosis (pinpoint pupils)
- Respiratory suppression

Opioid Withdrawal

- Dysphoric mood
- Nausea/vomiting
- Muscle aches
- Lacrimation
- Rhinorrhea
- Pupil dilation
- Pilorection
- Sweating
- Diarrhea
- Yawning
- Fever
- Insomnia

3 Waves of the Rise in Opioid Overdose Deaths



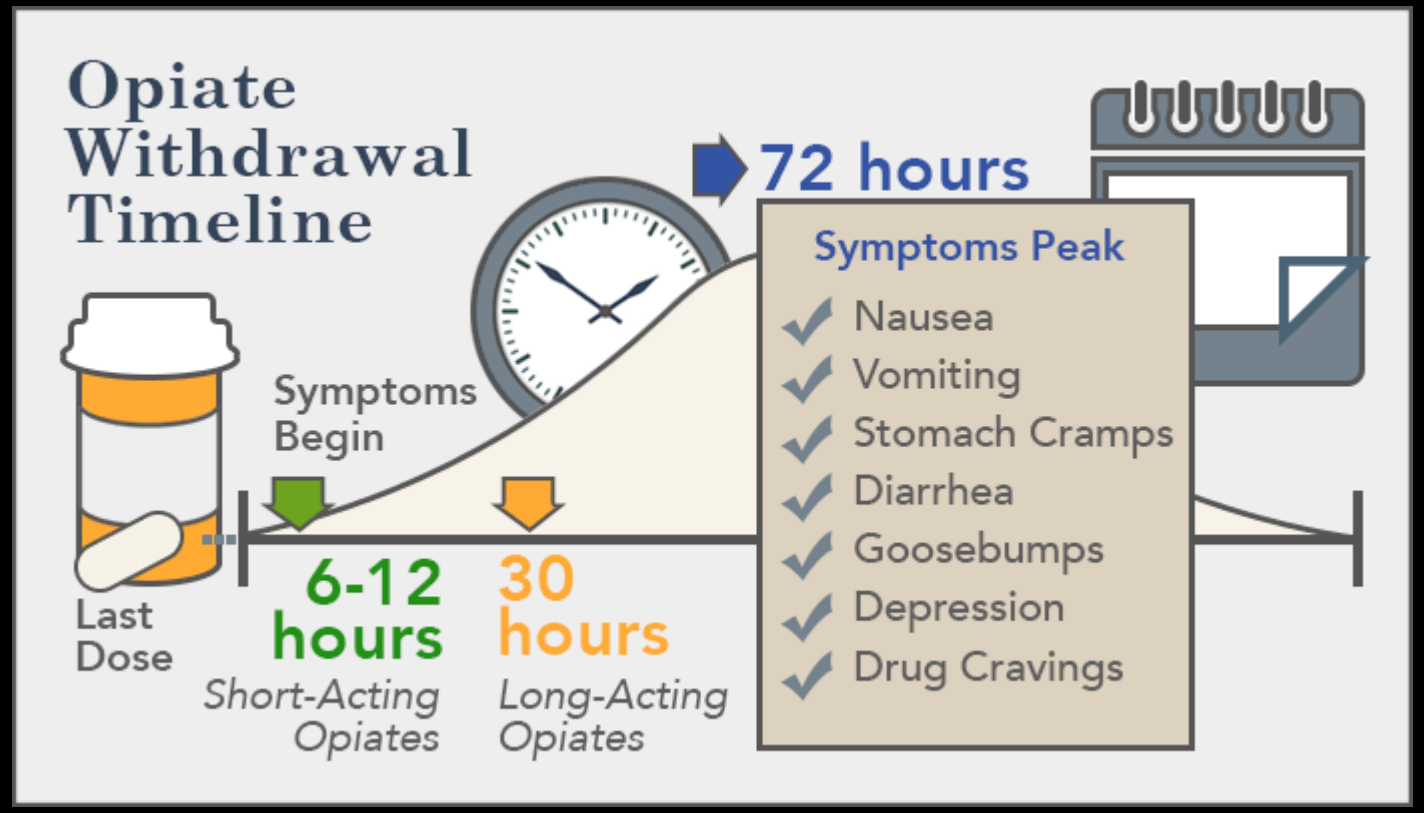
SOURCE: National Vital Statistics System Mortality File.


HEROIN
FENTANYL
CARFENTANIL


2 mL Single-dose
I.V. or I.M. use
Fentanyl Citrate
Inj., USP
100 mcg Fentanyl/2 mL
(50 mcg/mL)
Hospira, Inc.
Lake Forest, IL 60045 USA
2 mL Single-dose
I.V. or I.M. use
Fentanyl Citrate
Inj., USP
100 mcg Fentanyl/2 mL
(50 mcg/mL)
Hospira, Inc.
Lake Forest, IL 60045 USA

Treatment


Detox



Acute withdrawal

7 days for heroin

Up to 25 days for methadone

Post-Acute Withdrawal Syndrome (PAWS)

Can be up to 1 year

Post-Acute Withdrawal Syndrome (PAWS)

