



Singer Amy Winehouse performs in Dingle

Wall Street Journal

“THEY TRIED TO MAKE ME GO TO REHAB”

Mary ET Boyle, Ph. D.
Department of Cognitive Science
UCSD

THE WALL STREET JOURNAL.

A Tribute to Amy Winehouse

Updated July 20, 2012, 5:42 a.m. ET

ARTS & ENTERTAINMENT

One wet and windy December evening in 2006, a 23-year-old Amy Winehouse arrived in Dingle, a fishing town of 2,000 souls in County Kerry, southwest Ireland, "at the edge of the known world before we found out that it was round," as one resident describes it. There, in front of some 70 people gathered in the small St. James Church, Winehouse performed songs that have forever inscribed her in the musical firmament—"Back to Black," "Tears Dry On Their Own," "You Know I'm No Good."

Singer Amy Winehouse performs in Dingle



South Wind Blows

With her second album "Back to Black" not even two months old, the English singer was in Dingle to record "Other Voices," an Irish TV show that every winter brings musicians from all over the world to this remote corner of Europe. This month, a year after her premature death at 27 from alcohol poisoning, those few hours she spent in the town

have been turned into a touching tribute to the tormented artist.

"Arena: Amy Winehouse—The Day She Came to Dingle," by Irish director Maurice Linnane, brings together unseen footage from Winehouse's heartfelt performance, archival recordings of her musical idols and the recollections of locals who met her that evening.

"We decided we would just tell a story of that day, of what happened when Amy came to Dingle," says Mr. Linnane, whose film stays away from the rumors and controversies that surrounded the soul artist's last years. "My rule was, if they weren't in the room that day, they weren't allowed to talk about it."

So we hear about Winehouse from Paddy Kennedy, the Dingle bus driver who picked the singer up at the airport and thought she was Amy Winehouse's daughter. "I hadn't a clue who the lady was," he recalls in the documentary. Mr. Linnane adds that she sang in the back of the bus, "half the way from Dingle to Cork."

We hear from Aoife Woodlock, a music producer on "Other Voices," whom Winehouse asked to hold her hair while she backcombed it for her signature beehive style. "She came with her spindly, little legs and her mental hair, and sung her heart out, in Kerry, for us," Ms. Woodlock says.

no

no

no

THE WALL STREET JOURNAL.

Amy Winehouse's Killers

Her Talent as Fierce as her Heartache.

By SALLY SATTEL Jul. 27, 2011

Her addictions killed her. That was it that quickly formed following the death of Amy Winehouse, the British soul singer who discovered in her London home on Saturday. A released Monday were inconclusive. But, prior drinking massive quantities of alcohol in the day

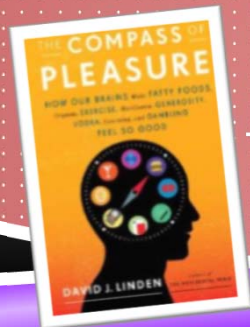


“As for Ms. Winehouse, her talent was as fierce as her heartache.”

