Reward Circuits and Drug Addiction (IV) Ch.4

- Dopamine, drug reinforcement and drug reward
- Neural changes that occur following repeated drug exposure
- Animal Models of Drug Relapse
- The Incentive – Sensitization Hypothesis

- **PLEASE FILL OUT YOUR TEACHING EVALUATIONS!**

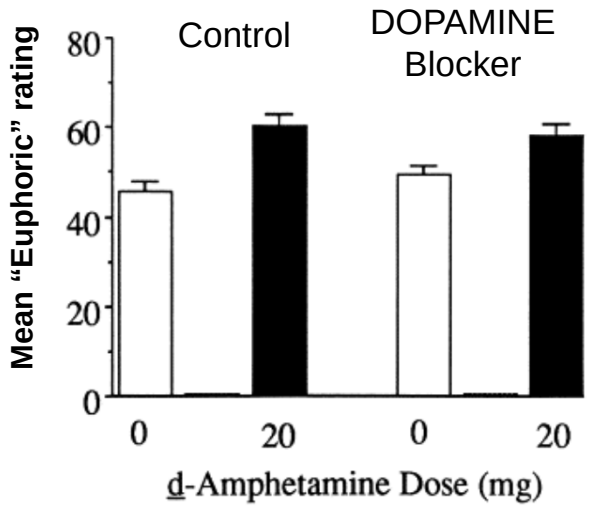
Dopamine and Drugs of Abuse- what it's not

- So, rewards are pleasurable, rewards increase dopamine release, so dopamine is pleasure?
  - Note that "Reward" has 2 components
    - **"Liking"** = pleasurable, hedonic effects of rewards
    - "**Wanting" =** craving, willingness to work for rewards

➢ **Study: *Blockade of dopamine receptors in humans does not alter subjective ratings*** of drug euphoria

- It is now relatively well-accepted (by *most* scientists) that dopamine is **not involved** in the pleasurable effects of drugs of abuse (or natural rewards)

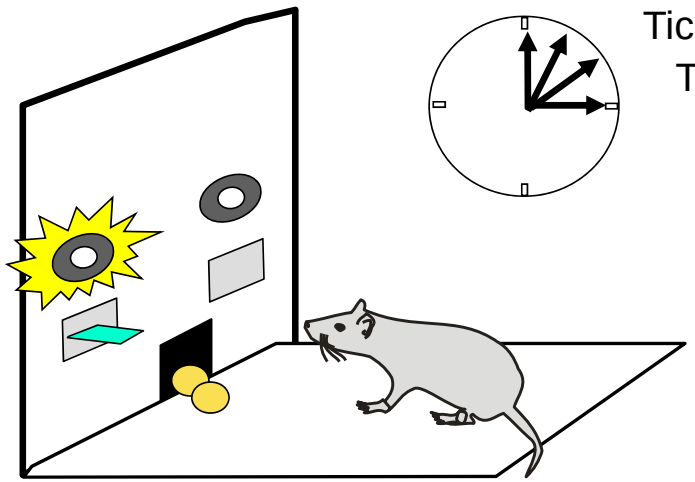
Dopamine antagonism does not affect reported euphoria induced by amphetamine



- Dopamine more involved in the preparatory/approach behaviours associated with rewards and conditioned stimuli, NOT their pleasurable effects
  - Endogenous opioids (e.g.: endorphins) play a role in pleasurable aspects of rewards

➢ **So, dopamine helps get you to the good things in life (wanting), but doesn't seem to be involved in you liking them**

Dopamine and Approach Towards Reward-Related Stimuli

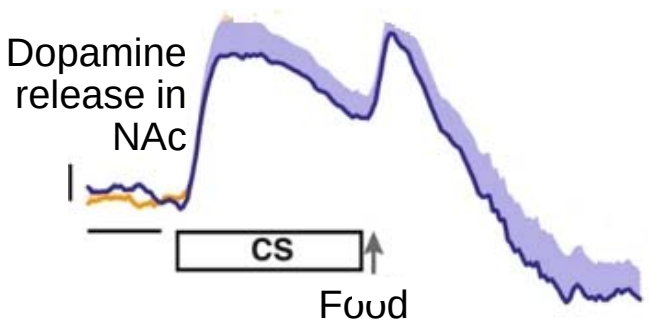


Tick…
Tick…
Tick…

Pavlovian Approach (Autoshaping): Cue comes on, predicts food delivery 5 s later

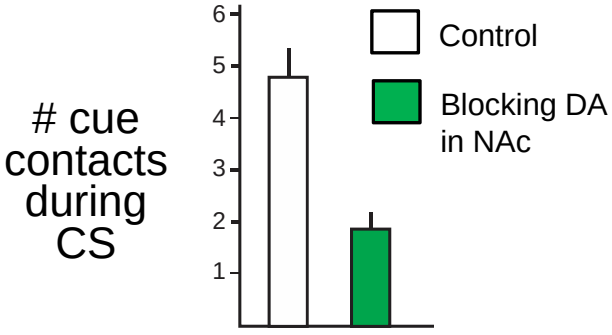
→Food ALWAYS delivered, regardless of whether animal interacts with lever