- Alcohol or drug cravings
- Irritability
- Anxiety
- Presence of a dysphoria state or depression
- Trouble sleeping
- Decreased ability to feel pleasure (anhedonia)
- Decreased libido (interest in sex)
- A reduction in short-term memory
- Chronic and lasting fatigue
- Struggling to concentrate
- Difficulty focusing on tasks
- Impaired decision-making skills
- Reduced control of executive functions
- Physical problems, especially pain, that may not be attributed to a specific cause

HUFFPOST

THE BLOG 08/27/2013 02:56 pm ET | **Updated** Oct 27, 2013

Death by Detoxification

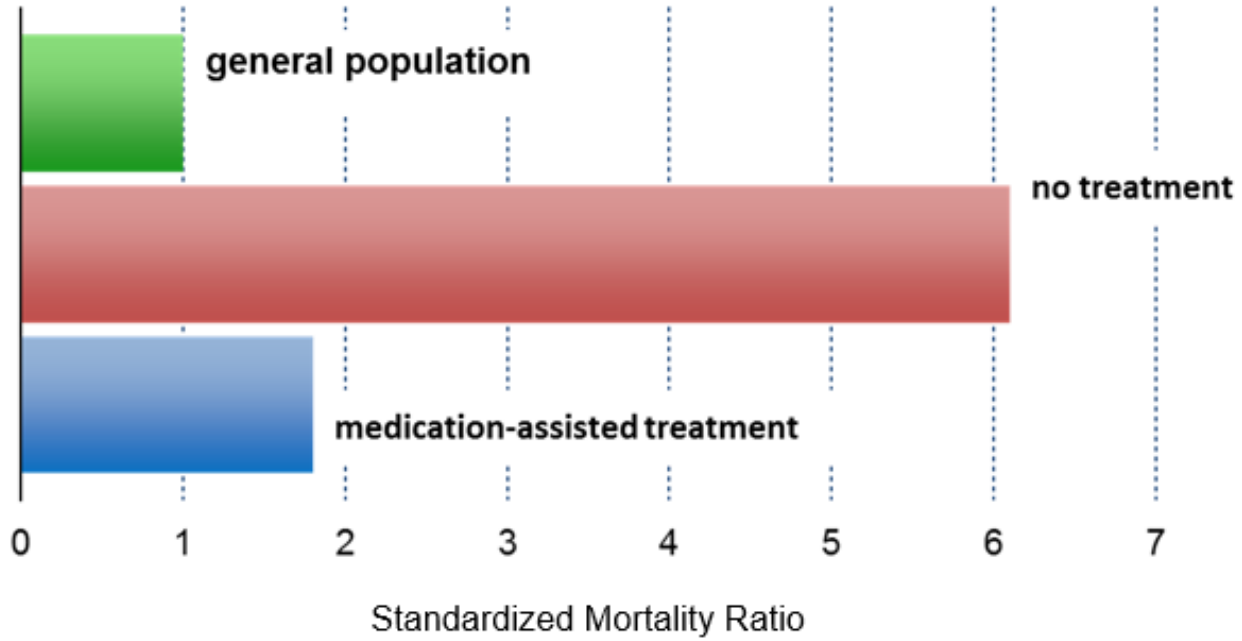
By Adam Bisaga, M.D., Maria A. Sullivan, M.D., Ph.D.

Hardly a day passes when we do not hear reports from many different areas of the country about young people dying from overdoses of narcotics. The recent death of the actor Cory Monteith was a stark public reminder of this recurring tragedy. Many of these incidents are even more tragic since they happen not too long after discharge from a treatment program. These headlines are a wake-up call: What more can be done to save the lives of young people with drug addictions, especially those who come to us seeking help?

Monteith was taking heroin, but we know that taking opioid painkillers — such as Vicodin or Oxycontin — affect the brain similarly to heroin and could have resulted in the same tragic outcome. He died of an overdose, a leading cause of death in individuals who use heroin or misuse painkillers. Overdoses, which are most often unintentional, are too common among people who regularly use heroin or misuse painkillers. Drug overdose death rates in the U.S. have more than tripled since 1990. In the past decade, deaths from opioids have surpassed motor vehicles as a cause of death in some states.

Benefits of MAT: Decreased Mortality

Death rates:



Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

129 times the overdose death risk as compared to gen. pop.

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Release from Prison — A High Risk of Death for Former Inmates

Ingrid A. Binswanger, M.D., Marc F. Stern, M.D., Richard A. Deyo, M.D., Patrick J. Heagerty, Ph.D., Allen Cheadle, Ph.D., Joann G. Elmore, M.D., and Thomas D. Koepsell, M.D.

ABSTRACT

BACKGROUND

The U.S. population of former prison inmates is large and growing. The period immediately after release may be challenging for former inmates and may involve substantial health risks. We studied the risk of death among former inmates soon after their release from Washington State prisons.