— Sally Sattel

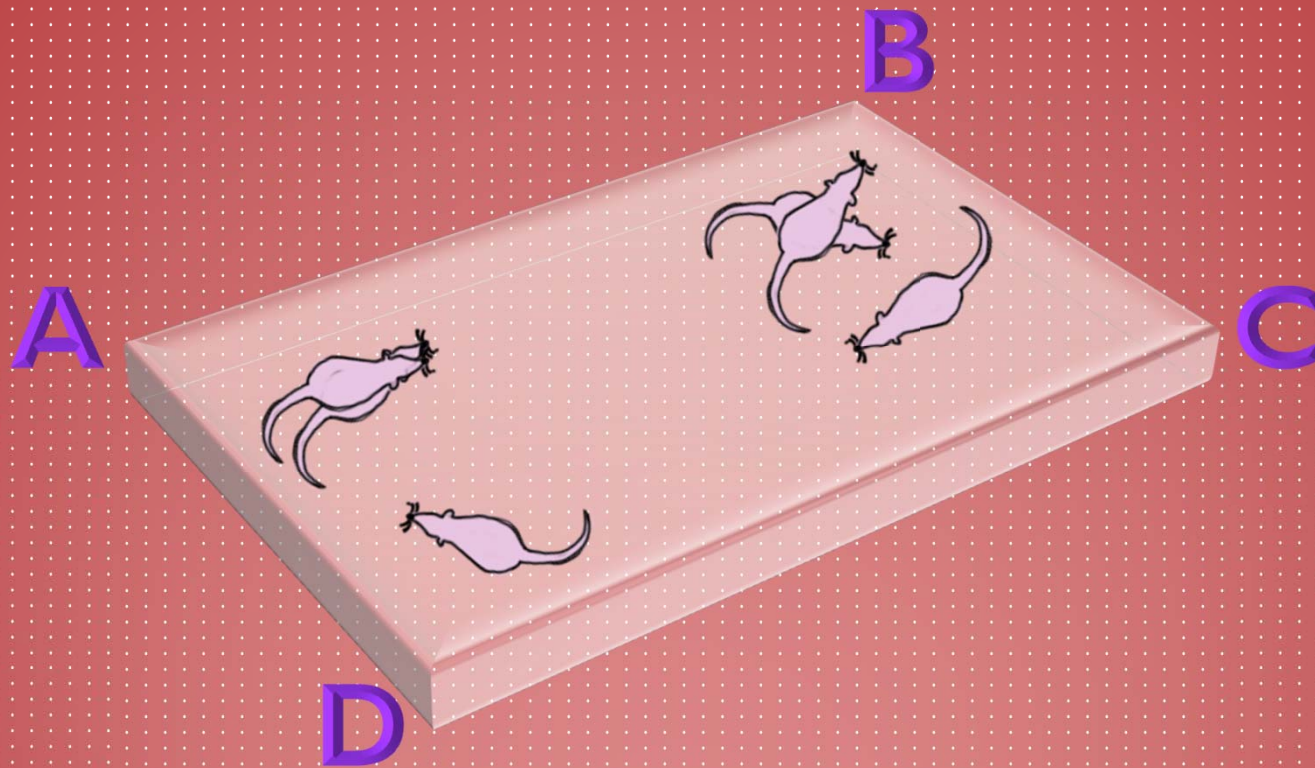


“ The rat in question was placed in a large rectangular box with corners labeled A, B, C, and D and was allowed to explore freely. Whenever the rat went to corner A, Olds pressed a button that delivered a brief, mild electrical shock through the implanted electrodes. (Unlike the rest of the body, brain tissue does not have the receptors that allow for pain detection, so such shocks don't produce a painful sensation within the skull.) After a few jolts, the rat kept returning to corner A and finally fell asleep in a different location. The next day, however, the rat seemed even more interested in corner A than the others. Olds and Milner were excited: They believed that they had found a brain region that, when stimulated, provoked general curiosity. However, further experiments on this same rat soon proved that not to be the case. By this time, the rat had acquired a habit of returning often to corner A to be stimulated. The researchers then tried to coax the rat away from corner A by administering a shock every time the rat made a step in the direction of corner B. This worked all too well—within five minutes, the rat relocated to corner B. Further investigation revealed that this rat could be directed to any location within the box with well-timed brain shocks—brief ones to guide the rat to the target location and then more sustained ones once it arrived there. ”



The Compass of Pleasure by David J. Linden

The next day...





ingestion

Preferred for many drugs

Easy and safe

Carried via bloodstream

Unpredictable dosage



injection

Preferred by medical professionals

Predictable: fast; strong drugs

Drug users: IV injection

Dangerous – allergic rxn or overdose.



