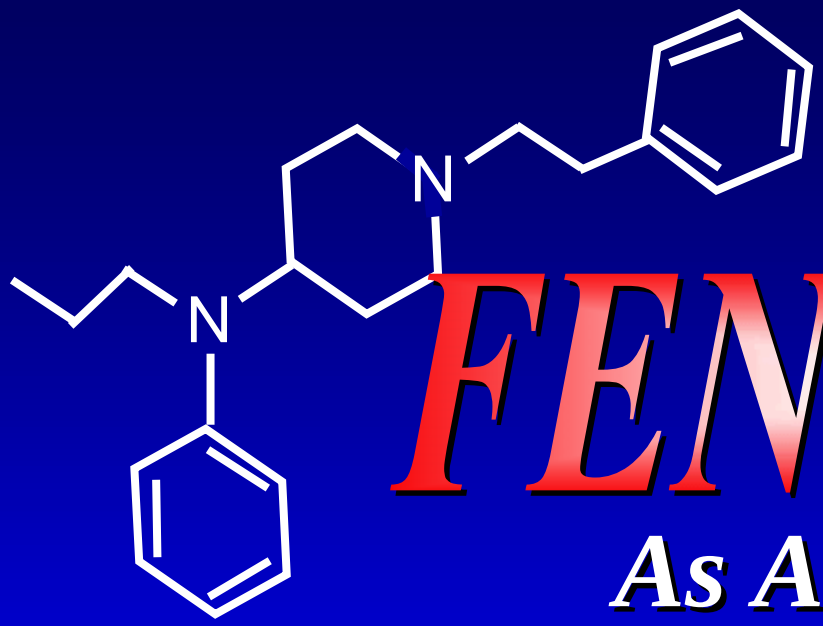
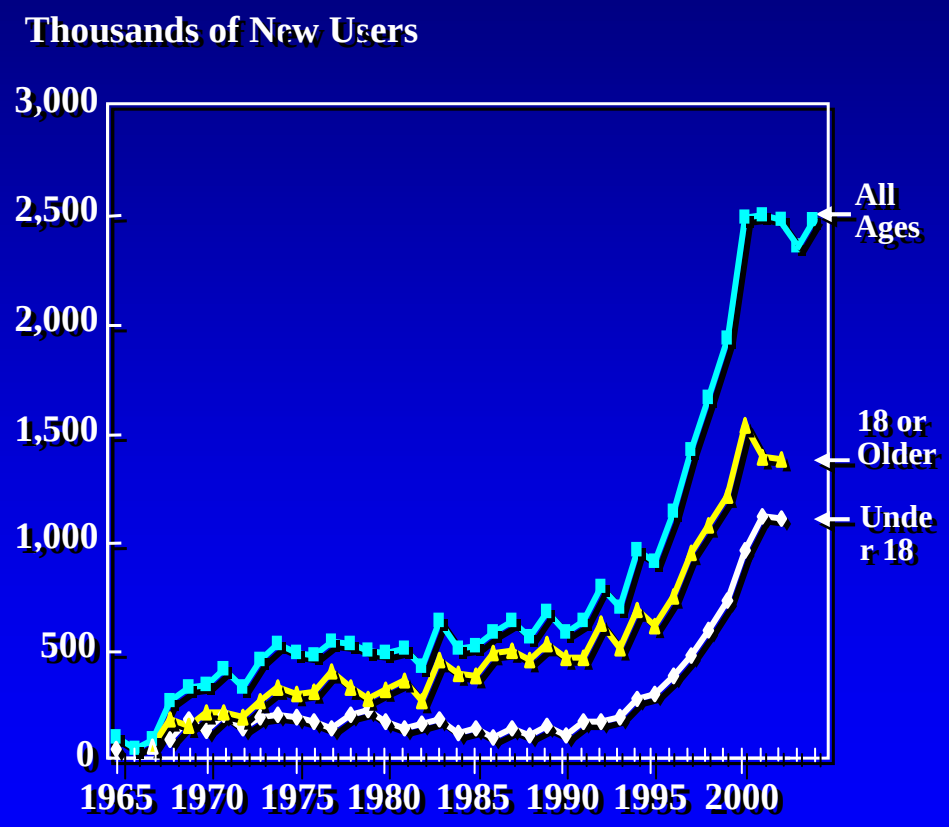


FENTANYL

As A Drug of Abuse

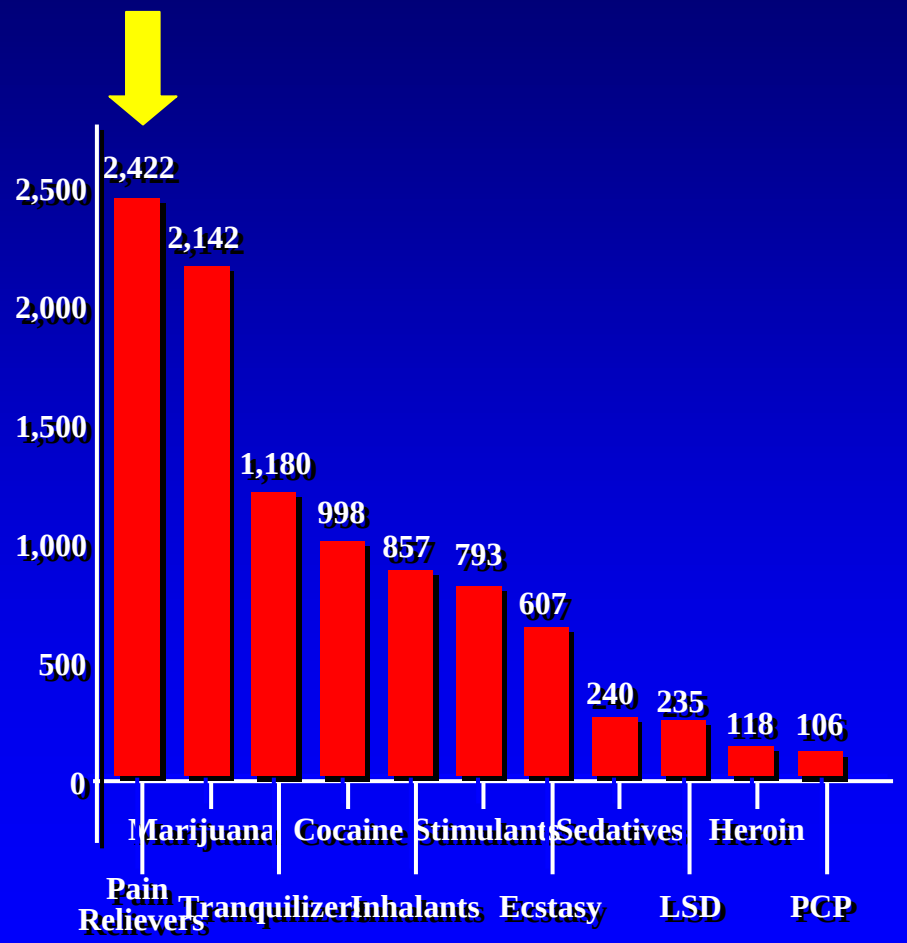
Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

Annual Numbers of *New* Nonmedical Users of Pain Relievers: 1965-2004



Source: 2003 & 2004 NSDUH, SAMHSA

Numbers of Past Year Initiates
(In Thousands)



Source: SAMHSA, 2004 NSDUH

Opioids

Examples: OxyContin, Vicodin, Fentanyl

How They Work…

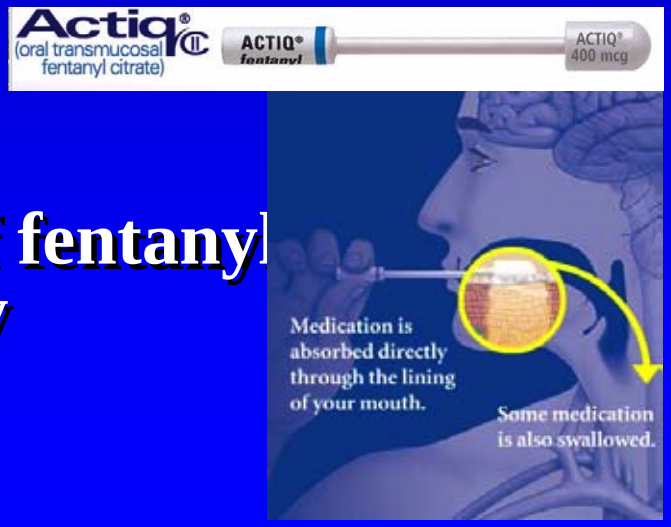
Attach to Opioid Receptors in the Brain and Spinal Cord, Blocking the Transmission of Pain Messages to the Brain

Opioids Are Generally Prescribed For:

- **Anesthesia**
- **Management of acute or chronic severe pain**
- **Relief of coughs and diarrhea**