METHODS

We conducted a retrospective cohort study of all inmates released from the Washing-

other state residents, with a markedly elevated relative risk of death from drug overdose (129; 95% CI, 89 to 186). The leading causes of death among former inmates

RESULTS

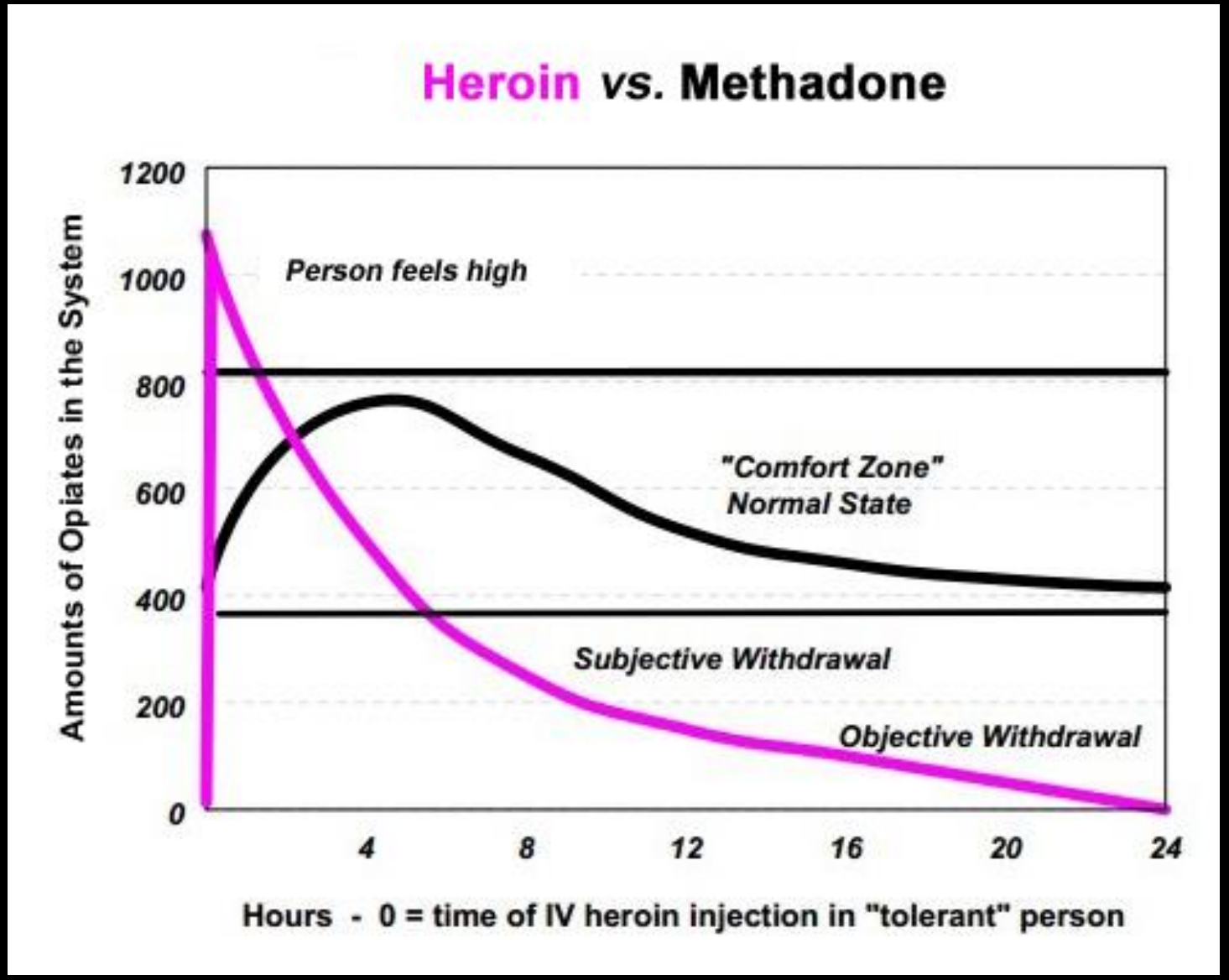
Of 30,237 released inmates, 443 died during a mean follow-up period of 1.9 years. The overall mortality rate was 777 deaths per 100,000 person-years. The adjusted risk of death among former inmates was 3.5 times that among other state residents (95% confidence interval [CI], 3.2 to 3.8). During the first 2 weeks after release, the risk of death among former inmates was 12.7 (95% CI, 9.2 to 17.4) times that among other state residents, with a markedly elevated relative risk of death from drug overdose (129; 95% CI, 89 to 186). The leading causes of death among former inmates were drug overdose, cardiovascular disease, homicide, and suicide.