inhalation

Through the lungs
into the capillaries

Anesthetics; tobacco
& marijuana

Difficult to regulate
dose

Can damage lungs

absorption

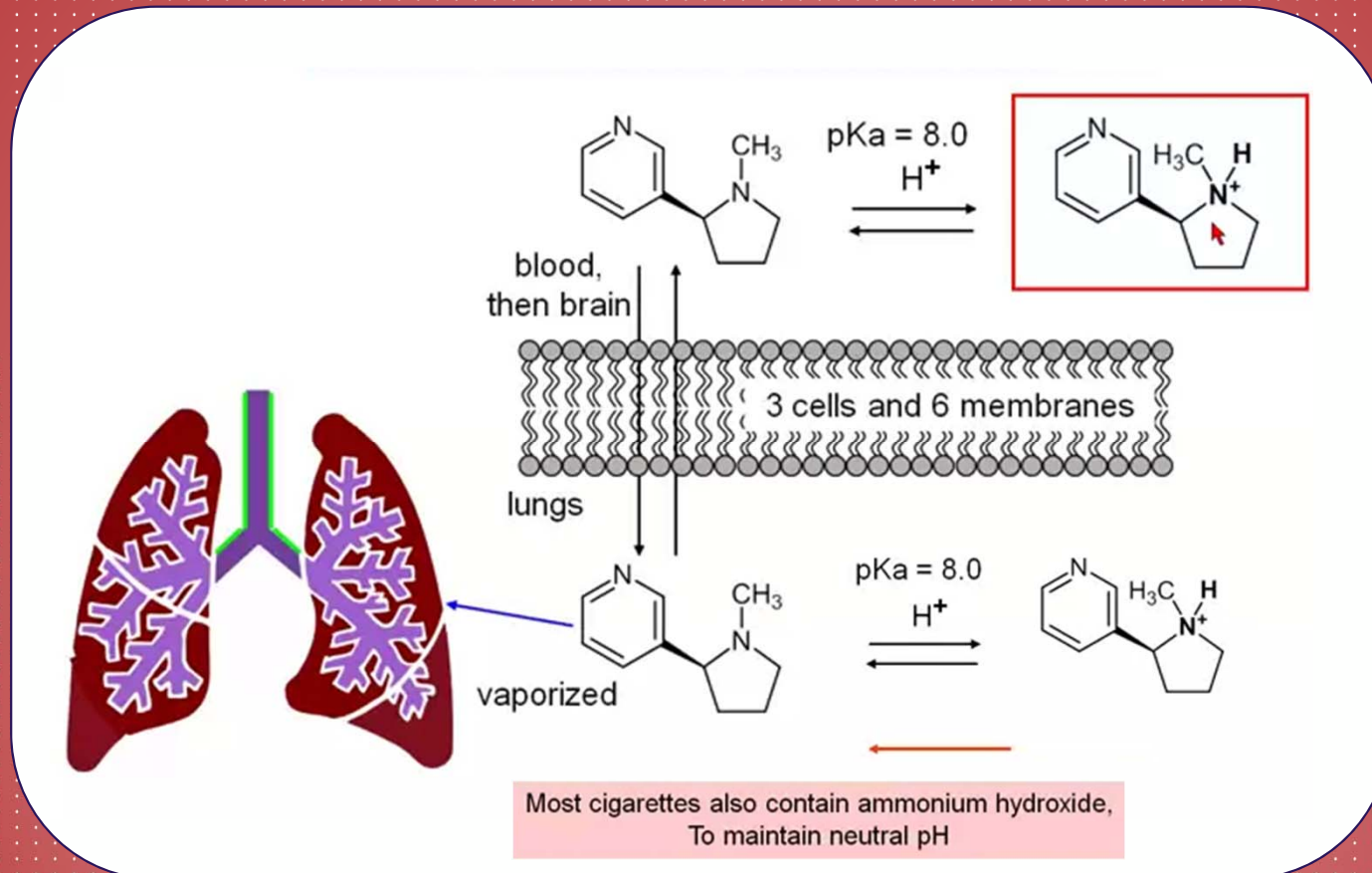
Mucous membranes

Nose; mouth

Snort cocaine

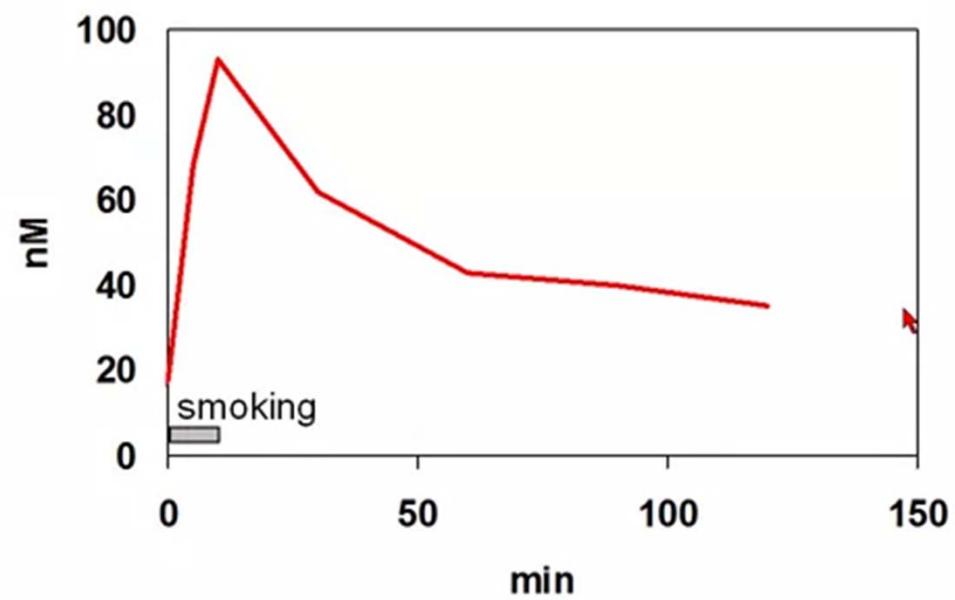


NICOTINE'S PATH TO THE BRAIN



From H. Lester, CalTech

Blood nicotine concentrations during and after a cigarette



CLASSIFICATION OF DRUG ACTIONS

stimulants

- Enhance and speed up CNS activity
- Temporary effect → crash

depressants

- Slow down or impair CNS activity

Hallucinogens

- Distort sensory information processing

Drug Addiction, Dysregulation of Reward, and Allostasis

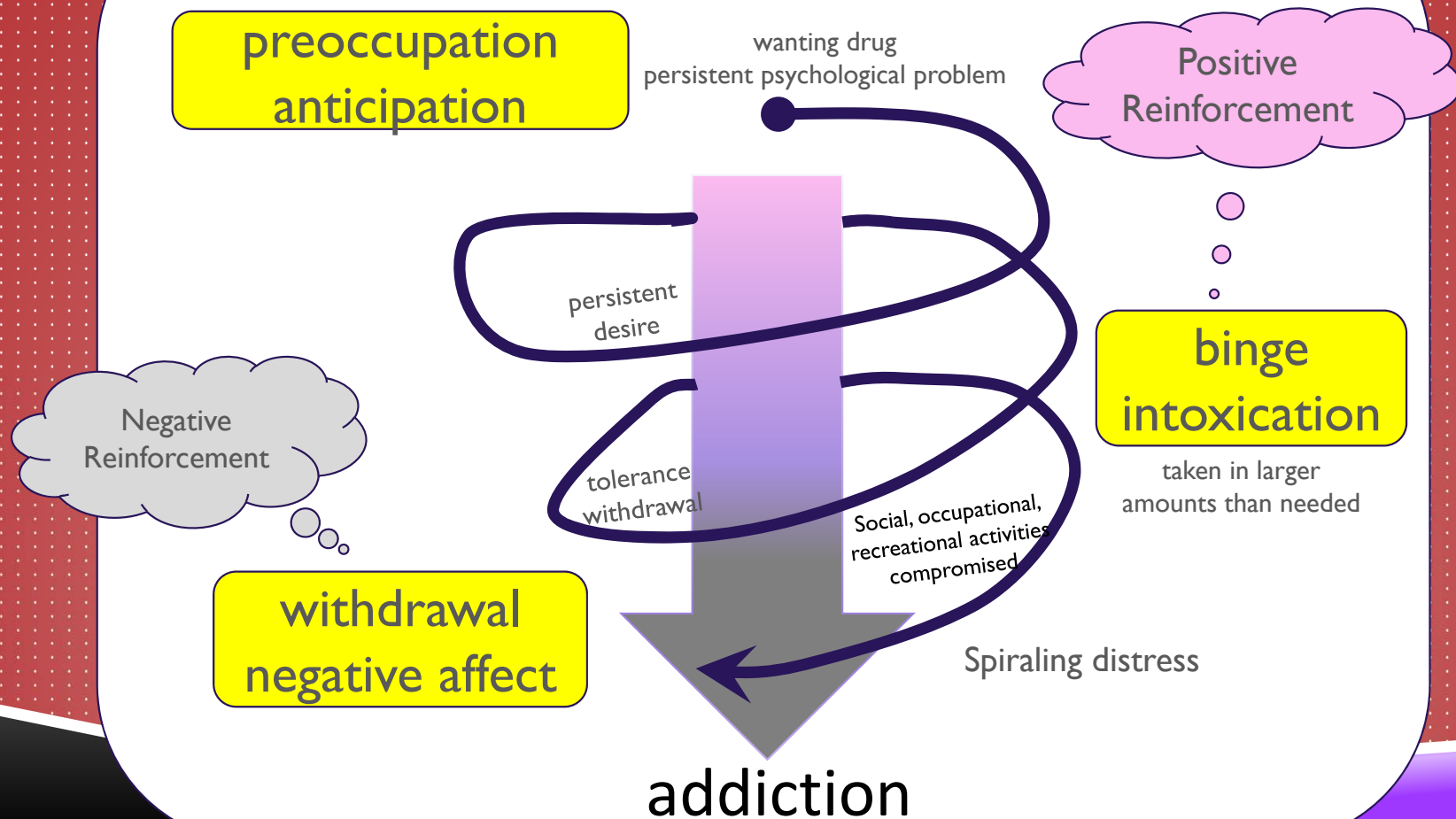
George F. Koob, Ph.D., and Michel Le Moal, M.D., Ph.D.

