



Biological Psychology

M5X00908 Brain, Behaviour, and Cognition (BBC)

Lecture 8: Drug Addiction and the Brain's Reward

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The impact of drugs on the brain



Focus of today's lecture:

- How the brain responds to chemicals in drugs
- Drug addiction
- Illegal drugs (e.g., heroin/cocaine) and legal drugs (e.g., nicotine/alcohol).

Addiction also relates to prescription medication.

- Important to understand pharmacological principles.
- And mechanisms involved to ascertain whether there is a point at which intervention could be implemented.

Basic Principles of Drug Action



- **How do drugs work? What happens in the body when someone takes a drug?**
- **Psychoactive drugs** – influence subjective experience and behavior by acting on the nervous system & change perception of reality.
- **Drug administration** – route of administration influences rate and degree to which drug reaches site of action.

Drug Administration & Absorption

Oral Ingestion (swallow):

- Dissolves in fluid of stomach & carried to intestine & absorbed into bloodstream.
- Quick & Easy, but unpredictable as influenced by other factors (food in stomach)

Injection: Strong, fast, predictable (bypass digestive tract)

- Subcutaneously: under skin
- Intramuscularly: into large muscle
- Intravenously: into veins, directly to brain
- No way to counteract effect of overdose, impurity of drug, or allergic reaction.
- Can lead to development of scar tissue, infections, and collapsed veins.

Absorption through mucous membranes:

- Nose, mouth, rectum

Inhalation (tobacco & marijuana):

- Absorbed through capillaries in lungs
- Difficult to regulate dose & damage to lungs if chronically inhaled.

Mechanisms of Drug Action



- For a drug to have an effect, it must get to the brain & pass through blood-brain barrier.
- Psychoactive drugs affect the nervous system in many ways – some (e.g., alcohol) act diffusely on neural membranes.
- Others act in a specific way by binding to particular synaptic receptors, or by influencing the synthesis, transport, release, or deactivation of a particular neurotransmitter, or by influencing the chain of reactions in postsynaptic neurons.
- Action of most drugs are terminated by enzymes in the liver – called drug **metabolism**.
- Drug metabolism eliminates a drug's ability to pass through lipid membranes of cells so it cannot penetrate the blood-brain barrier
- Small amounts may also be excreted in urine, sweat, feces, breath, and mother's milk.

Drug Tolerance



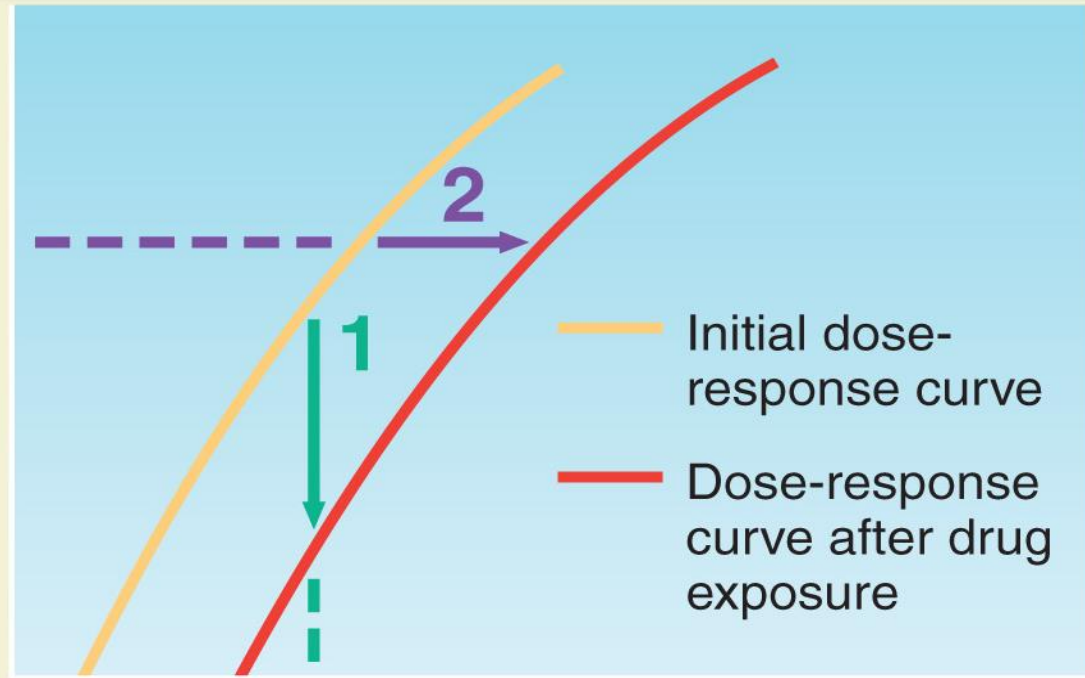
- People can become tolerant of a drug, where they experience decreased sensitivity to the drug due to repeated exposure.
- Demonstrated in 2 ways: either dose has less effect than before, or it takes more of the drug to produce the same effect.
- Drug tolerance = shift in dose-response curve: a graph of the magnitude of effect of different doses of the drug to the right.

