

Drug Addiction: A Brain Disease

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Trieste, 2009

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Levels of Drug Use

- Recreational use
- Tolerance
- Dependence
- Abuse (Intoxication, harm, illegal use)
- Addiction (loss of self control)

How does drug use lead to
addiction?

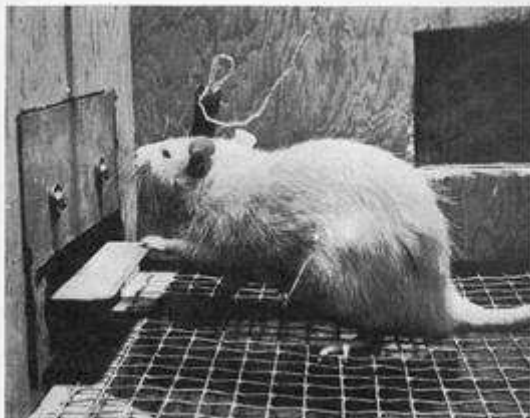
Addictive drugs act on the brain
to produce reward:
addiction is pathological learning

Addiction is harmful learning.

- 1) Drug consumption + environmental cues
- 2) Drug effect on brain → Reward
- 3) Reward → ↑Drug consumption
- 4) Environmental cues → Drug seeking

How do drugs produce reward?

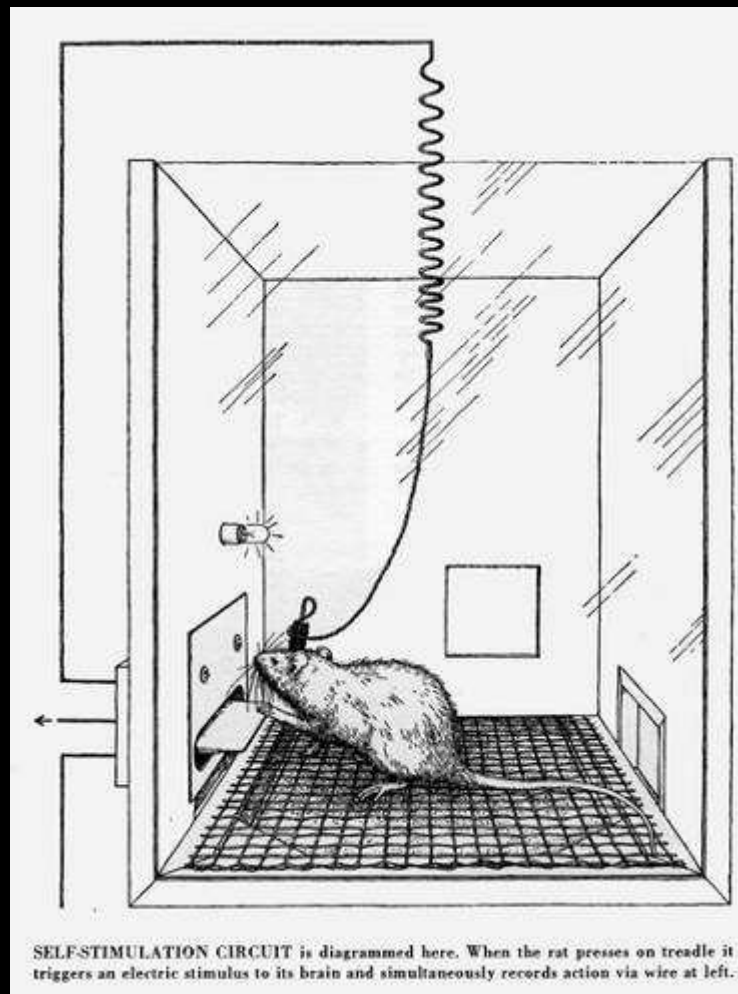
Intracranial self-stimulation



RAT SEEKS STIMULUS as it places its paw on the treadle. Some of the animals have been seen to stimulate themselves for 24 hours without rest and as often as 5,000 times an hour.