“Drug addiction is a chronically relapsing disorder that is defined by two major characteristics: **a compulsion to take the drug with a narrowing of the behavioral repertoire toward excessive drug intake**, and **a loss of control in limiting intake** (American Psychiatric Association 1994; World Health Organization 1992).

An important challenge for neurobiological research is to understand the **neuroadaptive differences between controlled drug use and loss of control**, and by extension, the molecular, cellular and system processes that lead to addiction (Koob and Le Moal, 1997).”

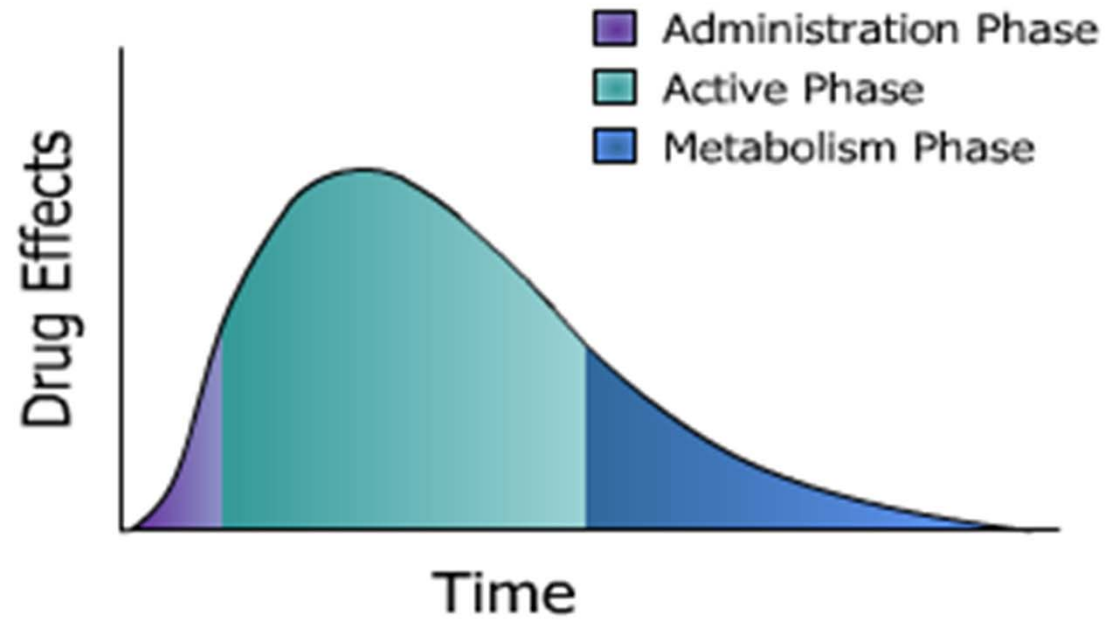
Neuropsychopharmacology (2001) **24**, 97–129