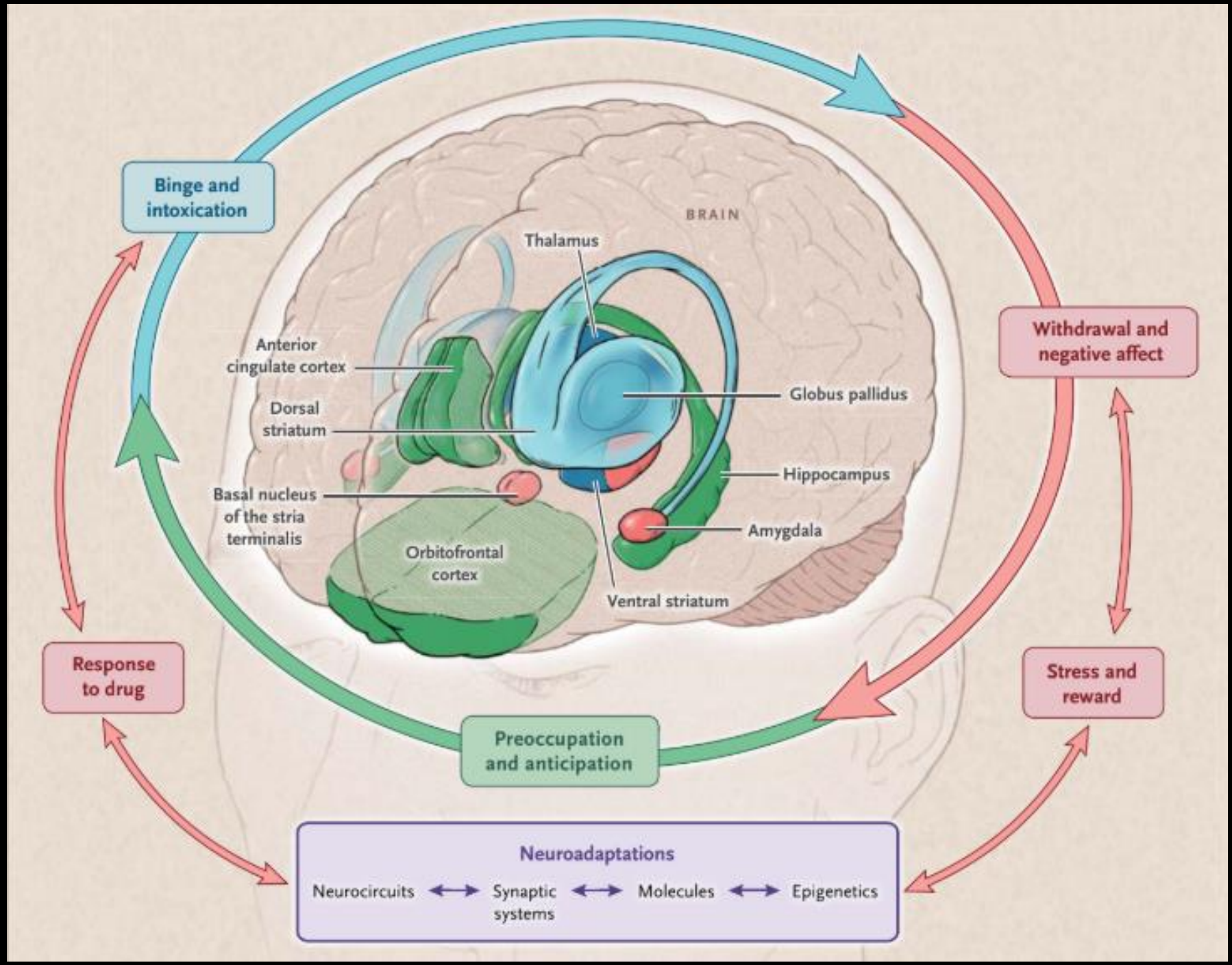
From the Puget Sound Veterans Affairs Medical Center, Seattle (I.A.B., T.D.K.); the Departments of Medicine (I.A.B., R.A.D., J.G.E.), Health Services (I.A.B., R.A.D., A.C., T.D.K.), Biostatistics (P.J.H.), and Epidemiology (J.G.E., T.D.K.), University of Washington, Seattle; the Department of Medicine, University of Colorado at Denver and the Health Sciences Center, Denver (I.A.B.);

N Engl J Med 2007;356:157-65.

- Methadone
- Buprenorphine
- Naltrexone

Why do methadone and buprenorphine work?