Drug tolerance is a shift in the dose-response curve to the right. Therefore,

1 In tolerant subjects, the same dose has less effect.

2 In tolerant subjects, a greater dose is required to produce the same effect.

Magnitude of Drug Effect



Dose of Drug

Drug Tolerance



- 3 aspects about the specificity of drug tolerance

1. **Cross tolerance** – one drug can produce tolerance to similar drugs – e.g., alcohol & benzodiazepines.
2. Tolerance often develops to some effects & not others of a drug. Can also have an “**inverse tolerance**,” or sensitization.
3. Drug tolerance is not a unitary phenomenon – no single mechanism underlies all examples of tolerance

Drug Tolerance



2 categories of changes that underlie drug tolerance:

Metabolic

- Reduced amount of drug is getting to the site of action

Functional

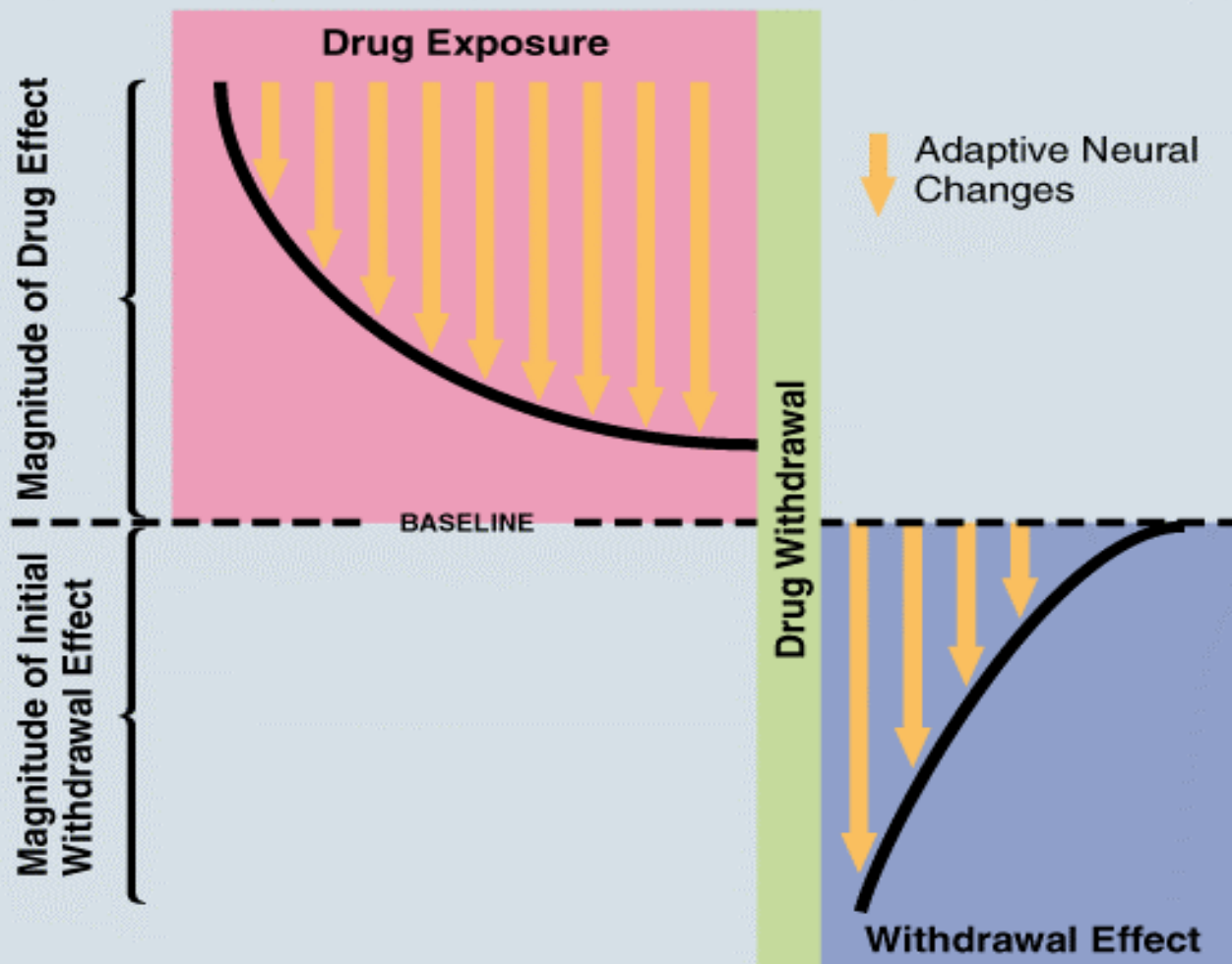
- Decreased responsiveness at the site of action; fewer receptors; decreased efficiency of binding at receptors; receptors less responsive