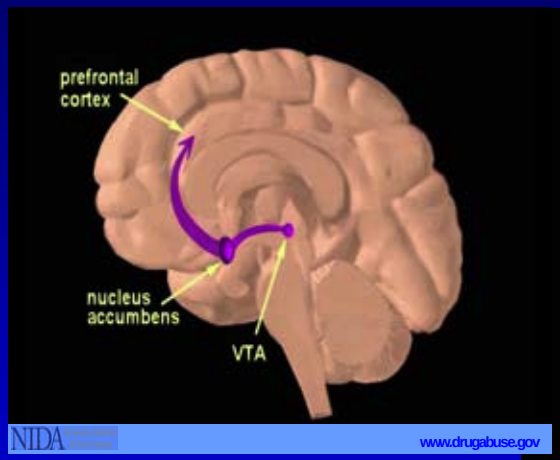
Fentanyl

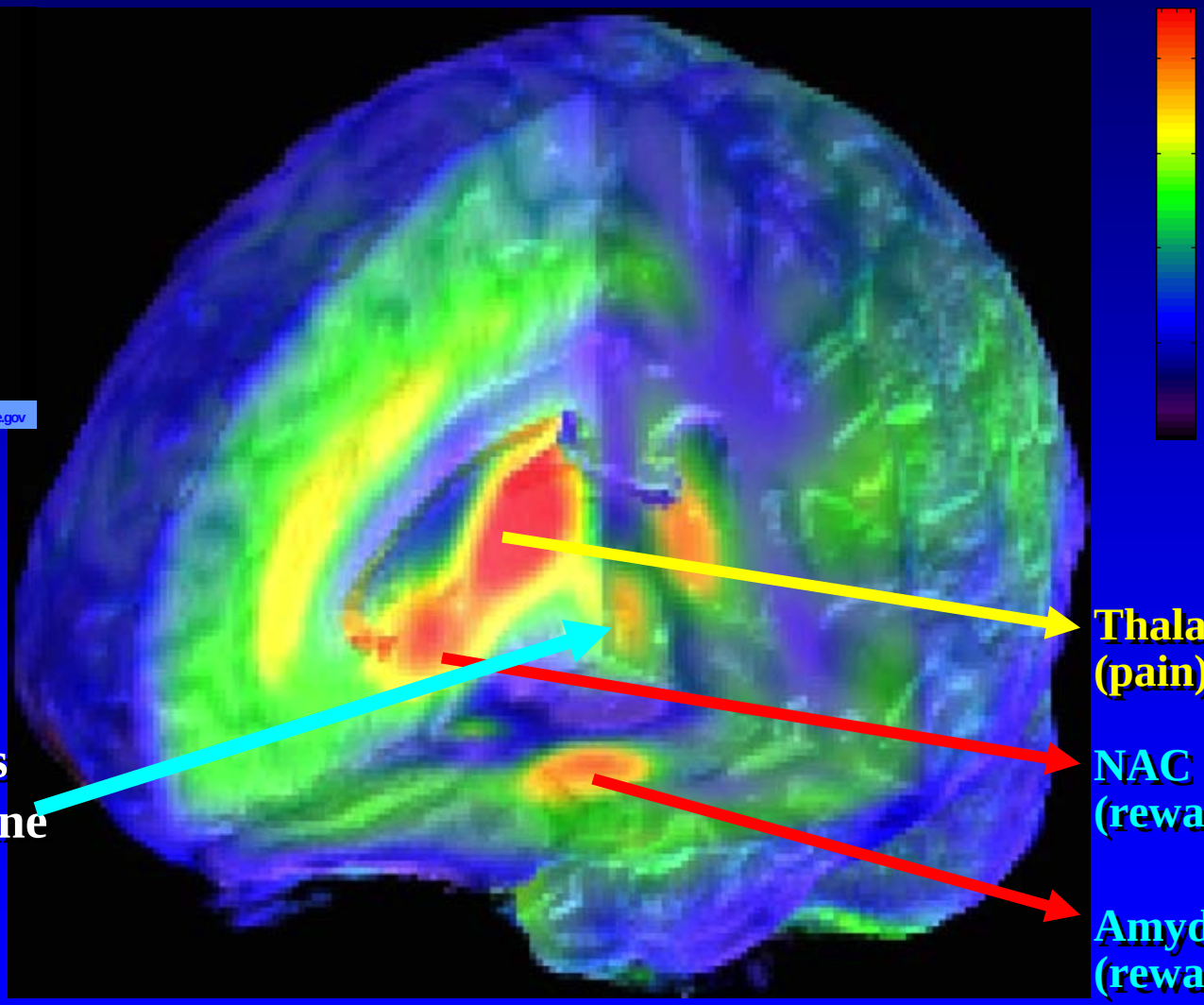
- μ-opioid receptor agonist
- potency = 50-100 times that of morphine
- high lipid solubility: easy access to brain
- rapid onset; short duration of action
- injectable (Sublimaze®), transdermal (Duragesic®), & transmucosal (Actiq®)
- more than 12 different analogs of fentanyl have been produced clandestinely



Narcotic Pain Killers

(Oxycontin, Vicodin, Fentanyl, Demerol, Dilaudid)
Activate Opiate Receptors, which Modulate Pain and Reward

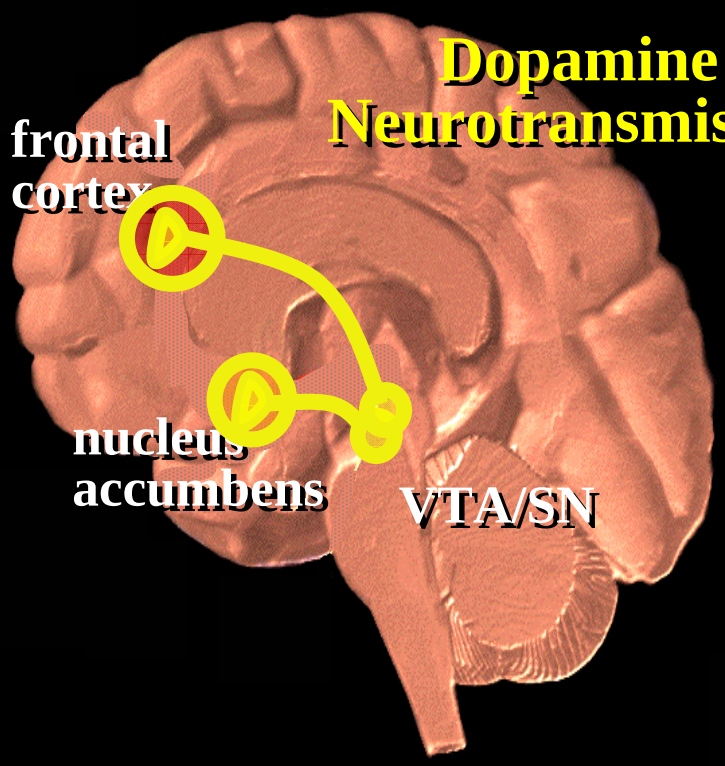


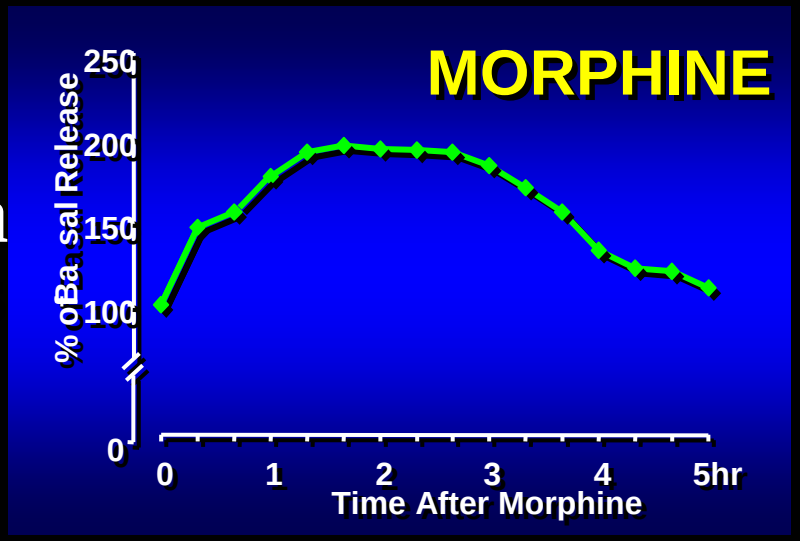


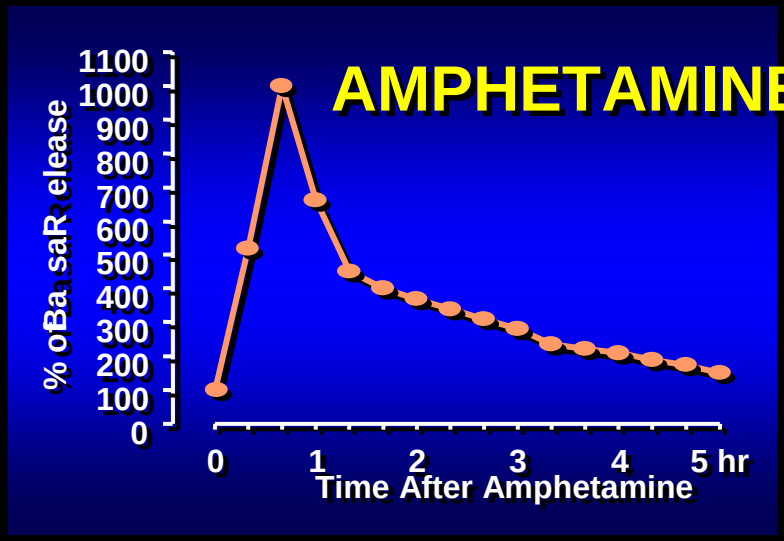
Opiate Receptors Activate Dopamine Cells

Why Do People Abuse Prescription Drug

These prescription drugs, like other drugs of abuse (cocaine, heroin, marijuana raise brain dopamine levels