The spiraling distress/addiction cycle

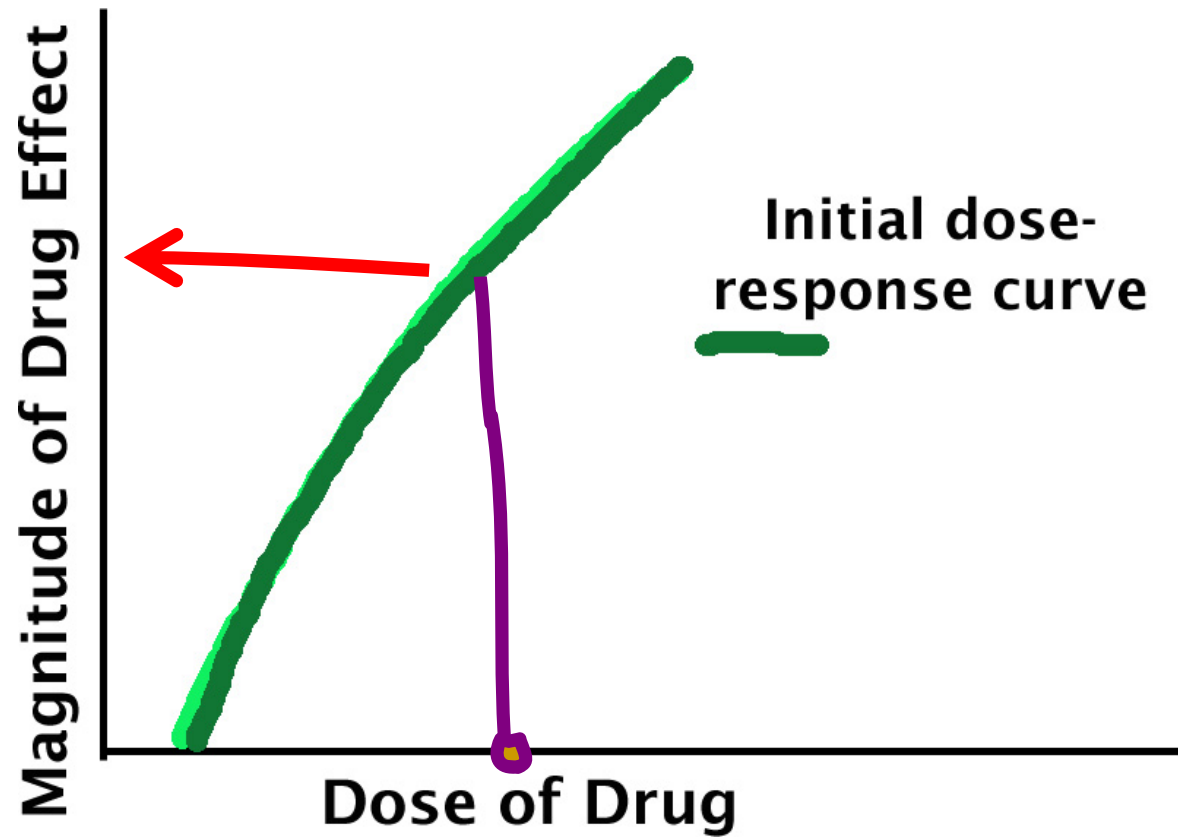


Adapted from Koob & Le Moal (2001) *Neuropsychopharmacology* 24, 97–129

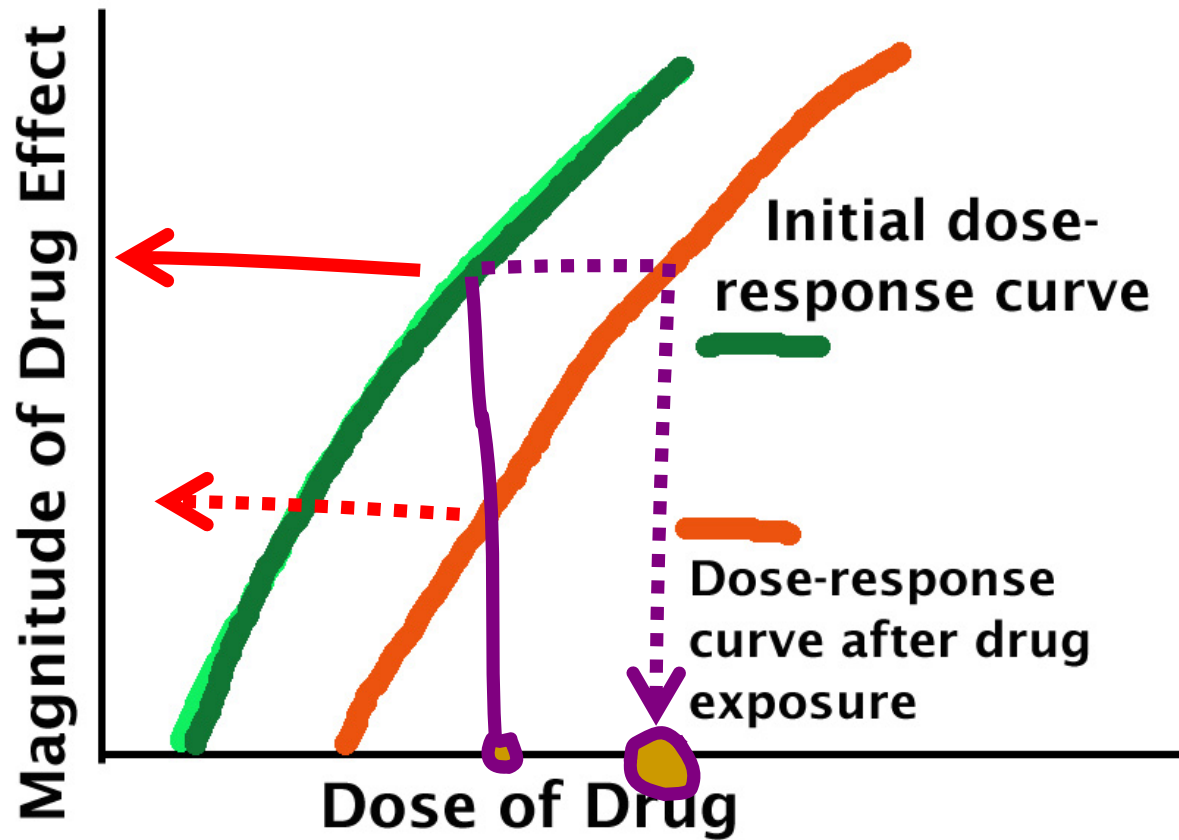
Drug Effects Over Time



DOSE RESPONSE CURVE...



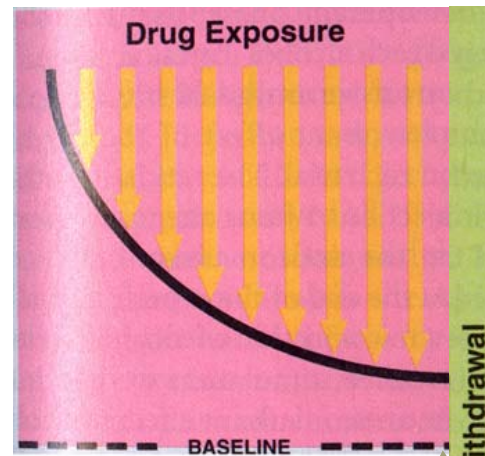
DOSE RESPONSE CURVE...



TOLERANCE & WITHDRAWAL

REWARD SYSTEM DYSREGULATION

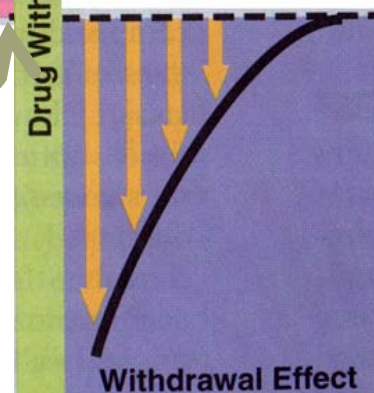
Drug effect decreases with increased exposure



Drug exposure leads to the development of **adaptive** neural changes that produce tolerance by counteracting the drug effect.

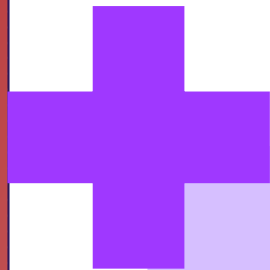
Withdraw from drug

With no drug to **counteract** them, the neural adaptations produce withdrawal effects **opposite** to the effects of the drug.