Volkow Koob
2016 NEJM

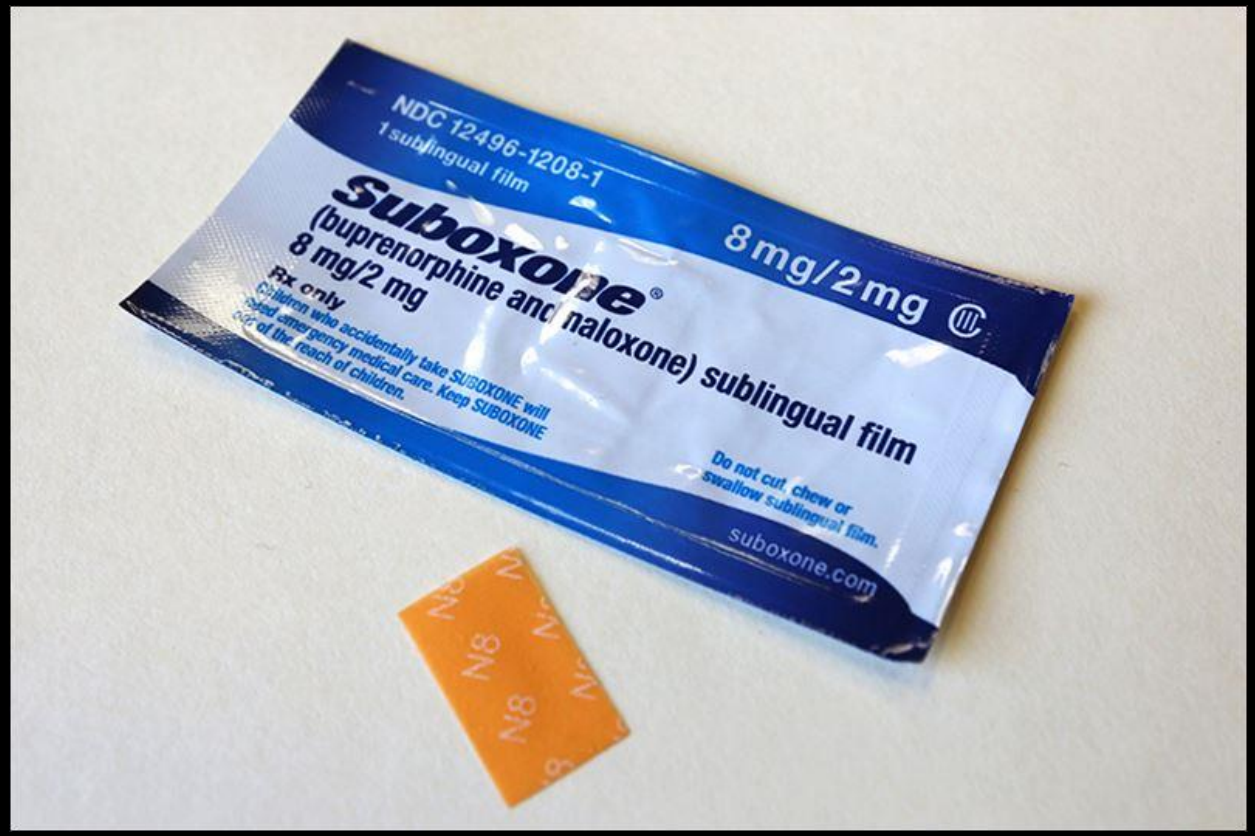
reddit


When you're dope sick AF and your plug finally calls back after you've already taken your sub

Methadone


5mg
10mg
40mg
(Dispersible Tablet)
Methadose
Methadone IR Tablets
Mallinckrodt

Buprenorphine



Buprenorphine / Naloxone Tablets
Photo by Psych0naut. © 2010 Erowid.org

XR-Naltrexone

380mg IM every 4 weeks

Vivitrol injection preparation - YouTube
https://www.youtube.com/watch?v=IZBaDCIWSwg

The Duration Dilemma

RESEARCH

Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies

Luis Sordo,[1,2,3] Gregorio Barrio,[4] Maria J Bravo,[1,2] B Iciar Indave,[1,2] Louisa Degenhardt,[5,6] Lucas Wiessing,[7] Marica Ferri,[7] Roberto Pastor-Barriuso[1,2]

[1]National Centre for Epidemiology, Carlos III Institute of Health, Madrid, Spain

[2]Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain

[3]Department of Preventive Medicine and Public Health, Faculty of Medicine, Complutense University, Madrid, Spain

[4]National School of Public

ABSTRACT

OBJECTIVE

To compare the risk for all cause and overdose mortality in people with opioid dependence during and after substitution treatment with methadone or buprenorphine and to characterise trends in risk of mortality after initiation and cessation of treatment.

DESIGN

Systematic review and meta-analysis.