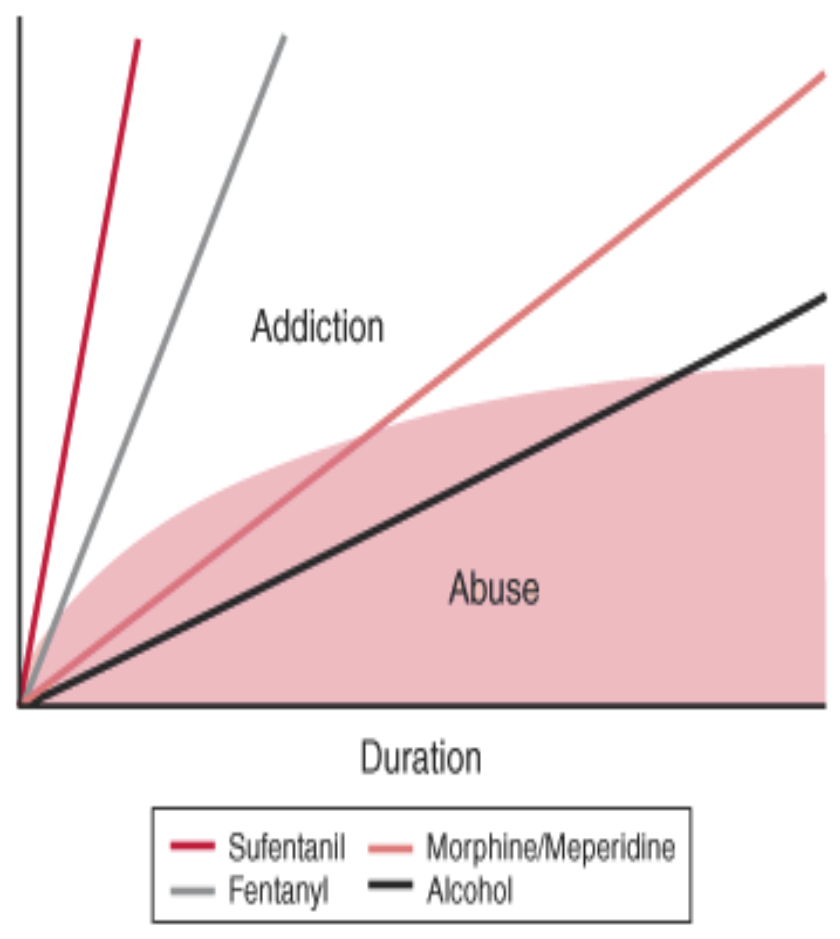




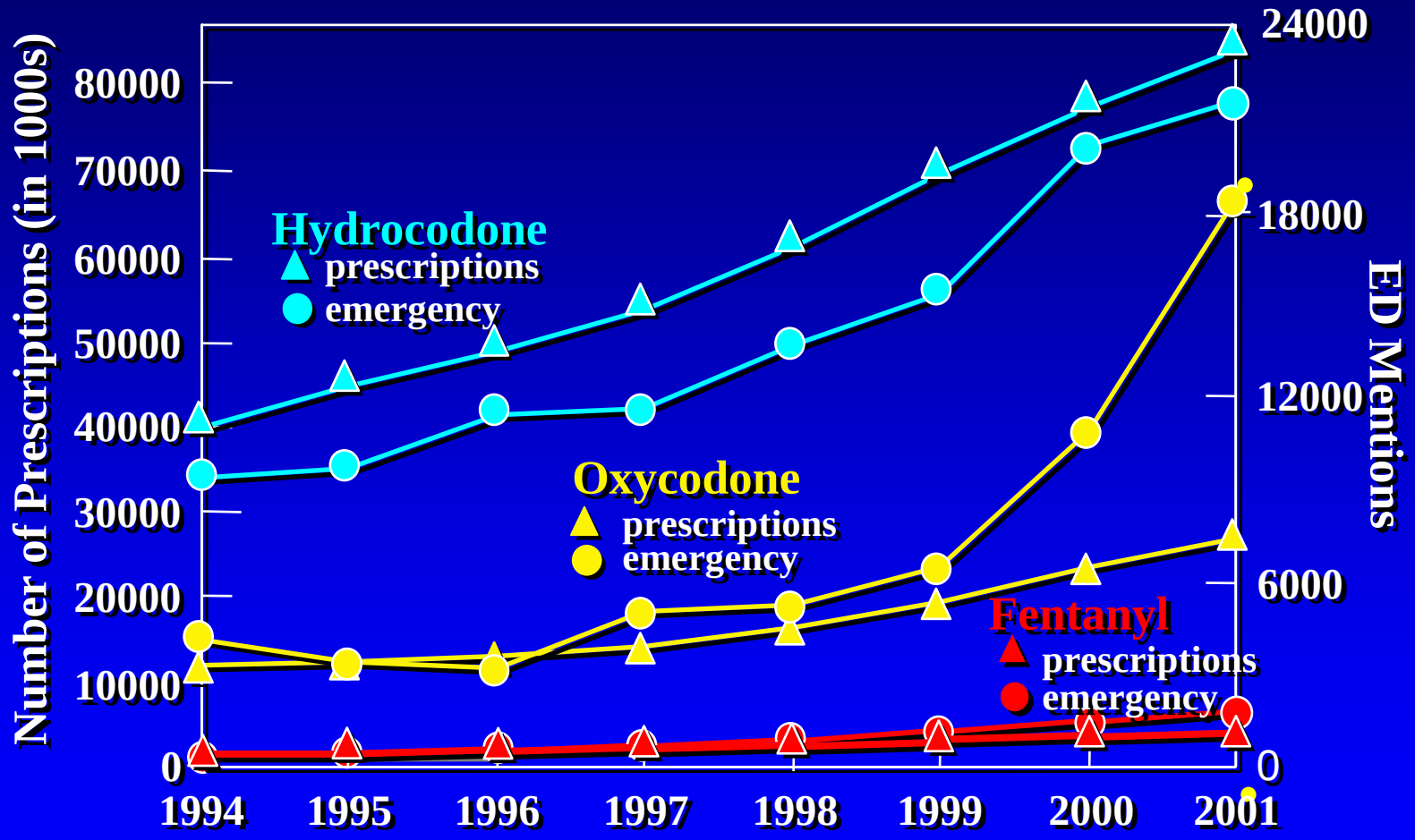
Di Chiara et al.

BUT dopamine is also elevated by natural reinforcers

The Speed at which Drugs Increase Dopamine Affects their Rewarding Effects

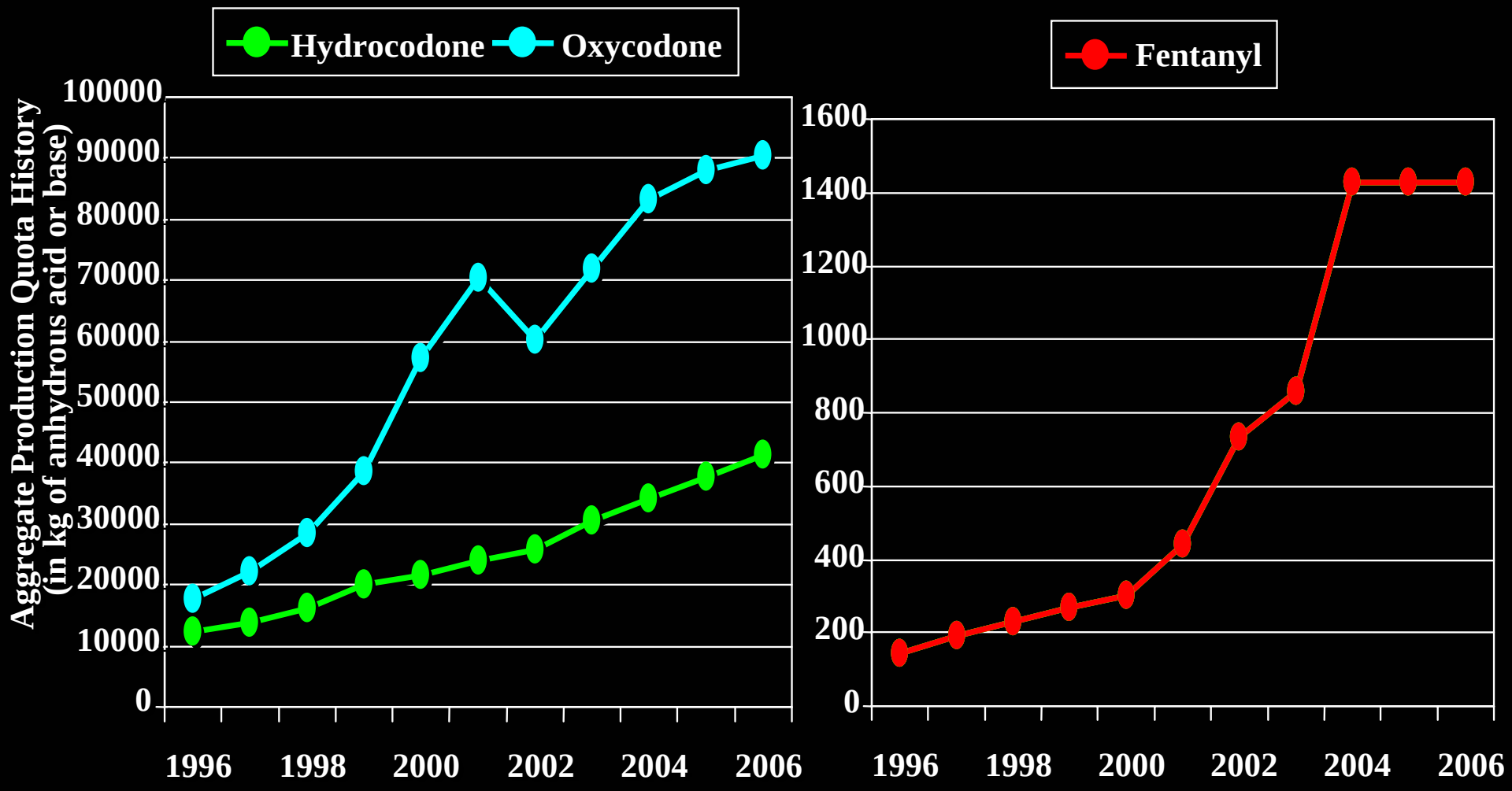


As Prescriptions Increase Emergency Room Visits For Non-Medical Abuse Have Also Increased



Source: SAMHSA, DAWN, 2002

Aggregate Production Quota History



Source: DEA, Office of Diversion Control

Availability on the Internet

Delivered in the Privacy of your Home

24/7 Pharmacy - Buy Prescription Drugs without Prescription - Netscape

http://www.247-pharmacy.com/

24/7 PHARMACY

Buy prescription drugs and medicine online - No prescription required - Free Worldwide delivery

Weight Loss | Sexual | Hair Loss | Pain Relief | Depression | Antibiotics | Venereal | Sleeping Aids

Wednesday 28 Januari 16:12 — Prescription Drugs without a Prescription — FAQ | Testimonials

Prescription Drugs

See our complete assortment of prescription drugs

Best Selling Drugs

- Alaxan, Carisoprodol
- Buy Ambien, Zolpidem
- Soma, Carisoprodol
- Buy Clenbuterol
- Buy Codeine
- Codipront, Codeine
- Buy Dolgesic Codeine
- Buy Cialis
- Buy Florinal Codeine
- Buy Furosemide
- Termalgin Codeine
- Buy Tylenol, Codeine
- Buy Codeisan Syrup
- Buy Dihydrocodeine
- Buy Dolmen Codeine
- Buy Depranocol

24/7 Pharmacy - the best and easiest way to buy prescription drugs online!

Some reasons why you should consider using this pharmacy!

- No consultation fees
- No prescription required
- Free Worldwide delivery
- Discrete packaging
- Mail order to your door
- Drugs at low prices

All major credit cards are accepted with 100% secure transactions!

How Customers appreciate 24/7 Pharmacy

Hi Majken,

Pain Relief Drug

New

FLUDETEN

Fludeten, Codein

used to relieve mild to moderately severe pain.

[Buy Fludeten]

Price: 65,00 US$

Anxiety Drug

New

Xanax, Alprazolam

medicine is a benzodiazepine used to treat anxiety and panic disorder.

[Buy Xanax]

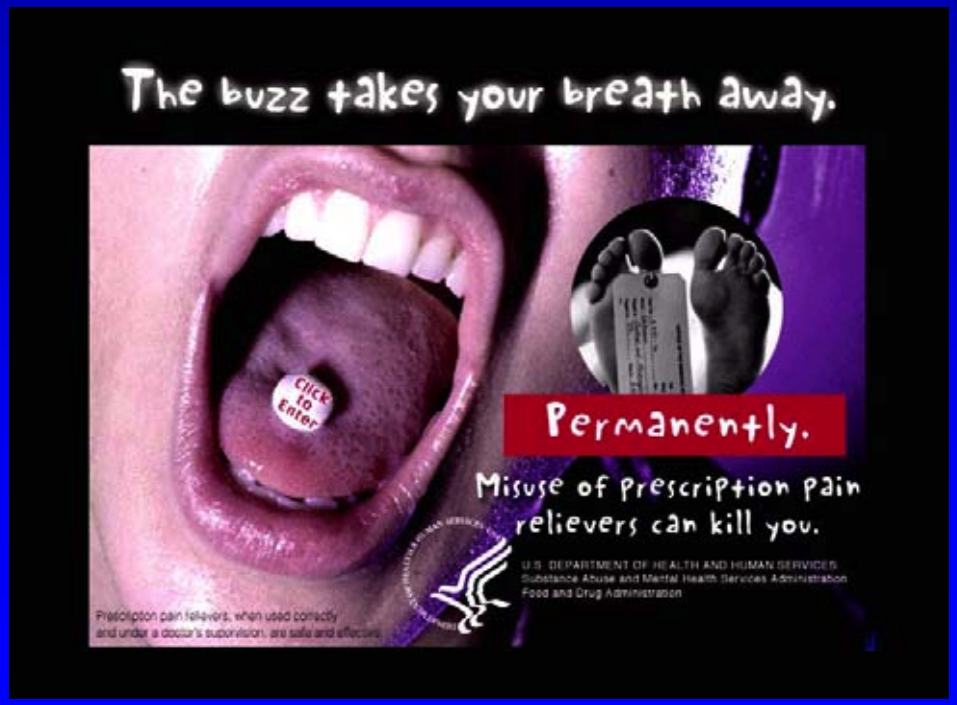
"Some reasons why you should consider using this pharmacy"