→Over training, animals start to approach/press/bite lever while waiting for food delivery – cue becomes "attractive", elicits approach



→Cue evokes DA release, associated with approach

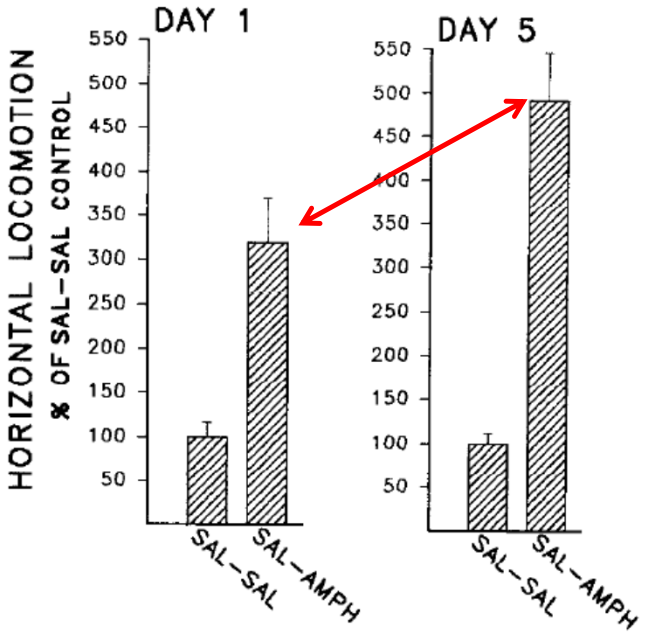
→ DA increases again when reward delivered



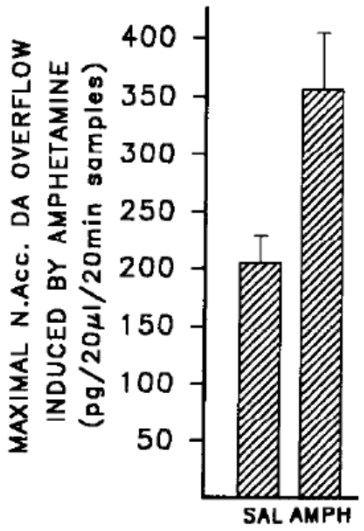
→Blocking NAc DA receptors ***reduce approach to cue*** (but DOES NOT disrupt approach/consumption of food reward)

- **So, dopamine promotes behaviors directed towards reward-related stimuli**

Sensitization of the Dopamine System

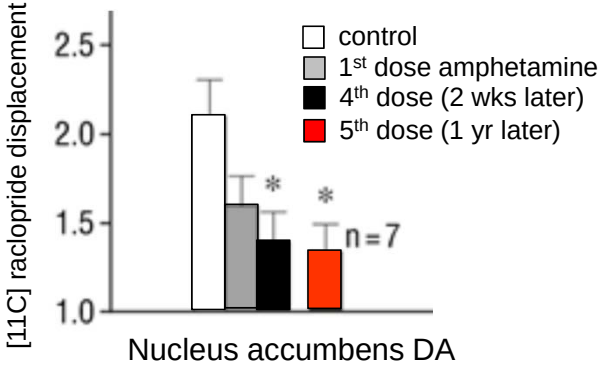


Day 5-
dopamine response



- Repeated exposure to **all drugs** with a high addictive potential (like cocaine) can induce **sensitization** of DA release
  - Also enhances DA release to reward-cues
- Studies in humans have shown these effects can be long lasting!

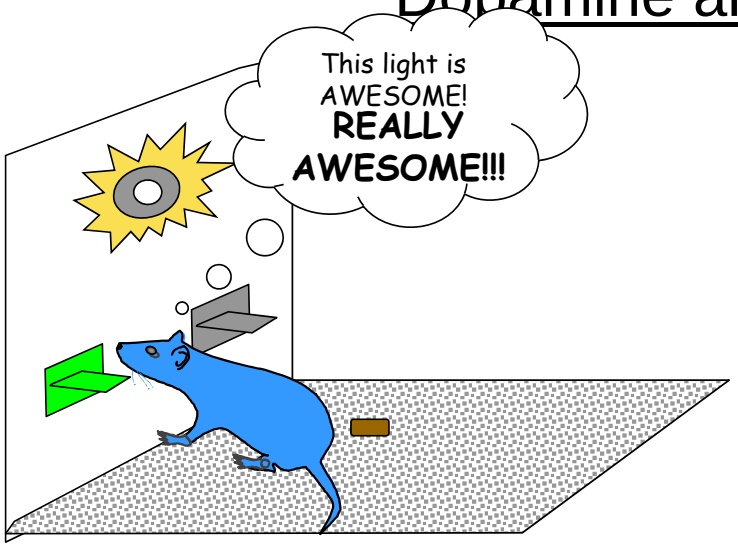
Human PET study
(lower values = greater DA release)