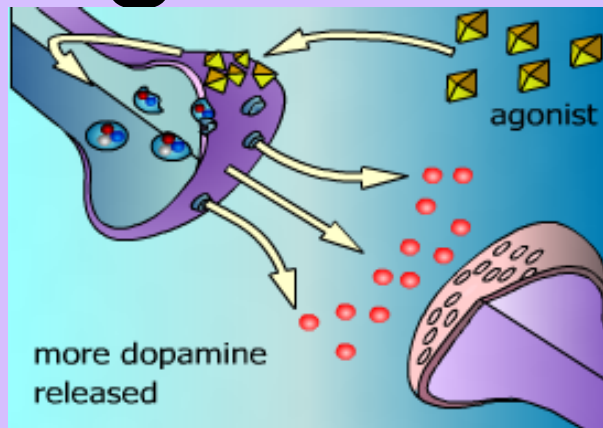
The magnitude of the withdrawal effect is **proportional** to the tolerance of the drug.

ALTERING THE FUNCTION OF NEUROTRANSMITTERS CAN CHANGE BEHAVIOR.



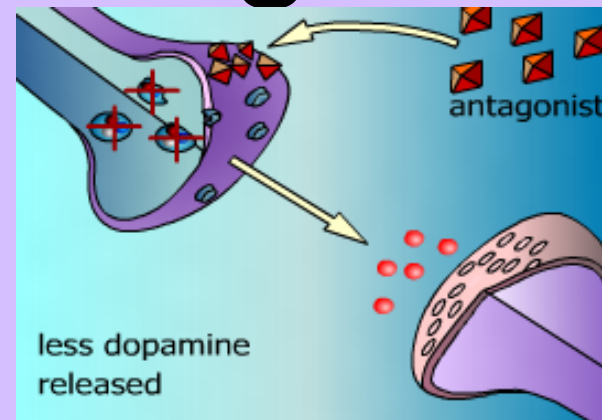
mimics or
facilitates
the release

agonist

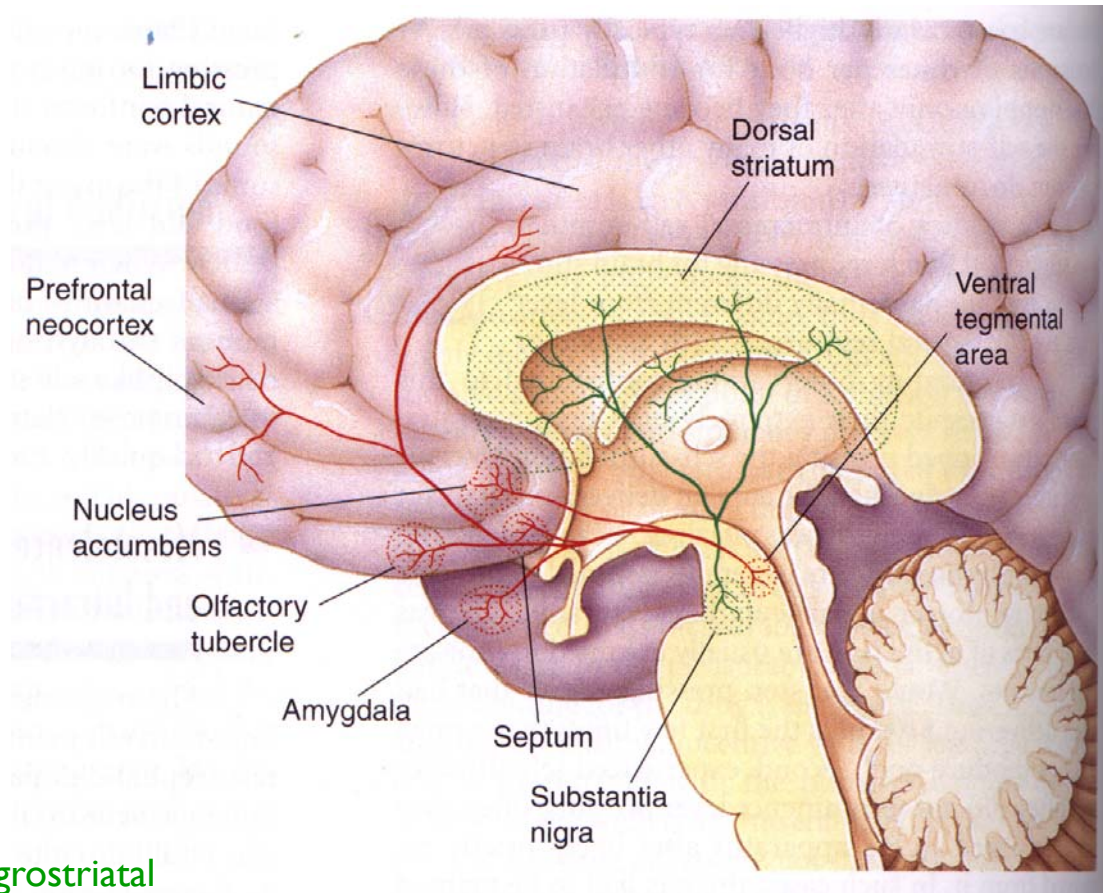