No prescription required!

www.drugabuse.gov

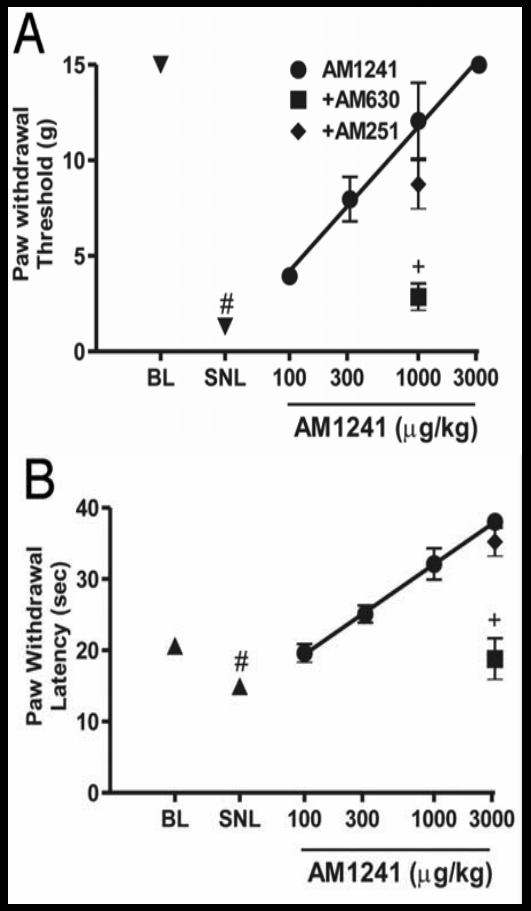
NIDA

What Are We Doing About All of This?



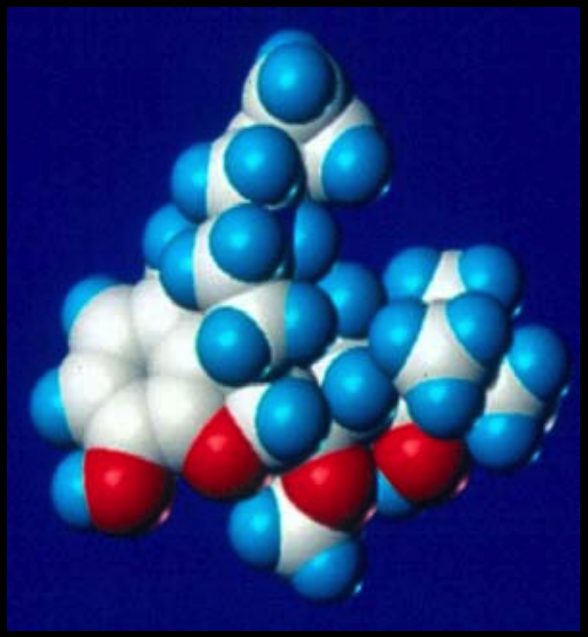
Development of Alternative Medications with no Drug Abuse Potential

Activation of CB2 Cannabinoid Receptors by AM1241Inhibits Experimental Neuropathic Pain



Source: Ibrahim et al., PNAS, September 2, 2003.

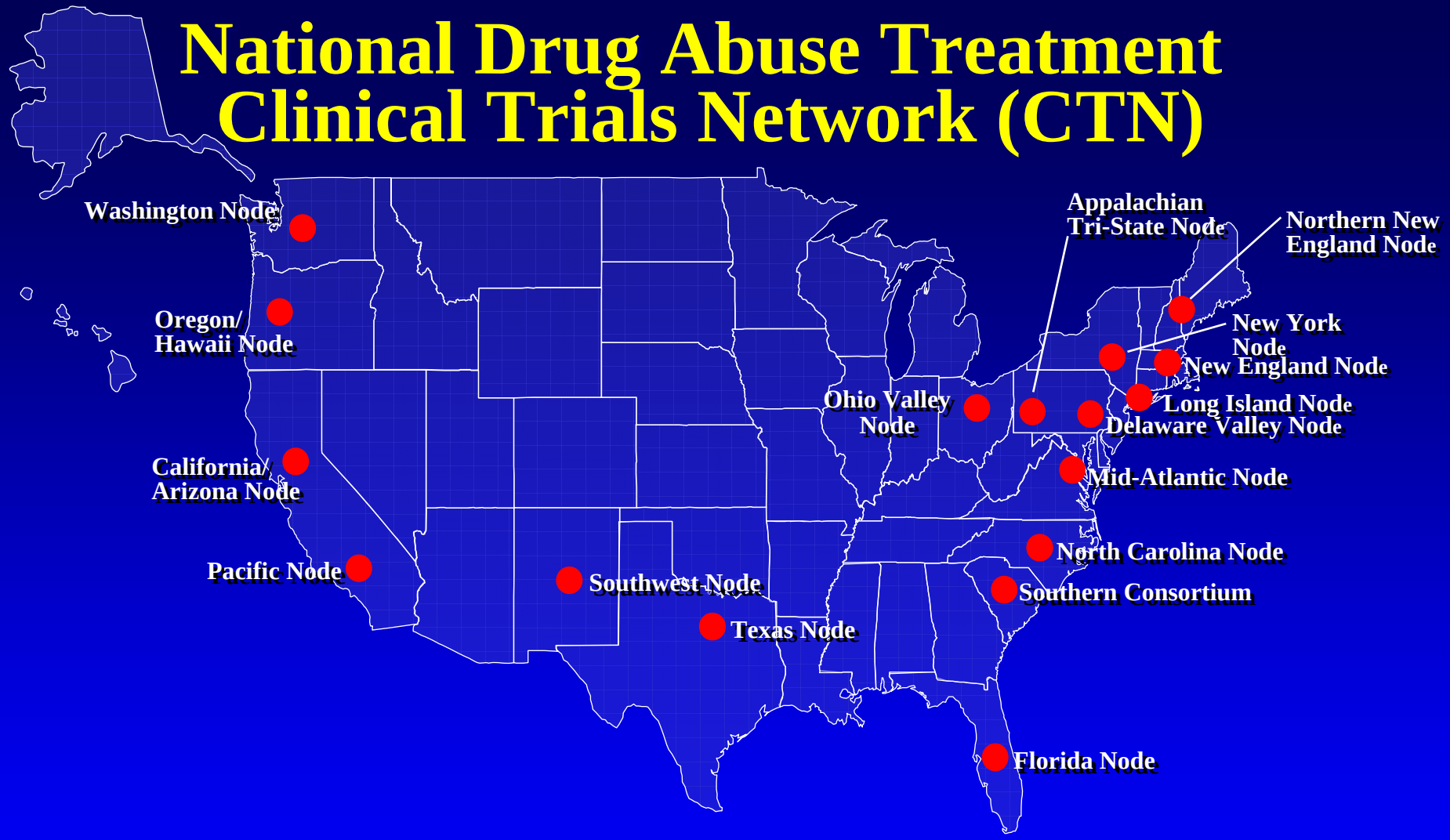
Suboxone® Buprenorphine monotherapy product



Subutex® Buprenorphine + *naloxone* combination product

(addition of opioid antagonist reduces abuse liability)

National Drug Abuse Treatment Clinical Trials Network (CTN)



NIDA Has Launched New Clinical Trials On:

- *Treatment of addiction to opiate analgesics*

Expanded Research Efforts

- Prescription Drug Abuse Program Announcement (PA-04-110)
- Prescription Opioid Use and Abuse in the Treatment of Pain (RFA-DA-06-005) (with NIA & NIDCR)

We've Developed and Widely Disseminated Materials Detailing the Facts About Prescription Drug Abuse…

www.drugabuse.gov

Director's Column
Vol. 19, No. 5 (January 2005)

Confronting the Rise in Abuse of Prescription Drugs

By NIDA Director Nora D. Volkow, M.D.

The misuse and abuse of prescription medications is a growing public health concern. The National Survey on Drug Use and Health (NSDUH), conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA), estimates that in 2003, 6.3 million Americans aged 12 and older abused prescription drugs (that is, took medications not prescribed for them or took medications solely for pleasure or entertainment) in the month preceding the survey. Most abused pain relievers (4.7 million); others abused tranquilizers (1.8 million), stimulants (1.2 million), and sedatives (0.3 million).

The abuse of prescription medications has increased in all segments of the population, and in recent years the increase in abuse of prescription painkillers has been particularly sharp and worrisome. In 2002, the NIDA-supported Monitoring the Future survey initiated questions about the prescription pain medications oxycodone (OxyContin) and hydrocodone (Vicodin). In that year and in 2003, about 4 percent and 4.5 percent, respectively, of high school seniors reported nonmedical use of oxycodone in the 12 months preceding the survey. Roughly 10 percent of seniors reported nonmedical use of hydrocodone, making it the third most widely abused illicit substance (after marijuana and amphetamine) in this age group.

The abuse of prescription pain medications is increasing among adult Americans as well. Among young adults aged 18 to 25, the rate increased from 22.1 percent in 2002 to 23.7 percent in 2003, NSDUH data show. Abuse of oxycodone increased among all age groups from 2002 to 2003: by more than 10 percent among Americans aged 12 to 17, by nearly 40 percent among 18- to 25-year-olds, and by 60 percent for Americans aged 26 or older.

NIDA is responding to the increase in prescription drug abuse on several fronts. In September, a Consultant Workgroup meeting brought together researchers and physicians with expertise in pain management and the epidemiology, prevention, and treatment of opiate abuse. This panel developed an outline for a large-scale clinical study of treatment for prescription opiate abuse that will be designed and conducted by NIDA's Clinical Trials Network. NIDA research also is expanding our understanding of the risks posed by prescription medications in different populations—women, adolescents, racial and ethnic groups, health professionals, those with comorbid substance abuse and mental health disorders, and those with HIV/AIDS and other infectious diseases. One group that may be especially at risk is the elderly. Age-related changes may influence the way in which their bodies metabolize and respond to prescription drugs. Older adults are more likely to have undiagnosed psychiatric and medical illness. They also are more likely to be taking several medications in complex drug regimens, increasing the risk of

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NATIONAL INSTITUTE ON DRUG ABUSE

Research Report SERIES

PRESCRIPTION DRUGS *Abuse and Addiction*

Most people who take prescription medications take them responsibly; however, the nonmedical use or abuse of prescription drugs remains a serious public health concern. Certain prescription drugs—opioids, central nervous system (CNS) depressants, and stimulants—when abused, can alter the brain's activity and lead to dependence and possibly addiction.

An estimated 4 million people aged 12 and older used prescription drugs for nonmedical reasons in 1999; almost half of that number reported using prescription drugs nonmedically for the first time in the previous year. We would like to reverse this trend by increasing awareness and promoting additional research on this topic.

The National Institute on Drug Abuse (NIDA) has developed this publication to answer questions about the consequences of abusing commonly prescribed medications. In addition to offering information on what research has taught us about how certain medications affect the brain and body, this publication also discusses treatment options.