Drug Withdrawal Effects & Physical Dependence



- After sig. amount of a drug has been in the body for several days, sudden elimination triggers adverse physiological reaction: withdrawal syndrome.
- Effects of drug withdrawal are usually opposite to initial effects of the drug.
- The body makes changes to compensate for a drug's presence – functions normally with the drug present
- Severity varies with drug and pattern of use
- Those suffering withdrawal when they stop taking a drug are said to be physically dependent on that drug.
- The fact that withdrawal effects are opposite to initial effects suggests withdrawal effects may be produced by the same neuronal changes that produce drug tolerance.

Drug Withdrawal Effects & Physical Dependence



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

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

Relation between Drug Tolerance and Withdrawal Effects

Longer exposure to greater doses followed by rapid elimination produces greater withdrawal effects.

Addiction: What Is It?



- **“Addicts” continue to use a drug despite adverse effects on health/social life and despite repeated efforts to stop using.**
- **Many equate addiction & physical dependence: they see addicts as trapped in cycle of drug taking, withdrawal, & further drug taking to combat withdrawal**
- **But this is inconsistent with evidence....**
- **Addicts sometimes take drugs to alleviate/prevent withdrawal symptoms but it is not the major factor.**
 - **If it was then people could be treated with a few days in hospital until symptoms subsided.**
- **However, addicts often start taking their drug again even after months or years without it.**

Role of Learning in Drug Tolerance

Research suggests learning plays a role in drug tolerance

- Focus has been on 2 phenomena:

1. Contingent drug tolerance: tolerance develops only to drug effects that are actually experienced.
 - Studies use before-and-after design: 2 groups of Ps receive same series of drug injections & same series of repeated tests, group 1 Ps receive drug before each test while the other group receive it after. Typically when the drug is given after some sort of test, tolerance does not emerge
 - Figure 15.3 in Pinel gives details of a study by Pinel et al. to examine contingent tolerance to the anticonvulsant effect of alcohol in rats.
2. Conditioned drug tolerance: tolerance effects are maximally expressed only when a drug is administered in the same situation in which it has previously been administered.
 - Figure 15.4 in Pinel shows findings from a study where rats were given alcohol and saline injections either in a testing lab or in their colony room. Tolerance only observed when rats were injected in the environment that had previously been paired with alcohol administration.

Conditioned Tolerance and Withdrawal



- The Situational specificity of drug tolerance is well documented.
- Siegel et al. suggest addicts are susceptible to lethal effects of drug overdose when the drug is administered in a new context.
- Hypothesis: addicts become tolerant when they repeatedly self-administer drug in same environment & thus start taking larger doses to counteract diminution of drug effect.
 - Then if they administer huge dose in new situation, tolerance effects are not present to counteract the effects of the drug.
 - Siegel et al. found that many more heroin-tolerant rats died following high dose of heroin administered in a novel situation than died in the usual injection environment.
- Views each incidence of drug administration as a Pavlovian conditioning trial with environmental stimuli that regularly predict administration of the drug as conditional stimuli and drug effects as unconditional stimuli.

Conditioned Tolerance and Withdrawal



- Main assumption: conditional stimuli that predict drug administration come to elicit conditional responses opposite to the unconditional effects of the drug.
- Siegel has termed this: conditioned compensatory responses.
- Most demonstrations of conditioned drug tolerance have used exteroceptive stimuli, but interoceptive stimuli are also effective.
- E.g., both the feelings produced by the drug-taking and the first mild effects of the drug experienced soon after can (through conditioning) come to reduce the full impact of the drug.
- Interoceptive stimuli is important because even just thinking about a drug can evoke conditioned compensatory responses.
- Although tolerance develops to many drug effects, the opposite which is drug sensitization can also occur, and it too can be situationally specific.