oppose
or *blocks*
the release

antagonist



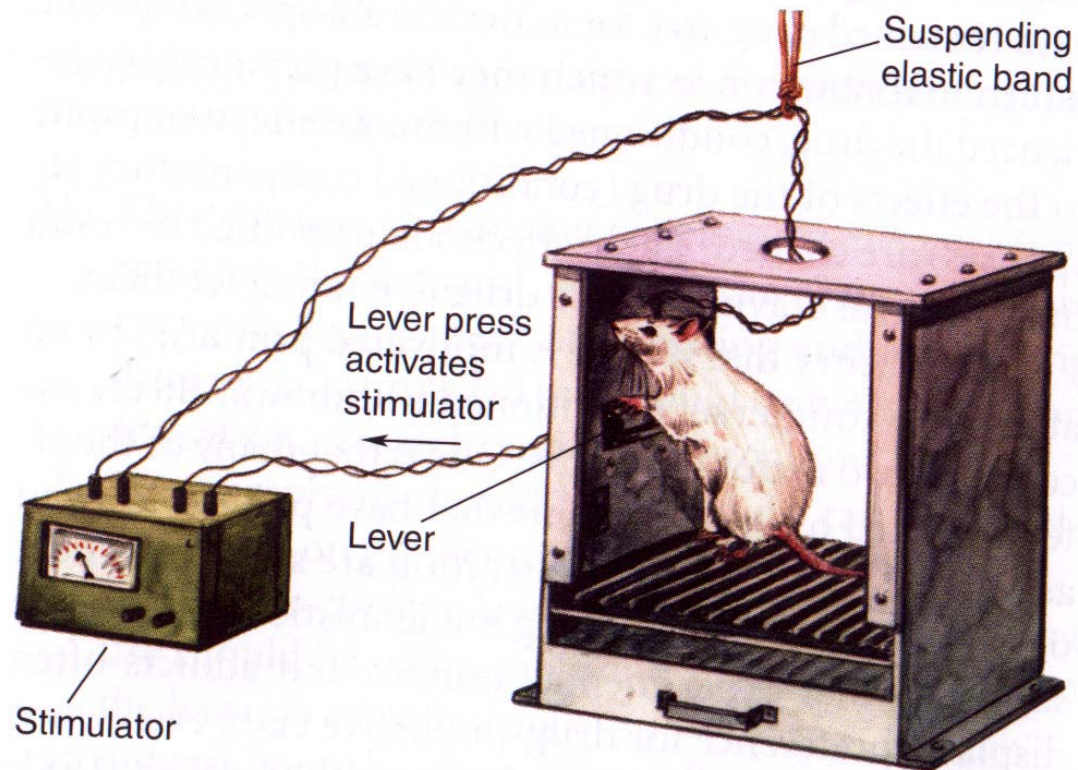
MESOTELECEPHALIC DA SYSTEM



Nigrostriatal
pathway

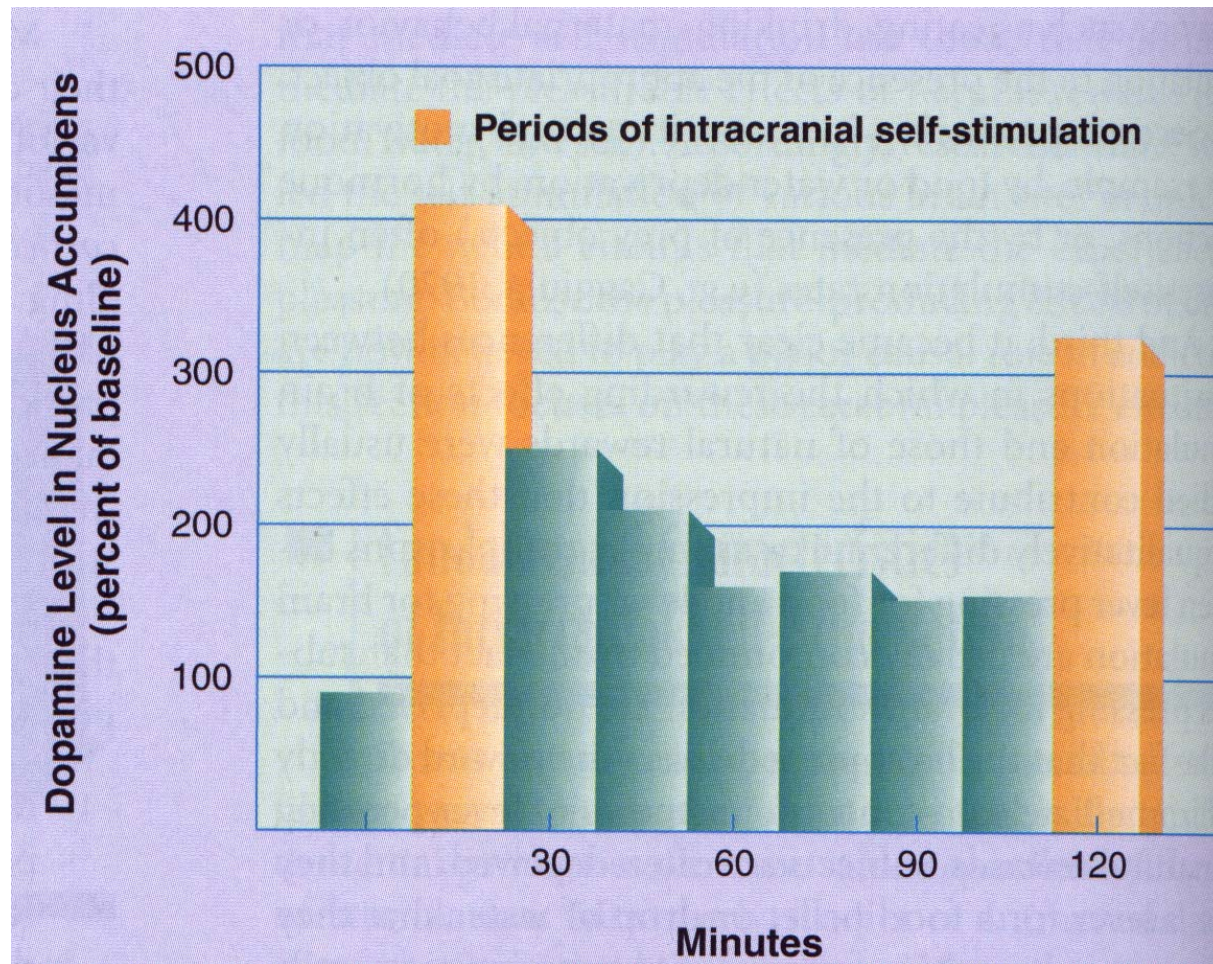
Mesocorticolimbic
pathway

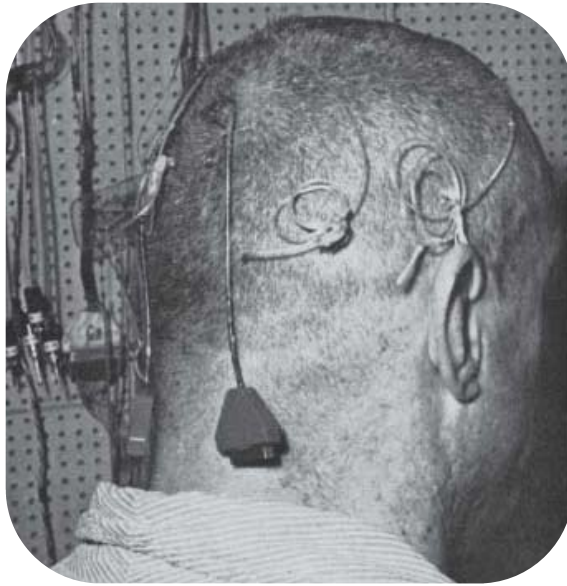
PLEASURE CENTERS OF THE BRAIN...