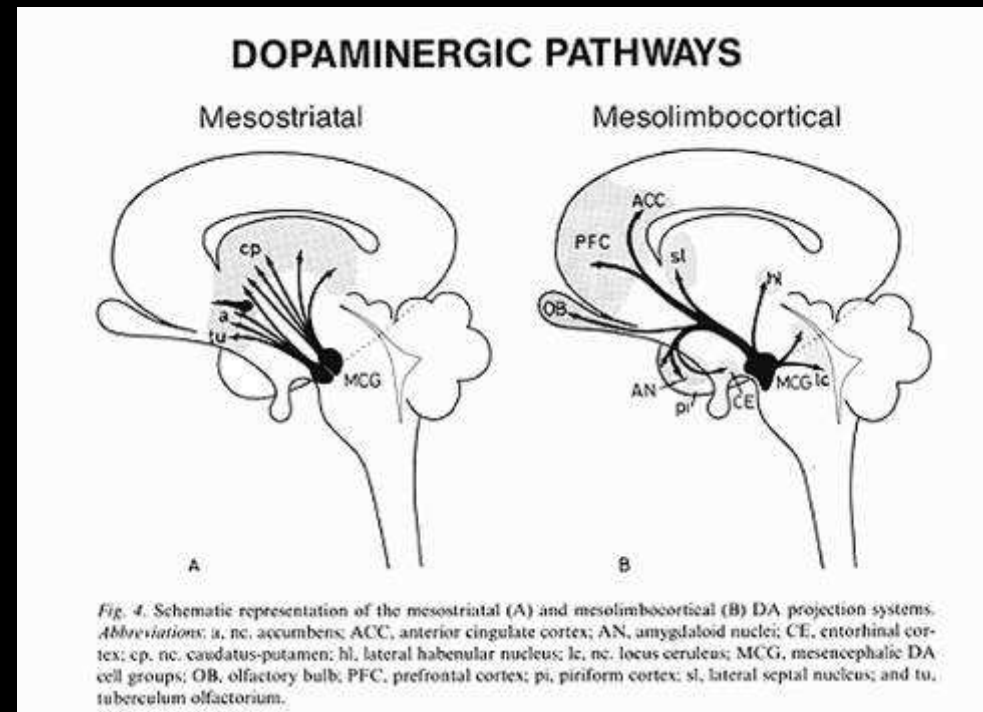
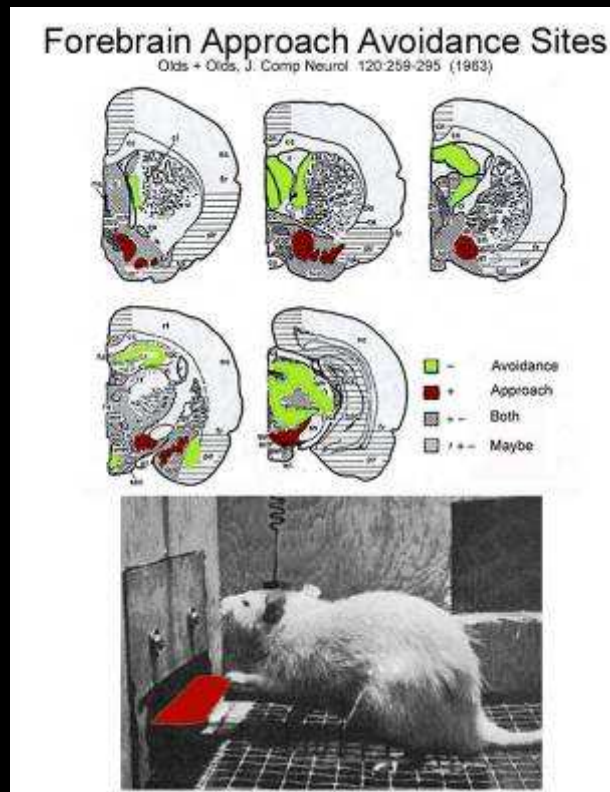
RAT FEELS STIMULUS as it presses on treadle. Pulse lasts less than a second; the current is less than .0005 ampere. The animal must release lever and press again to renew the stimulus.