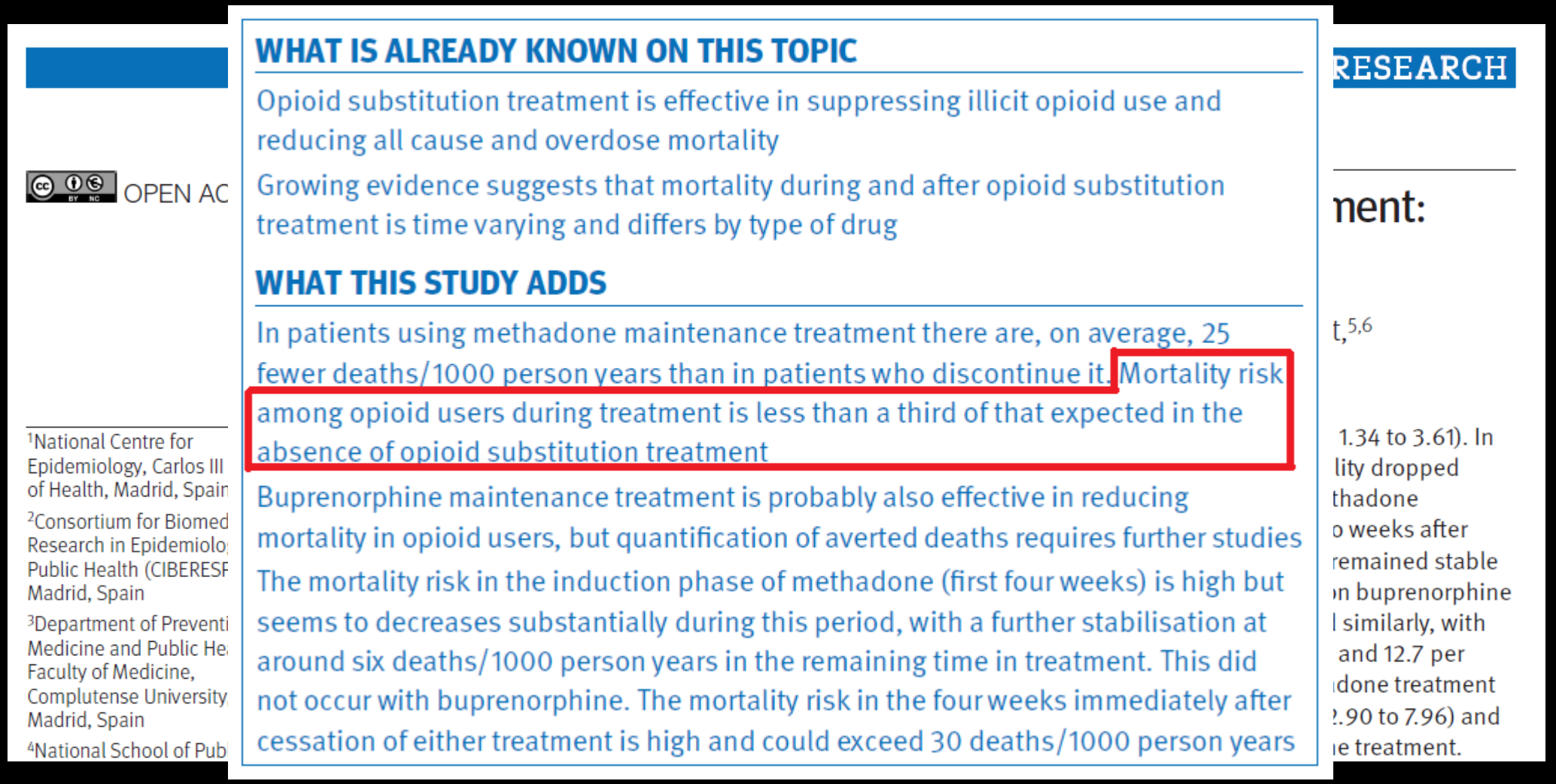
DATA SOURCES

Medline, Embase, PsycINFO, and LILACS to September

out of buprenorphine treatment (2.20, 1.34 to 3.61). In pooled trend analysis, all cause mortality dropped sharply over the first four weeks of methadone treatment and decreased gradually two weeks after leaving treatment. All cause mortality remained stable during induction and remaining time on buprenorphine treatment. Overdose mortality evolved similarly, with pooled overdose mortality rates of 2.6 and 12.7 per 1000 person years in and out of methadone treatment (unadjusted out-to-in rate ratio 4.80, 2.90 to 7.96) and 1.4 and 4.6 in and out of buprenorphine treatment.

BMJ 2017

The Duration Dilemma



OPEN AC

RESEARCH

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[2]Consortium for Biomed Research in Epidemiolo Public Health (CIBERESF Madrid, Spain
[3]Department of Preventi Medicine and Public He Faculty of Medicine, Complutense University Madrid, Spain
[4]National School of Pub

WHAT IS ALREADY KNOWN ON THIS TOPIC

Opioid substitution treatment is effective in suppressing illicit opioid use and reducing all cause and overdose mortality

Growing evidence suggests that mortality during and after opioid substitution treatment is time varying and differs by type of drug