This publication was developed to help health care providers discuss the consequences of prescription drug abuse with their patients. According to a recent national survey of primary care physicians and patients regarding substance abuse, 46.6 percent of physicians find it difficult to discuss prescription drug abuse with their patients.

Prescription drug abuse is not a new problem, but one that deserves renewed attention. We hope this scientific report is useful to the public, particularly to individuals working with the elderly, who because of the number of medications they may take for various medical conditions, may be more vulnerable to misuse or abuse of prescribed medications.

Alan I. Leshner, Ph.D.
Director
National Institute on Drug Abuse

What are some of the commonly abused prescription drugs?

Although many prescription drugs can be abused or misused, there are three classes of prescription drugs that are most commonly abused:

- **Opioids**, which are most often prescribed to treat pain;
- **CNS depressants**, which are used to treat anxiety and sleep disorders;
- **Stimulants**, which are prescribed to treat the sleep disorder narcolepsy, attention-deficit hyperactivity disorder (ADHD), and obesity.

Opioids

What are opioids?

Opioids are commonly prescribed because of their effective analgesic, or pain-relieving, properties. Medications that fall within this class—sometimes referred to as narcotics—include morphine, codeine, and related drugs. Morphine, for example, is often used before or after surgery to alleviate severe pain. Codeine, because it is less efficacious than morphine, is used for milder pain. Other examples of opioids that can be prescribed to alleviate pain include oxycodone (OxyContin), propoxyphene (Darvon), hydrocodone (Vicodin), and hydromorphone (Dilaudid),

NIDA PRESCRIPTION DRUG RESEARCH DISSEMINATION

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DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

Partnerships Are Essential In Advancing the Science of Addiction & in Translating Prevention & Treatment Strategies into Practice

NIAAA
National Institute Alcohol Abuse and Alcoholism

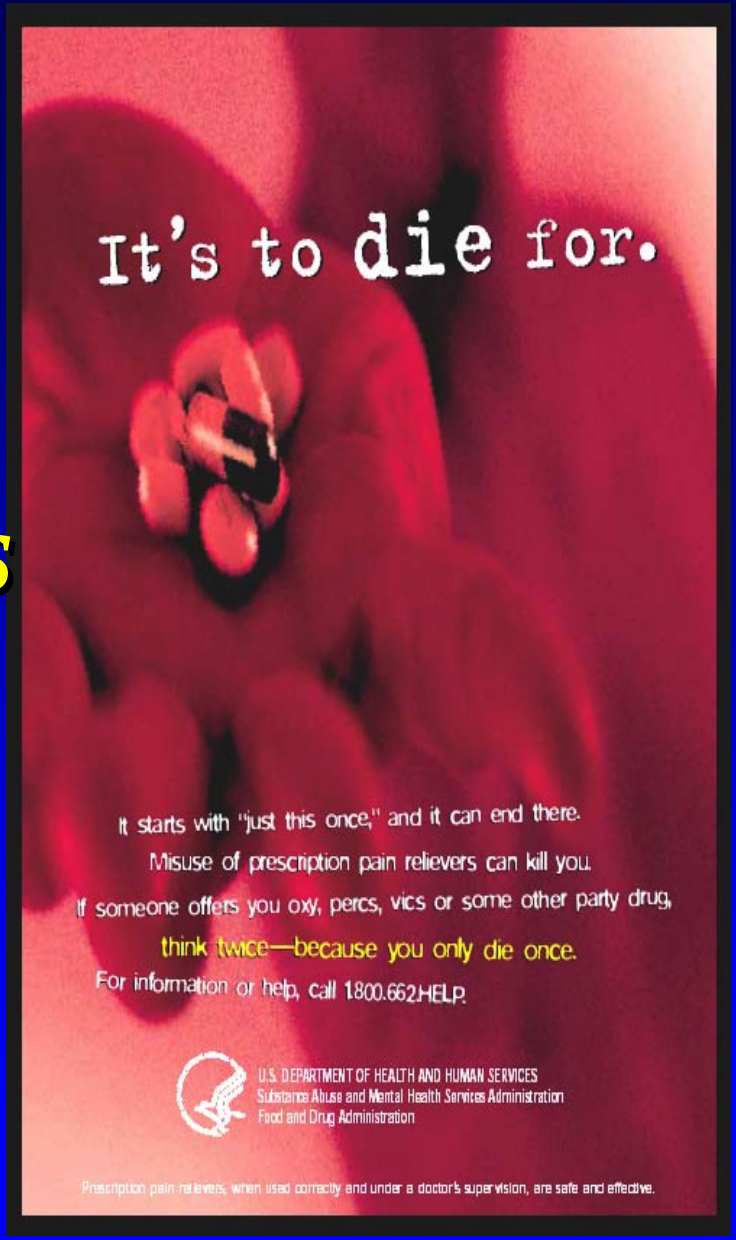
U.S. Department of Health & Human Services
SAMHSA

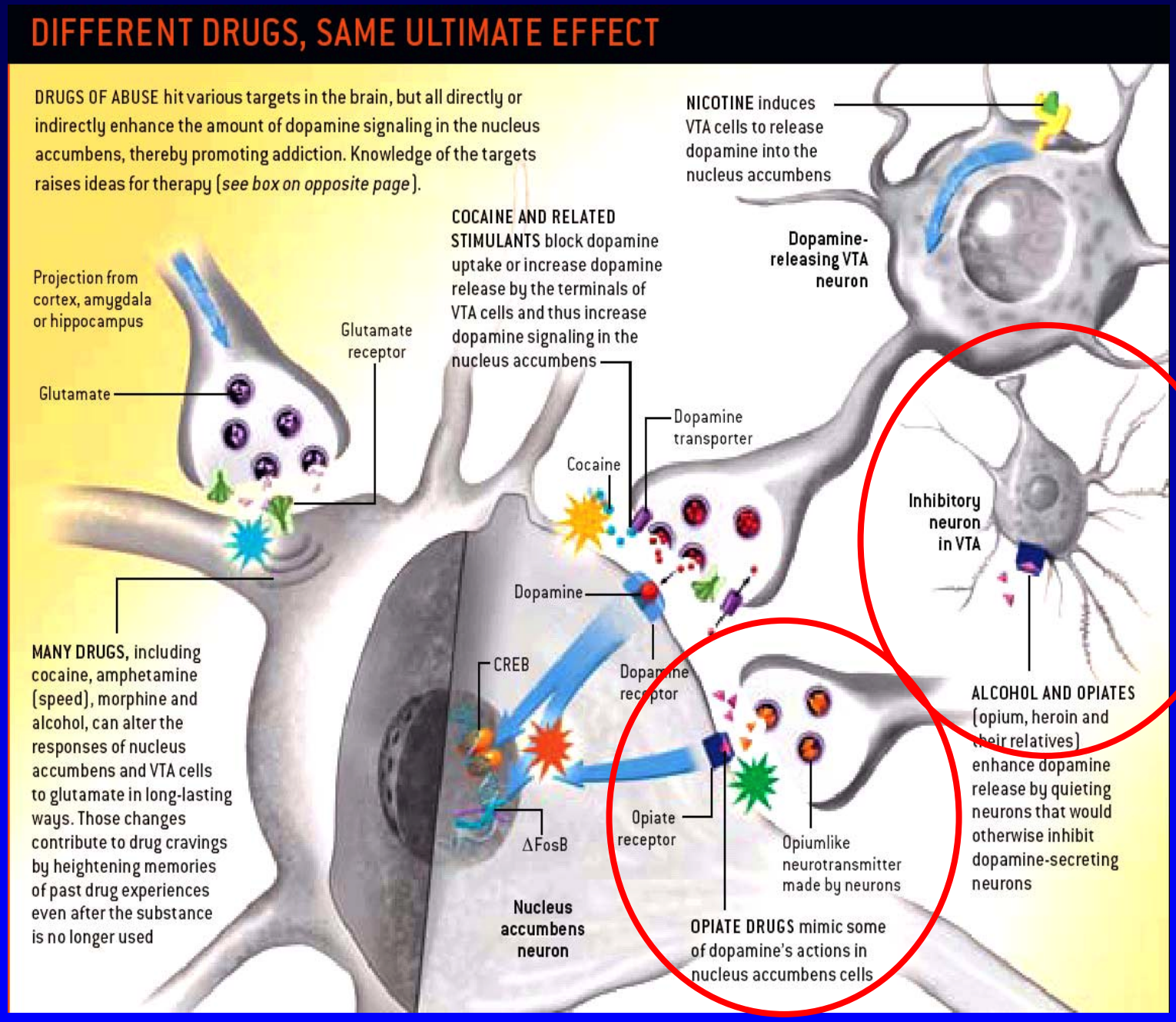
ONDCP
Office of National Drug Control Policy

DEA
U.S. DRUG ENFORCEMENT ADMINISTRATION

U.S Department of Justice
Office of Justice Programs
Partnerships for Safer Communities

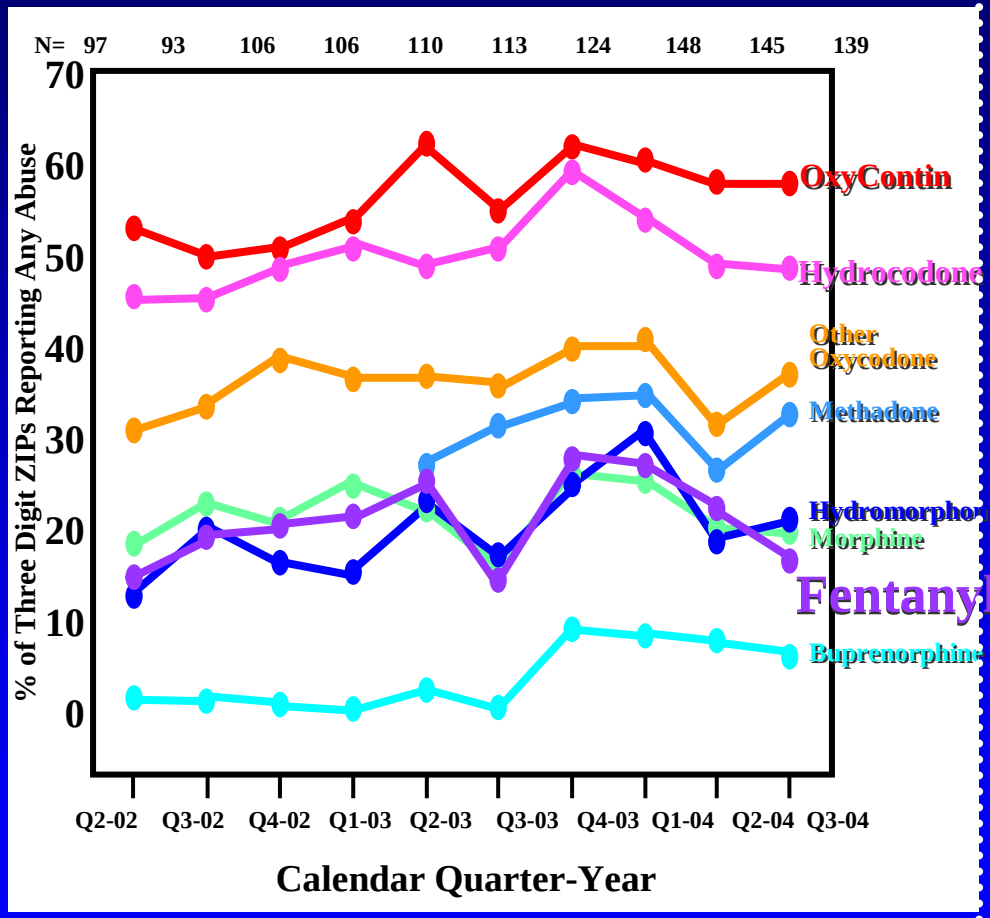
Why Has the Abuse of Prescription Drugs Been Increasing?