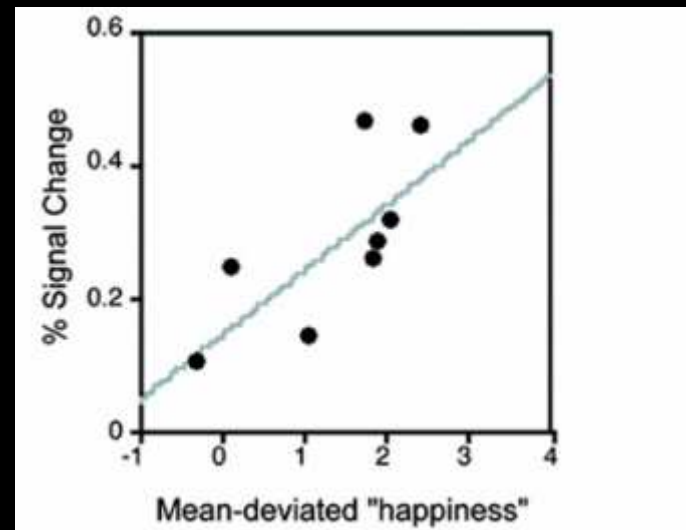
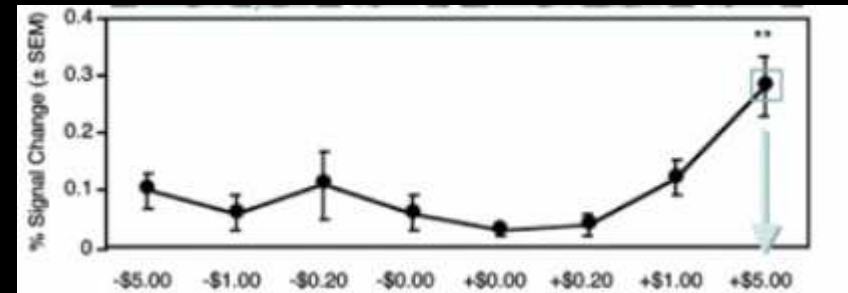
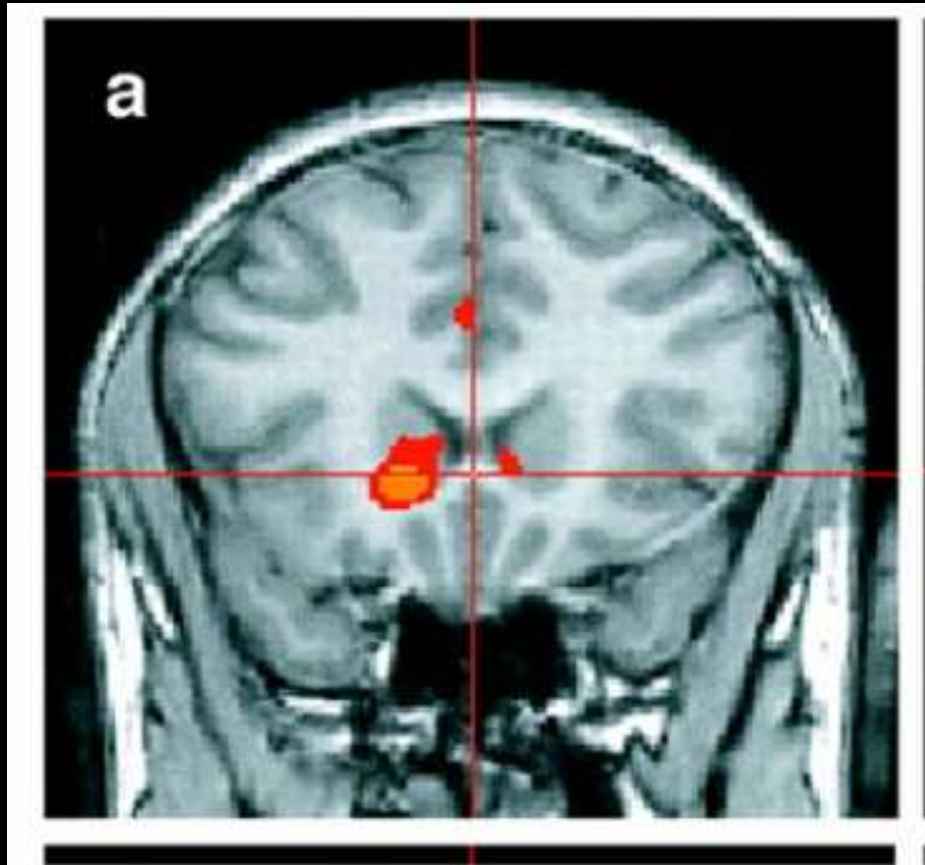
SELF-STIMULATION CIRCUIT is diagrammed here. When the rat presses on treadle it triggers an electric stimulus to its brain and simultaneously records action via wire at left.