➢ **So, repeated drug exposure can put you into a hyperdopamine state**

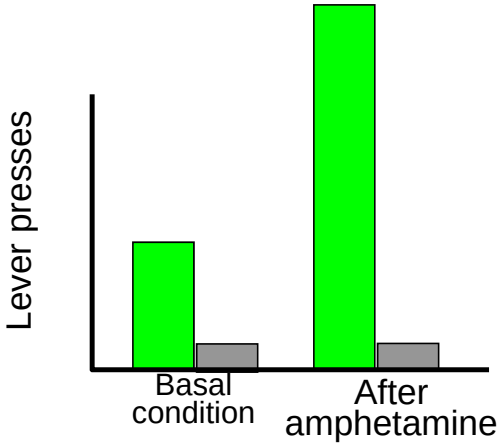
Can lead to sensitized DA release in response to cues associated with drug

Dopamine and conditioned reinforcement



Conditioned Reinforcement:
-**Phase 1:** CS light comes on and then reward is presented (e.g.; food)
-**Phase 2**: Levers are inserted to chamber
-One lever gives CS light, other gives nothing

- Animals will press lever **just for the CS**, even though lever press never gives reward
- Reward-associated cue is now reinforcing, animals will work for it



- Give amphetamine (ie: increase DA release) rat ***responds much more*** for conditioned reinforcer
- ***Important point:*** Rats sensitized to drugs like cocaine respond more for conditioned reinforcement **even when tested drug-free** weeks after treatment (effects persist)

➢ **So, in a hyperdopamine state, the cues exert a much more powerful influence over behaviour**

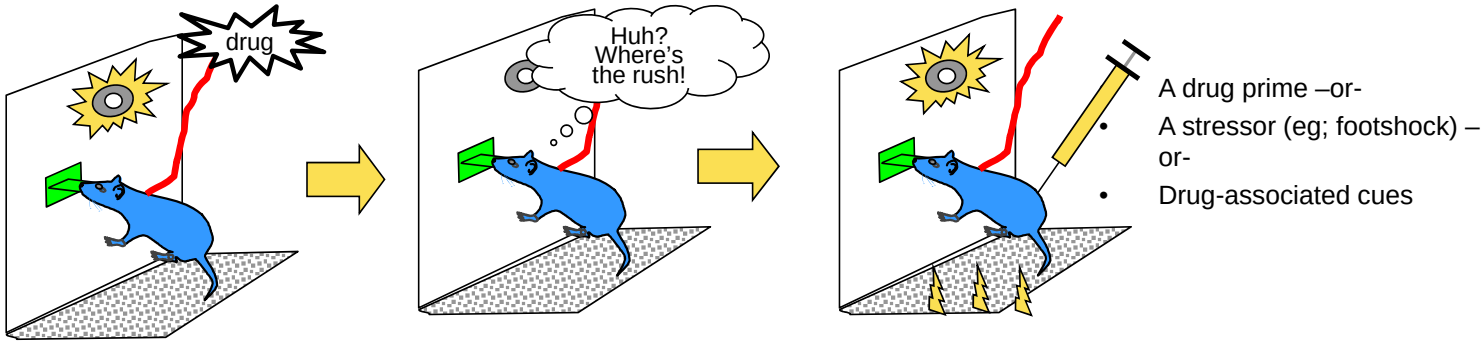
Reinstatement of Drug Seeking

- A key aspect of drug addiction is the relapse of drug taking after abstinence
  - •Can be triggered by "taste of the drug", cues associated with drug taking or stress
  - •In animals, this aspect of addiction can be modeled with a "reinstatement" paradigm

Step 1: train rats to administer drug (cues can be presented with drug infusion)

Step 2: Take rat thru extinction (lever press no longer delivers drug or cues, rats stop responding)

Step 3: On test day, lever pressing still **PROVIDES NO DRUG**, *but*, reinstatement of lever pressing can be induced by…