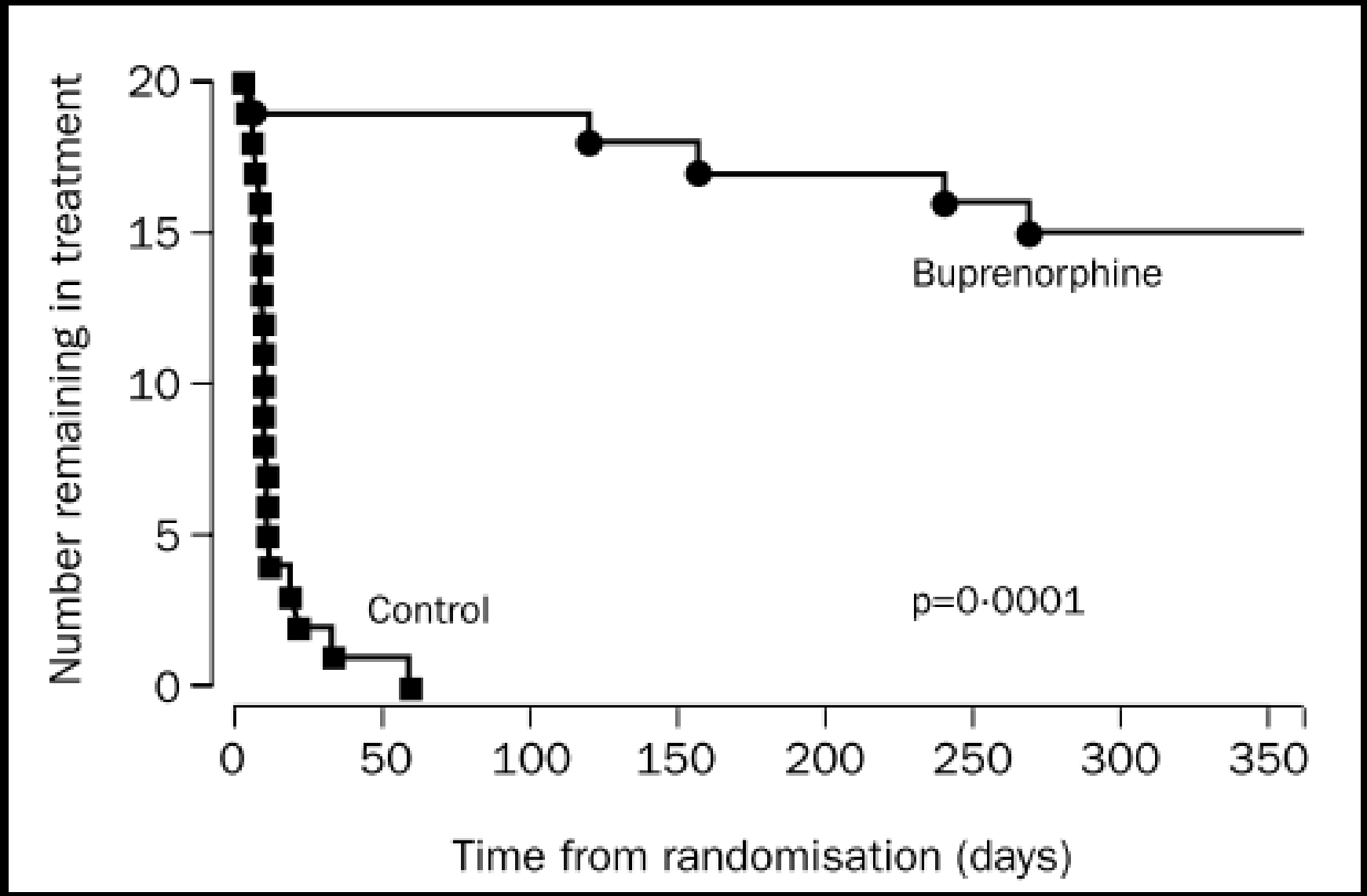
WHAT THIS STUDY ADDS

In patients using methadone maintenance treatment there are, on average, 25 fewer deaths/1000 person years than in patients who discontinue it. Mortality risk among opioid users during treatment is less than a third of that expected in the absence of opioid substitution treatment

Buprenorphine maintenance treatment is probably also effective in reducing mortality in opioid users, but quantification of averted deaths requires further studies

The mortality risk in the induction phase of methadone (first four weeks) is high but seems to decreases substantially during this period, with a further stabilisation at around six deaths/1000 person years in the remaining time in treatment. This did not occur with buprenorphine. The mortality risk in the four weeks immediately after cessation of either treatment is high and could exceed 30 deaths/1000 person years

BMJ 2017



Mortality:

4/20 in placebo group

0/20 in buprenorphine group

Kakko et al, 2003

If you do detox…

When prescribing MAT…

1. Continue despite opioid relapses
2. Continue despite other substance use
3. Can start even if just cravings and no relapse

MAT: A Summary

1) **Methadone**
- Federally-regulated methadone maintenance programs (1970s)
- Decreases overdose deaths, improves psychosocial adjustment, reduces criminal activity, decreases rates of HIV/HCV

80 - 120mg daily

2) **Buprenorphine**

8mg BID

- Similar outcomes as for methadone
- Used since 2002
- DATA 2000 waiver allows office-based prescriptions

3) **XR- Naltrexone (Vivitrol® injection)**

380mg IM q 4 wks

- Opioid antagonist (blocks receptor)
- Much less evidence

Opioids Are Different

- Post-acute withdrawal syndrome → high relapse rates
  (we need our endogenous opiates)
- Detoxification doesn't work
- Overdose death most likely after period of abstinence
  - Inpatient rehab
  - Incarceration
- MAT is the gold standard of treatment

RUTGERS
New Jersey Medical School
Department of Psychiatry

You may be eligible to receive $750* financial reimbursement

BUPRENORPHINE
TRAINING COURSE

This conference is designed to meet the requirement for a buprenorphine waiver certification under the DATA 2000 federal law. Participants will learn about opioid use disorder and how to prescribe buprenorphine for their patients.

Training is FREE and includes complimentary breakfast, lunch and CMEs

Registration

CLICK below to Register

All Courses are 8:30 am to 3:00 pm

Friday, April 19, 2019	Newark, NJ Rutgers New Jersey Medical School
Friday, May 10, 2019	Park Ridge, NJ Park Ridge Marriott
Friday, July 12, 2019	Somerset, NJ RWJ University Hospital Somerset
Friday, July 19, 2019	Union, NJ Clubhouse at Galloping Hill Golf Course
Friday, August 2, 2019	Ringoes, NJ Heron Glenn Golf and Restaurant
Friday, August 23, 2019	Old Bridge, NJ Grand Marquis
Friday, Sept 27, 2019	Whippany, NJ Hanover Marriott

Petros Levounis, MD, MA
Professor and Chair,
Department of Psychiatry,
Rutgers New Jersey
Medical School

Erin Zerbo, MD
Assistant Professor,
Department of Psychiatry,
Rutgers New Jersey
Medical School

* This training is for Physicians, Physician Assistants and Advanced Practice Nurses. Eligible providers who complete this full day training and attain the DATA 2000 waiver may be eligible to receive financial reimbursement of $750.