Olds and Milner, 1954

Drugs act at specific brain sites

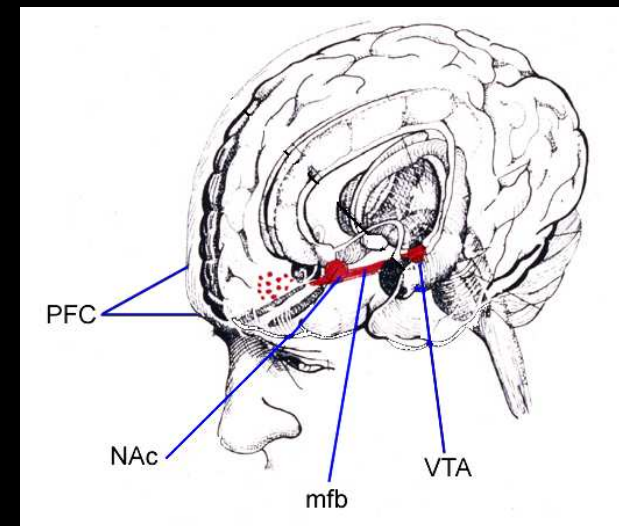
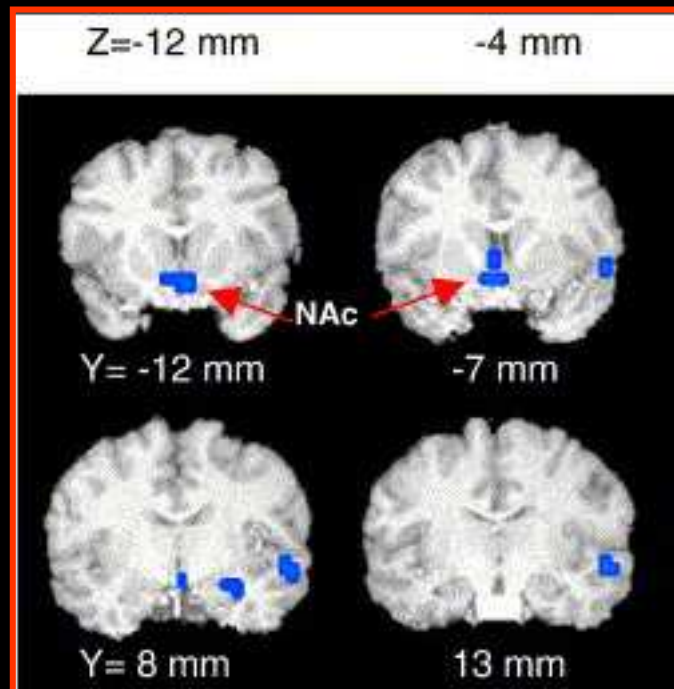