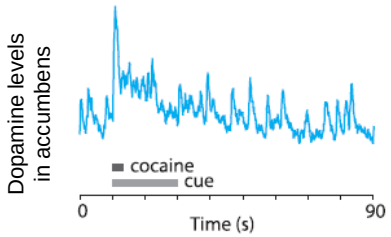


- A drug prime –or-
- A stressor (eg; footshock) –or-
- Drug-associated cues

Cue induced "relapse"

Each of these "triggers" evokes DA release in the accumbens

Dopamine release triggered by drug cue



- Blocking DA transmission REDUCES all types of reinstatement of drug-seeking

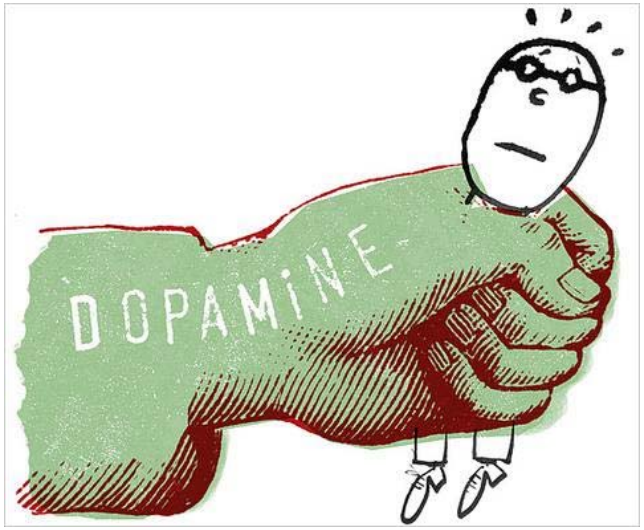
- **So, a drug "taste", cues associated with drug, or stress can**
  1) **Increase accumbens DA release and**
  2) **Trigger drug-seeking behaviour**

Dopamine and Addiction? Putting It All Together

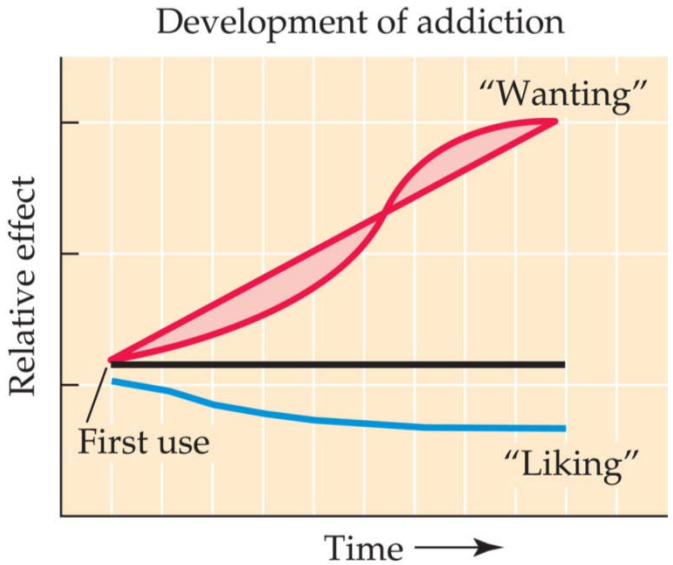
- 1) Addictive drugs dramatically increase mesolimbic DA levels
  - DA does not appear to mediate the hedonic effects of natural/drug rewards (*liking*), but plays a major role in associative learning and preparatory/approach behaviours (ie: *wanting*)

- 2) Drug-induced increases in DA "trick" your brain into thinking something important is going on, so it **starts to make associations with environmental cues/actions linked with drug-taking**

- 3) Reward-associated cues increase DA release in regions like the accumbens
  - This DA release can trigger the same behaviours that got you the rewards in the first place (drug-seeking)
- 4) Prolonged drug use leads a hyperactive (sensitized) DA system
  - Increased DA transmission can amplify the effects that drug-related cues exert over behaviour



Dopamine and addiction- an aberrant form of learning



- **Incentive-Sensitization Hypothesis:** cues associated with drug taking take over behaviour
  - Initial drug taking driven by pleasurable effects
  - Over time, tolerance develops to hedonic effects (*liking* the drug less), however, effects on the **dopamine system and** the **learning about drug-related cues** become sensitized
  - Drug-related cues (external, contextual, internal, temporal, or stress) activate neural networks (including dopamine system) that trigger unconscious conditioned responses that may be viewed as craving
    - These conditioned responses make you **THINK** you **WANT *the drug***
    - ***Similar to how food-related cues can make you hungry***
  - The associative memories between the effects of the drug and associated cues become amplified by the hyperdopaminergic state.
    - Essentially the brain is hijacked by the DA system. Drug cues trigger more craving and then more drug taking, even if the effects of the drug are not as pleasurable