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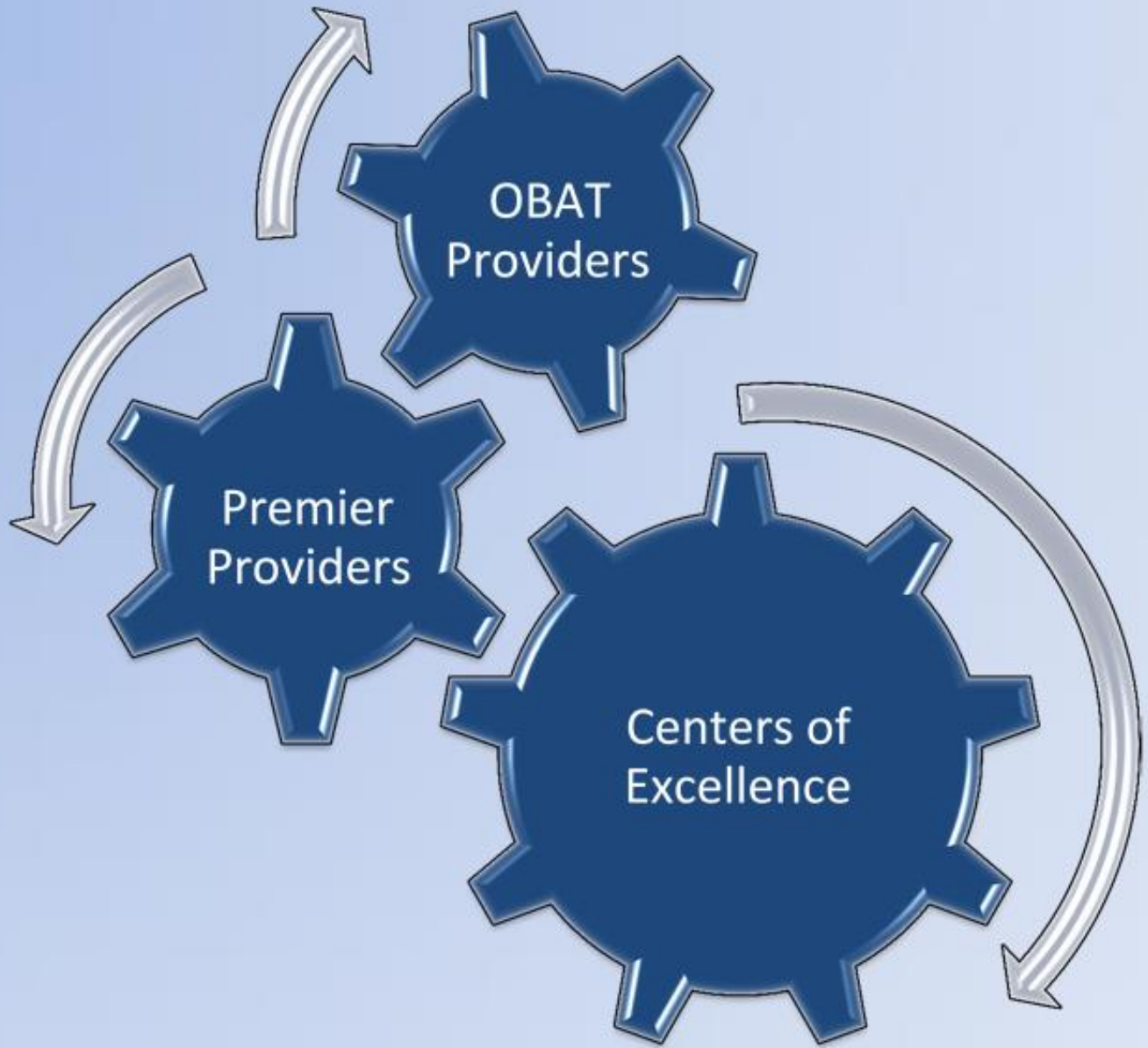
NJMS.Rutgers.edu/Psychiatry

This program is funded by the New Jersey Department of Human Services. Funding for this initiative was made possible (in part) by grant no. 5U79TI026556-03 from the Substance Abuse and Mental Health Services Administration (SAMHSA). The American Academy of Addiction Psychiatry (AAAP) is the Data Sponsor for this training. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the NJ Department of Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Friday, September 27, 2019

NJMS.Rutgers.edu/Psychiatry

The New Jersey **MATrx**



STATE OF NEW JERSEY
Department of Human Services
Division of Mental Health and Addiction Services

ADDICTION SERVICES TREATMENT DIRECTORY

Carole Johnson
Commissioner
Department of Human Services (DHS)

Valerie Mielke
Assistant Commissioner
Division of Mental Health and Addiction Services (DMHAS)

Home

In an emergency, always call 911. For 24/7 help finding treatment, please contact 1-844-REACHNJ (1-844-732-2465).

What type of treatment are you interested in?

- [x] Medication-Assisted Treatment (MAT)
- [x] Inpatient Services
- [x] Outpatient Services
- [x] Withdrawal Management

Near Zipcode / City — 10 Miles

County All

Provider Name Agency / Provider name

- [ ] Show only Intoxicated Driver Resource Center (IDRC)-affiliated agencies

Search Reset

njsams.rutgers.edu/TreatmentDirectory

Northern COE Counties

Please reach out to us!

Northern: COE@njms.rutgers.edu

Southern: SouthernNJCOE@rowan.edu

MAT Provider Hotline
866-221-2611
(Monday - Friday, 8am - 8pm)