Similar areas in human brain show activity with reward and pleasure



Knutson et al, J. Neurosci 2001

Human brain activation by cocaine: reward circuit



Kufahl et al
Neuroimage 2005

Drug self-administration in animals

Cable
for drug
delivery

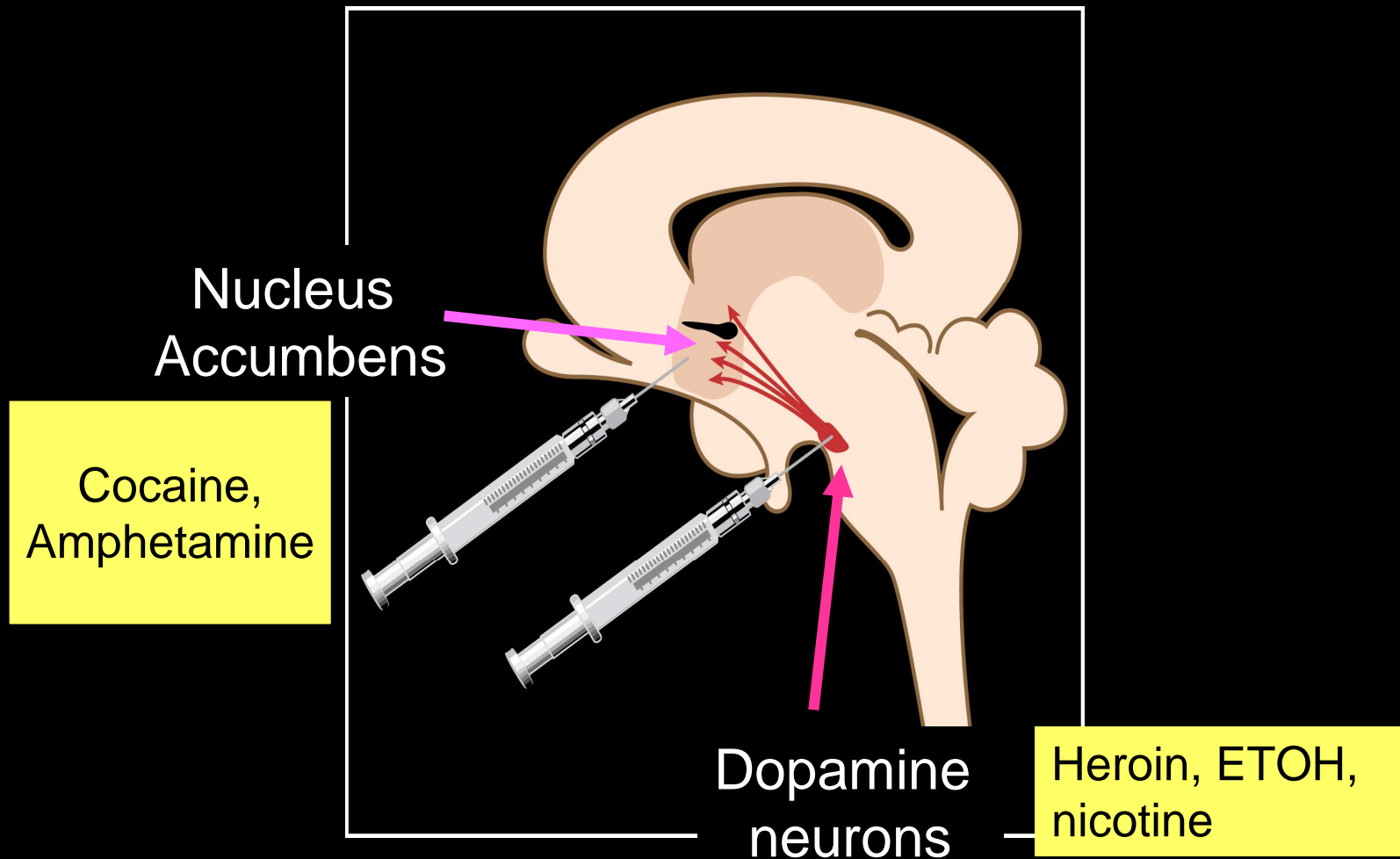


Lever
press
↓
drug



Graduate student

Rats self administer drugs directly into reward circuitry

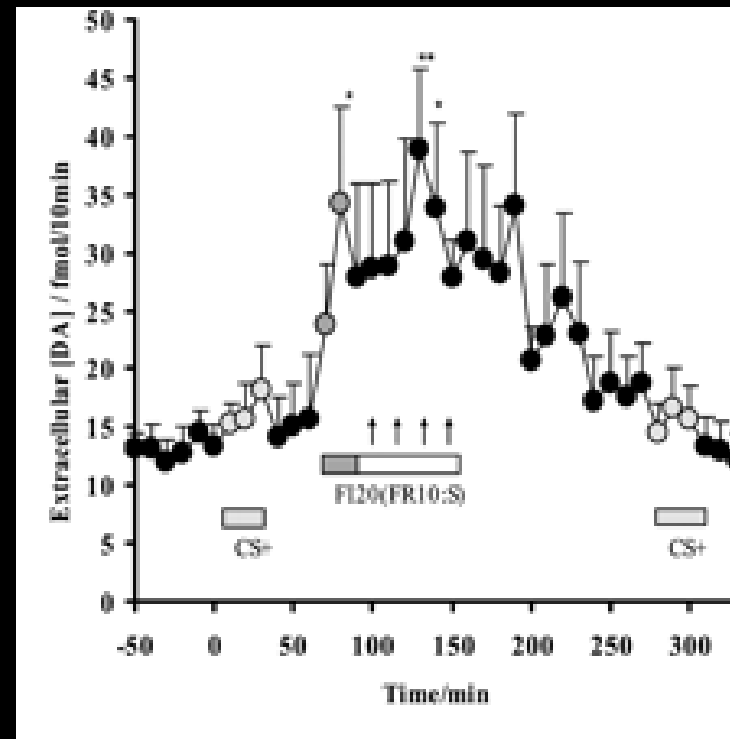
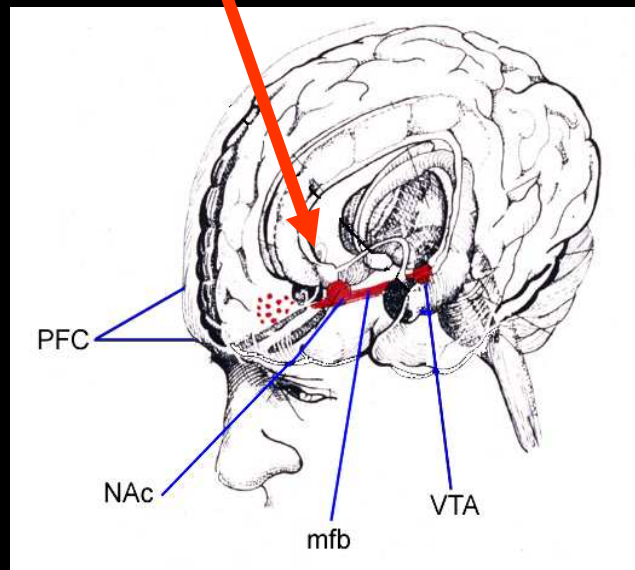


Environmental cues cause craving and relapse

- Drug associated cues (odors, taste, money, location of supply, needles)
- Drug action in brain → environmental cues cause craving and loss of control

Drug associated cues increase dopamine and activate the reward circuit

Dopamine sampling site



Ito et al, J. Neurosci. 2002

Whatever activates dopamine circuit can induce drug craving

- Drug
- Drug associated environmental cues
- Emotional Stress

Current approaches to treatment

I. Reduce drug reinforcement

- Remove drug (detoxification)
- Replacement (Nicotine gum/patch, methadone, buprenorphin)– prevents abstinence
- Reduce brain reward (e.g. naltrexone and acamprosate for ETOH)

Current approaches to treatment

II. Reduce environmental cues

- Reduce stress (Cognitive Behavioral or medication for anxiety and depression)
- Provide viable alternatives (work, education, recreation)

The future?

Determine neural mechanism of drug reward → better medical treatments

- Find specific location in brain
- Molecular mechanism
- Challenge: drug that blocks drug reward but not normal learning