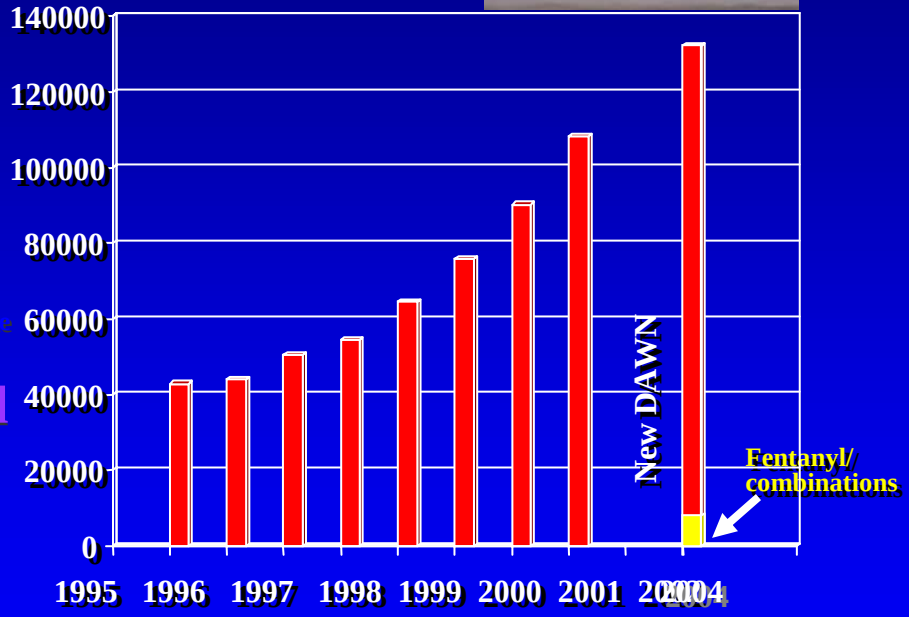
Source: Nestler, EJ and Malenka, RC, Scientific American, pp.78-85, March 2004.

Prevalence of Prescription Drug Abuse



Source: Cicero, TJ et el., The Journal of Pain. 6(10), pp. 662-672, October 2005.
Data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) system, Perdue Pharma.

Drug Abuse-Related ED Visits Involving Narcotic Analgesics

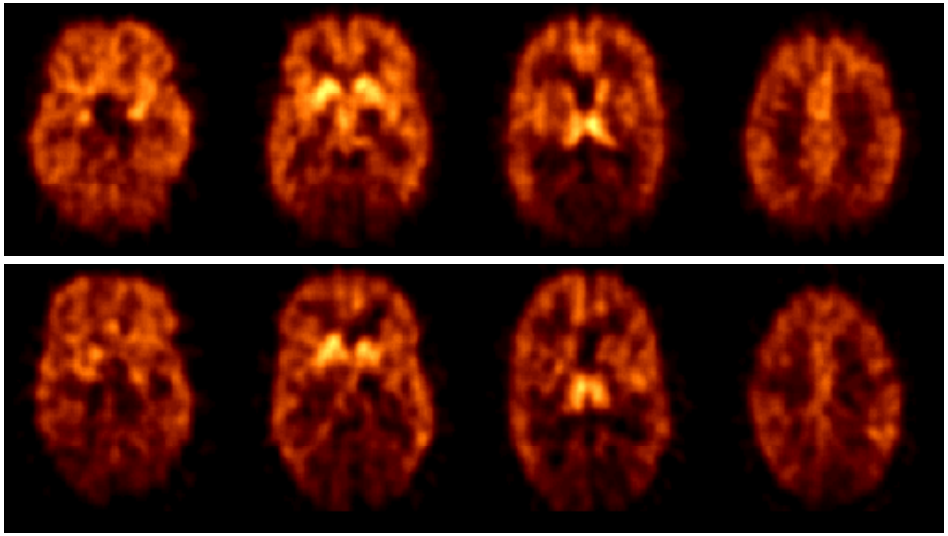


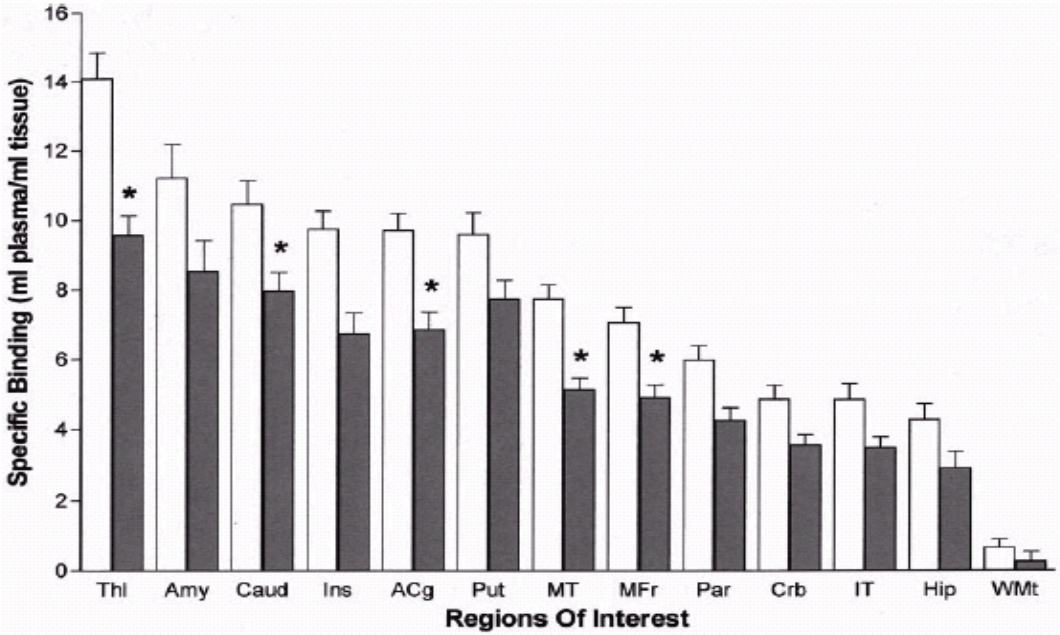
Source: SAMHSA, The DAWN Report: Narcotic Analgesics, 2002 Update, September 2004.

Specific Binding of [18F] cyclofoxy

Normal Control

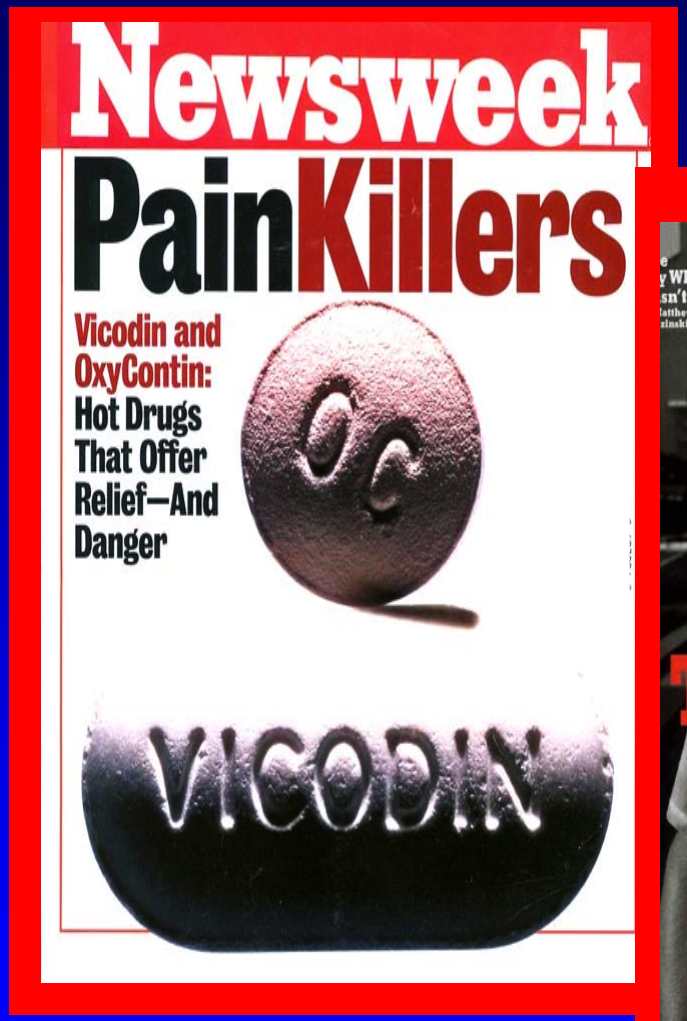
Methadone Maintained Patient

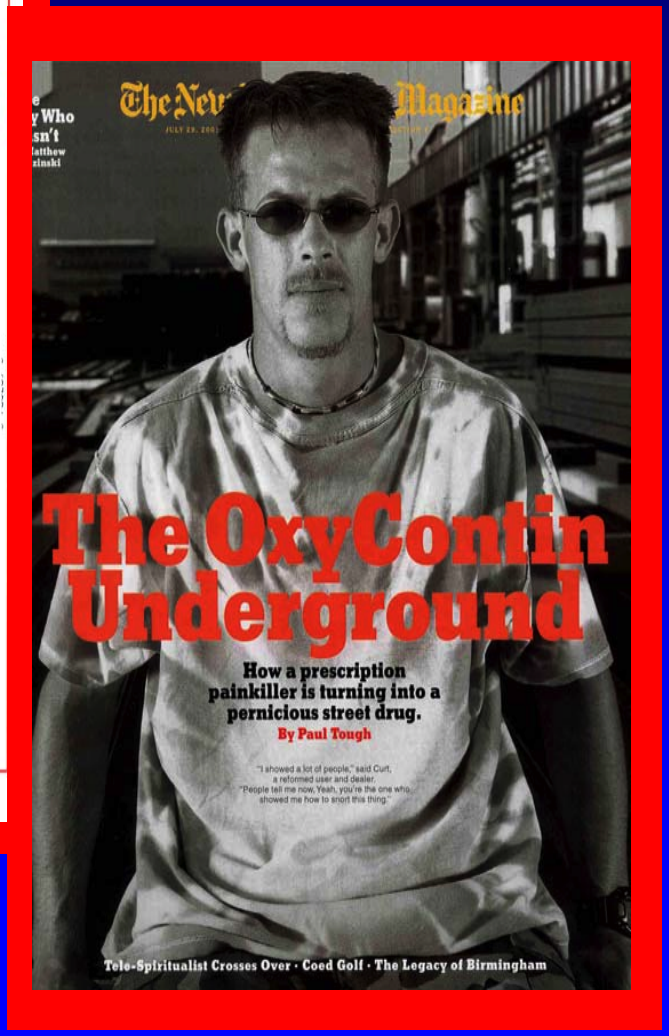




Source: Kling et al., JPET, 2000.