ICSS: intracranial self-stimulation

INCREASE IN DA RELEASE IN N.ACCUMBENS...





chronically implanted electrodes, one of which activated the medial forebrain bundle passing through the septum, a key part of the pleasure circuit. From Robert G. Heath, "Depth recording and stimulation studies in patients," in Arthur Winter, ed., *The Surgical Control of Behavior* (Springfield, Il.: Charles C. Thomas, 1971), 24. Reprinted with permission from Charles C. Thomas.

nature
neuroscience

Is there a common molecular pathway for addiction?

Eric J Nestler

Eric Nestler (2005) *Nature Neuroscience* 8, 1445 - 1449

Drugs of abuse

Diverse chemicals

Distinct targets & effects

Cause common effects:

acute

chronic

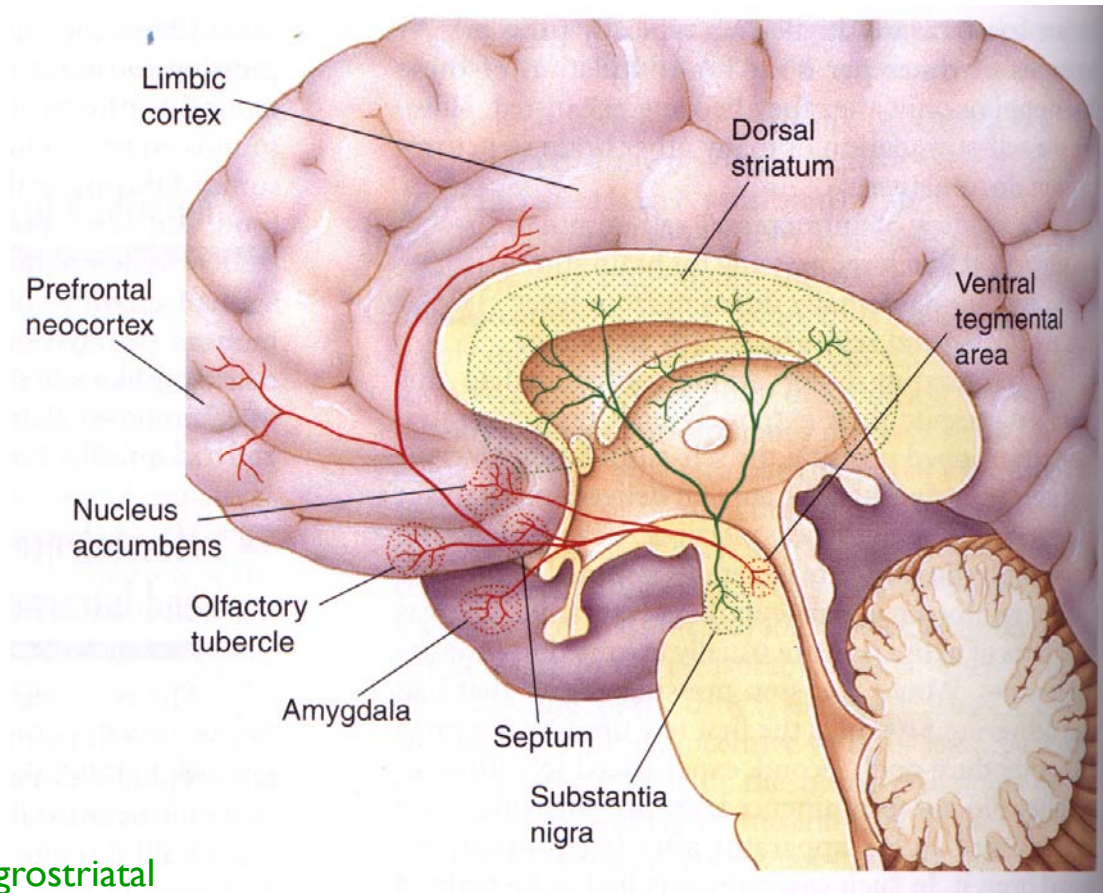
Characterized by:

immediate reward → repeated use → addiction

Loss of control over drug use.

Negative emotional symptoms withdrawal.

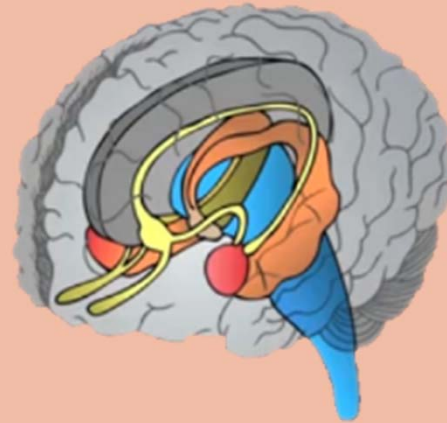
MESOTELECEPHALIC DA SYSTEM



Nigrostriatal
pathway

Mesocorticolimbic
pathway

Common
actions on brain
reward circuits



All drugs of abuse
affect **the limbic
system.**

Mesocorticolimbic
system →
dopaminergic
neurons in the
ventral tegmental
area → NAc.

Examples of common effects on the VTA-NAc.

- Stimulants directly *increase* dopaminergic transmission in the NAc.
- Opiates do the same (indirectly) they inhibit GABAergic interneurons in the VTA, which *disinhibits* VTA dopamine neurons.
- Opiates also *directly* act on opioid receptors on NAc neurons