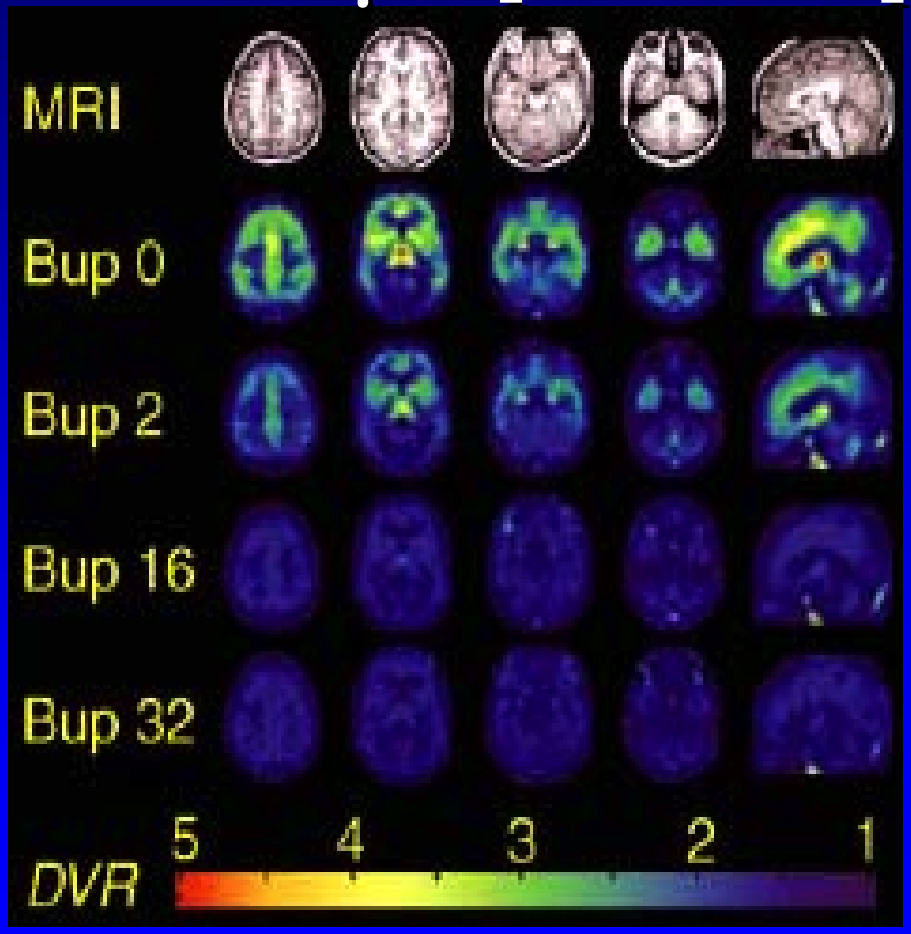
Increased Media Attention

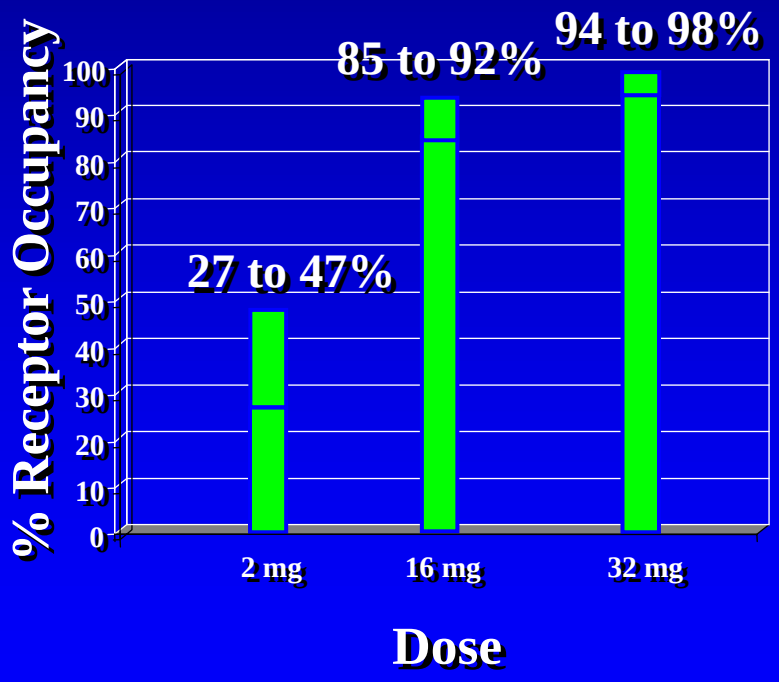




Medications to Treat Those Addicted

Effects of Buprenorphine Maintenance Dose on μ-Opioid Receptor Availability





Source: Greenwald, MK et al, Neuropsychopharmacology 28, 2000-2009, 2003.

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Students & Young Adults

Education resources & materials on drugs of abuse, marijuana, ecstasy, smoking, steroids, (more)

Parents & Teachers

Drug information & facts, education materials, curriculum guides, classroom tools, (more)

Researchers & Health Professionals

Grants & funding, research at NIDA, clinical trials, meetings, (more)

En Español

Recursos y materiales educativos sobre las drogas de abuso, manhuana, extasis,

Drugs of Abuse

- Acid/LSD
- Alcohol
- Club Drugs
- Cocaine
- Ecstasy/MDMA
- Heroin
- Inhalants
- Marijuana
- Methamphetamine
- PCP/Phencyclidine
- Prescription Medications
- Smoking/Nicotine

www.drugabuse.gov

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NIDA goes back to school

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Prescription Medications

Brief Description:	Prescription drugs that are abused or used for nonmedical reasons can alter brain activity and lead to dependence. Commonly abused classes of prescription drugs include opioids (often prescribed to treat pain), central nervous system depressants (often prescribed to treat anxiety and sleep disorders), and stimulants (prescribed to treat narcolepsy, ADHD, and obesity).
Street Names:	Commonly used opioids include oxycodone (OxyContin), propoxyphene (Darvon), hydrocodone (Vicodin), hydromorphone (Dilaudid), meperidine (Demerol), and diphenoxylate (Lomotil). Common central nervous system depressants include barbiturates such as pentobarbital sodium (Nembutal), and benzodiazepines such as diazepam (Valium) and alprazolam (Xanax). Stimulants include dextroamphetamine (Dexedrine) and methylphenidate (Ritalin).
Effects:	Long-term use of opioids or central nervous system depressants can lead to physical dependence and addiction. Taken in high doses, stimulants can lead to compulsive use, paranoia, dangerously high body temperatures, and irregular heartbeat.
Statistics and Trends:	According to NIDA's 2003 *Monitoring the Future* study, 9.3% of high school seniors used hydrocodone (Vicodin) in the past year. Source: NIDA InfoFacts: High School and Youth Trends.

Need a treatment referral?
Call 1-800-662-HELP or visit findtreatment.samhsa.gov

NIDA's Featured Publications

NIDA InfoFacts: Prescription Drugs and Pain Medications. Describes the health effects of abusing prescription drugs. For a general audience. (Report).

NIDA Research Report: Prescription Drugs: Abuse and Addiction. More detailed look at research findings on prescription drug abuse. For a general audience. (Report).

NIDA InfoFacts: Methylphenidate (Ritalin®). Overview of the health effects of Ritalin® when it is used for non-medical purposes. For a general audience. (Fact sheet).

See Also:

Other Recommended Reading

- Preventing Drug Use Among Children and Adolescents: A Research-Based Guide for Parents, Educators, & Community Leaders, 2nd edition
- NIDA InfoFacts: High School and Youth Trends
- NIDA InfoFacts: Hospital Visits (Trends and Statistics)
- NIDA InfoFacts: Nationwide Trends

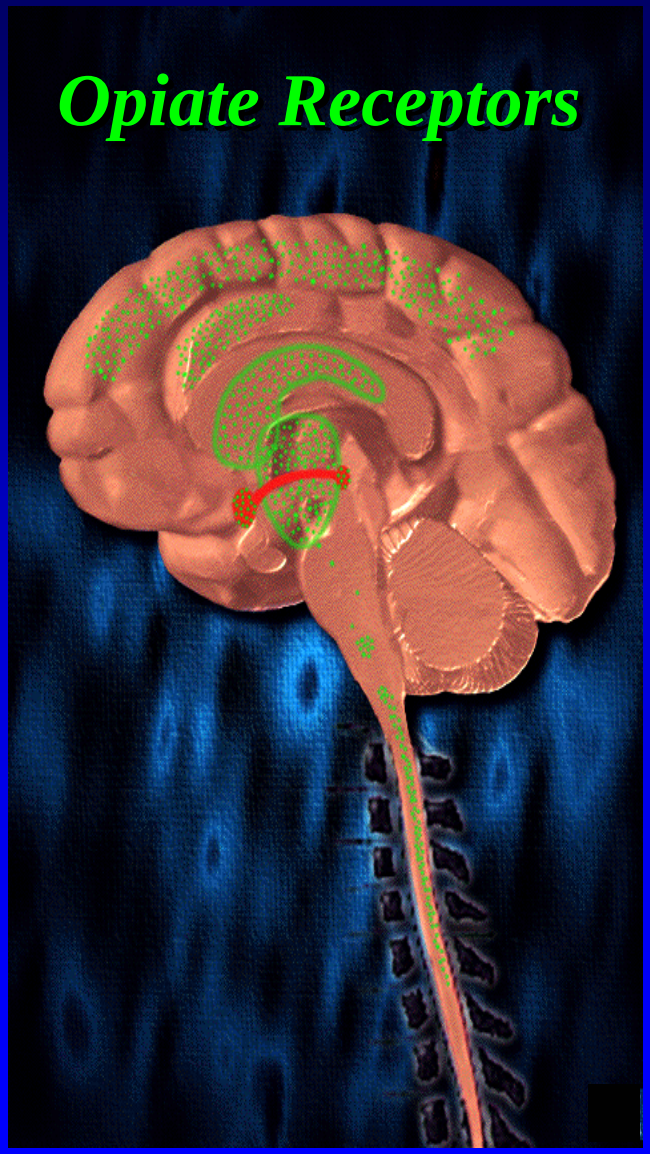
NIDA's Publication Series

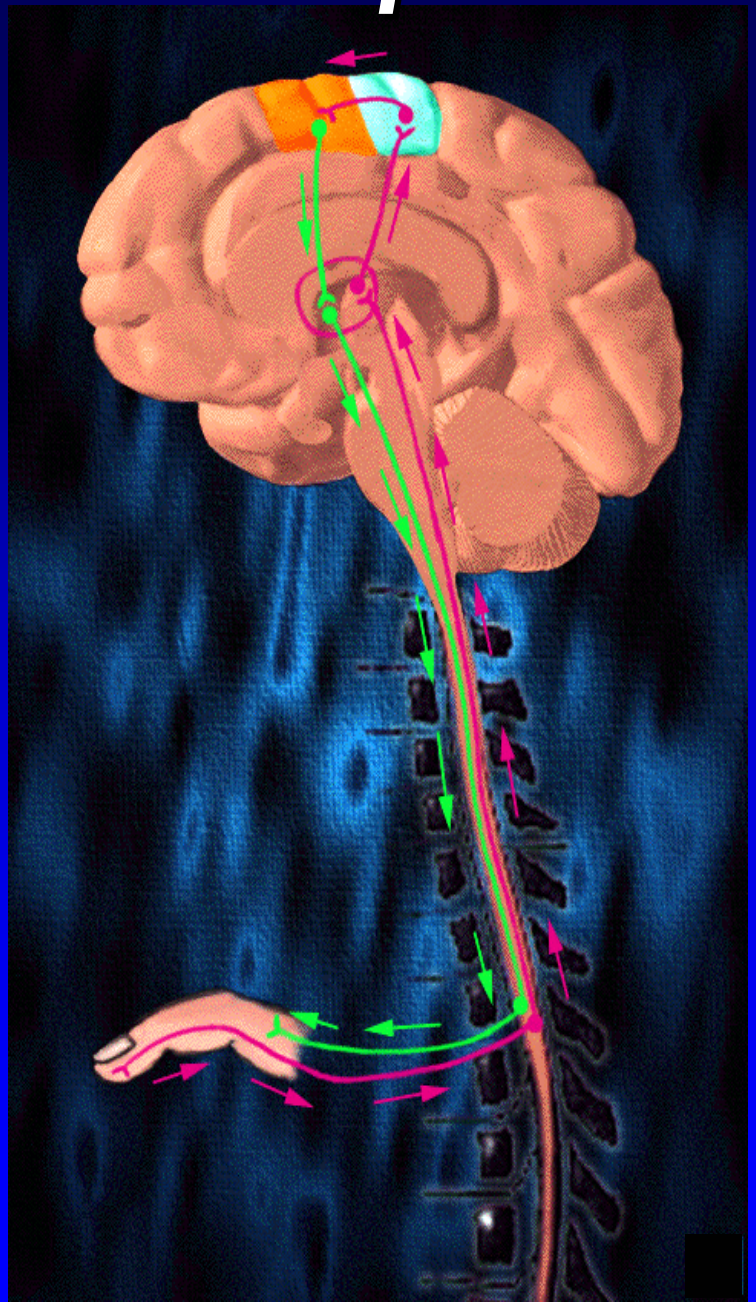
- Research Reports
- InfoFacts (fact sheets)
- NIDA Notes (newsletter)
- Science & Practice Perspectives (journal for researchers & health care providers)
- Mind Over Matter: Drug info for grades 5-9

Other Web Sites

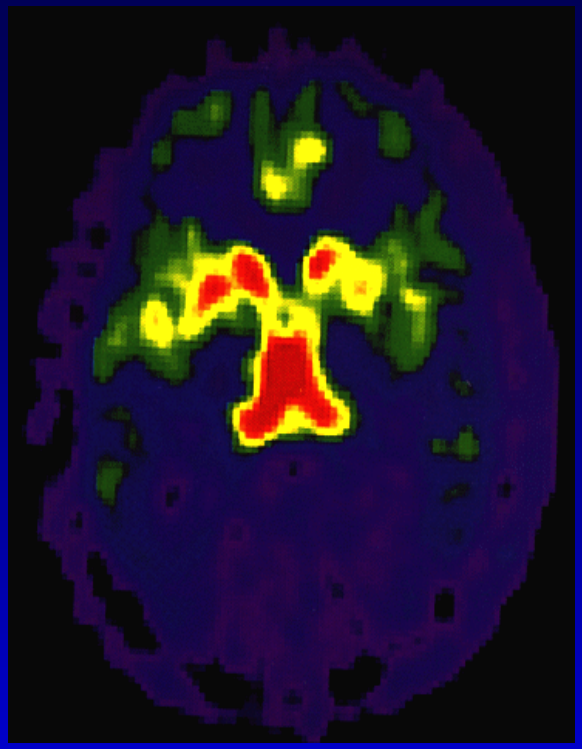
- ClubDrugs.org - a NIDA Companion Web site
- SteroidAbuse.org - a NIDA Companion Web site

Transmission of Pain Signals

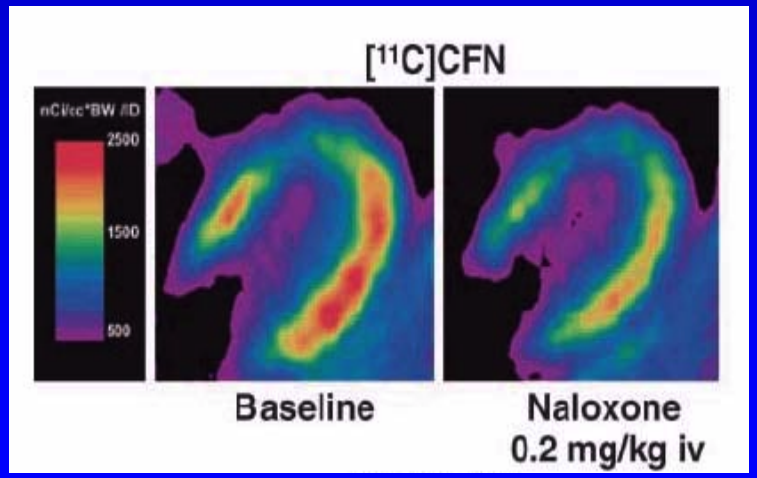




In Addition to Having Pain-Relieving Properties *Opiates, Including Fentanyl,* Affect Virtually All the Body's Organ Systems Including …

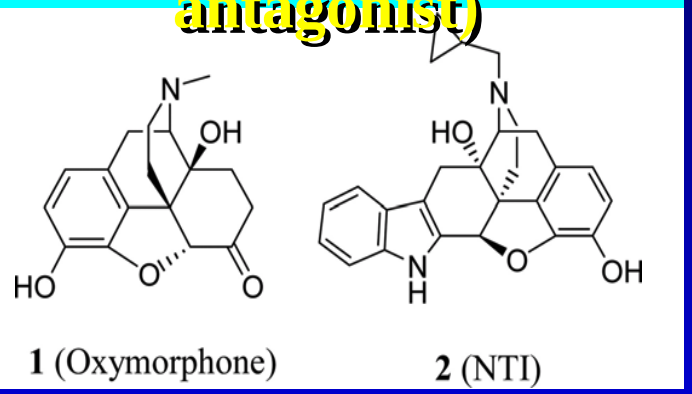


- Neuroendocrine
- Cardiopulmonary
- Gastrointestinal



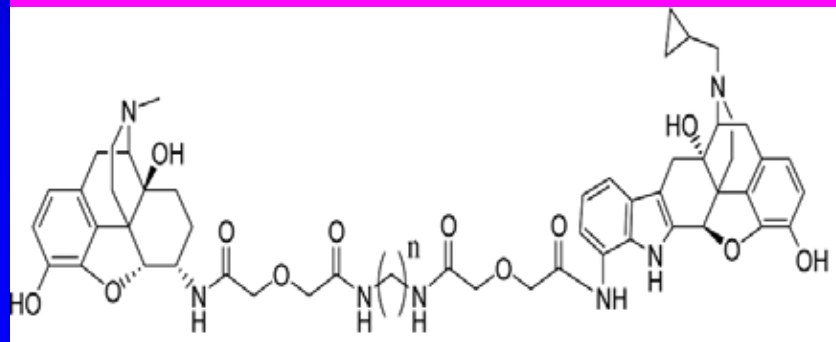
Involvement of δ Opioid Receptors in the Tolerance and Physical Dependence of μ Opioid Receptor Agonists

Key Pharmacophores: Oxymorphone (1, μ agonist) & NTI (2, δ antagonist)



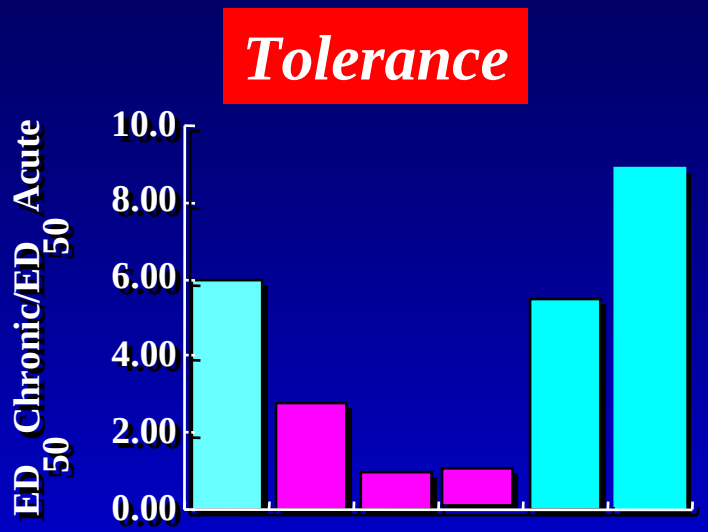
1 (Oxymorphone) 2 (NTI)

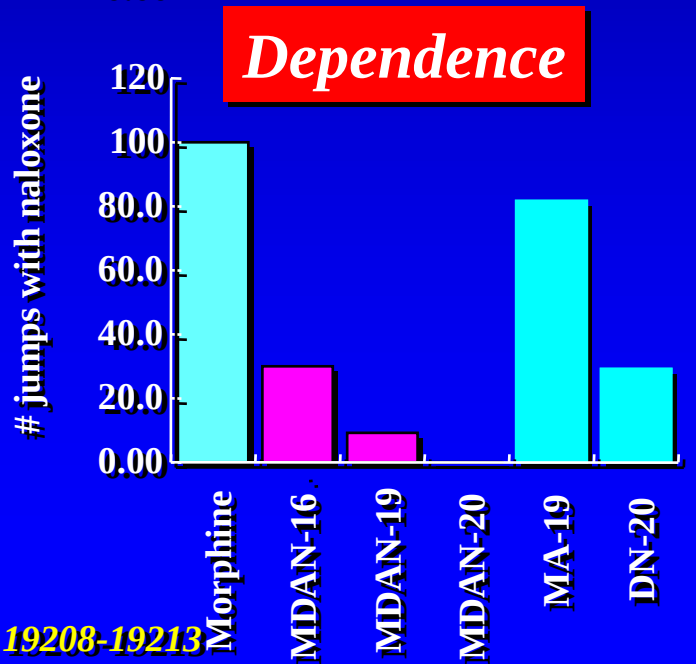
Final Compounds



3 - 8, MDAN Series

3(MDAN-16),
4(MDAN-17),
5(MDAN-18),
6(MDAN-19),
7(MDAN-20),
8(MDAN-21),





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Daniels, David J. et al. (2005) PNAS. USA 102, 19208-19213