5

Commonly Abused Drugs:

- Tobacco
- Alcohol
- Marijuana
- Cocaine
- Opiates

Tobacco



- When smoking a cigarette, nicotine (the major psychoactive ingredient of tobacco) & ~4,000 other chemicals referred to as tar are absorbed through the lungs.
- **About 70% of those who experiment with smoking become addicted**
- **Nicotine acts on nicotinic cholinergic receptors in the brain.**
- But because considerable tolerance develops to some of the immediate effects of tobacco, the effect on smokers vs. nonsmokers is remarkably different

Effects of Long-Term Tobacco Use

- Smoker's syndrome – chest pain, labored breathing, wheezing, coughing, susceptibility to respiratory infections
- Susceptible to lethal lung disorders – pneumonia, bronchitis, emphysema, lung cancer, cancer of larynx, mouth, kidneys, bladder, pancreas & stomach.
- Increased risk of cardiovascular disorders: can culminate in a heart attack or stroke.
- Can lead to Buerger's disease: blood vessels become constricted, especially those supplying blood to legs & in some cases toes, foot, ankle, leg, need to be amputated.
- Many claim to smoke to reduce tension but studies suggest smokers are more tense than nonsmokers.

Alcohol

- Alcohol molecules are so small & soluble in fat & water, they invade all parts of the body.
- Classed as a depressant because it reduces neural firing.
- Has a genetic component, heritability estimate for alcohol addiction ~ 55%
- Metabolic & functional tolerance develop
- Experience cognitive, perceptual, verbal, motor impairment as well as loss of control leading to unacceptable actions.



Effects of Chronic Alcohol Consumption

- **Severe withdrawal in 3 phases:**
 - 5-6 hrs post drinking: tremors, nausea, sweating, vomiting, headache, cramps, etc.
 - 15-30 hrs: convulsive activity
 - 24-48 hrs: delirium tremens (DTs) disturbing hallucinations, bizarre delusions, agitation, confusion, hypothermia: may last 3-4 days
- **Korsakoff's syndrome: brain damage, memory loss, sensory & motor dysfunction.**
- **Cirrhosis: scarring of the liver**
- Erodes heart muscles & increases risk of heart attack. Irritates lining of digestive tract & increases risk of oral & liver cancer, stomach ulcers, pancreatitis, and gastritis.
- **Fetal alcohol syndrome:** affects children of mothers drinking alcohol during pregnancy



Marijuana



- *Cannabis sativa* – common hemp plant
- Usually leaves are smoked or taken orally (baked).
- **THC** – primary psychoactive constituent – although 80 other cannabinoids are also present.
- Research on THC changed during 1990s with discovery of 2 receptors for it in the brain: CB1 & CB2.
- CB1: most prevalent G protein-linked receptor in the brain, while CB2 is found in brain stem & cells of the immune system.
- But why would we have THC receptors in our brain?
- This was answered with discovery of a class of endogenous cannabinoid neurotransmitter – called the endocannabinoids.

Marijuana



- First endocannabinoid isolated and characterized was called anandamide.
- At high doses marijuana impairs STM & ability to carry out tasks involving multiple steps.
- Speech becomes slurred/conversation lacks meaning
- Experience unreality, emotional intensification, sensory distortion, paranoia, and motor impairment.
- Some become addicted but rate is lower than other drugs and negative effects thought to be less severe than those associated with alcohol and tobacco.

Adverse Effects of Heavy Marijuana Use

- **Respiratory problems: cough, bronchitis, asthma.**
- **Elevated heart rate leading to heart attack.**
- **Single large doses can trigger heart attacks in susceptible individuals**
- **No evidence for permanent brain damage.**
- **But MRI shows prolonged use of large doses reduces hippocampus & amygdala volume.**
- **Possible correlation with schizophrenia, but no causal link has been shown.**

Medicinal Uses of Marijuana



**Treats
Nausea
in cancer
patients**

**Dilates
bronchioles
of asthmatics**

**Reduces
some
forms of
pain**

**Blocks
seizures**

**Decreases
Severity of
glaucoma**

Cocaine and Other Stimulants

- Increase neural and behavioural activity
- Cocaine is commonly abused - extracted cocaine (hydrochloride - white powder), is either snorted or injected.
- **Crack:** potent, cheap, smokable form
- Cocaine is an effective local anesthetic
 - But due to associated dangers, synthetic analogues (e.g., procaine and lidocaine) are used today.



Cocaine



- **Binges/sprees may lead to cocaine psychosis**
 - Mistakenly diagnosed as paranoid schizophrenia
 - Effects include tremors, nausea, hyperthermia, seizures, loss of consciousness, respiratory problems, heart attack, stroke.
- **During a spree, users become tolerant to euphoria, so larger doses are needed to feel the same effect.**
- **While tolerance may develop to most effects of cocaine (i.e., to the euphoria), sensitization is seen to its motor and convulsive effects**
- **Although highly addictive, withdrawal is relatively mild**

Other Stimulants

- **Amphetamine (“speed”)**

- Effects like cocaine – can produce psychosis
- Other amphetamines include methamphetamine (meth), which is used in an even more potent crystallized form (ice or crystal meth).

- **MDMA (“ecstasy”)**

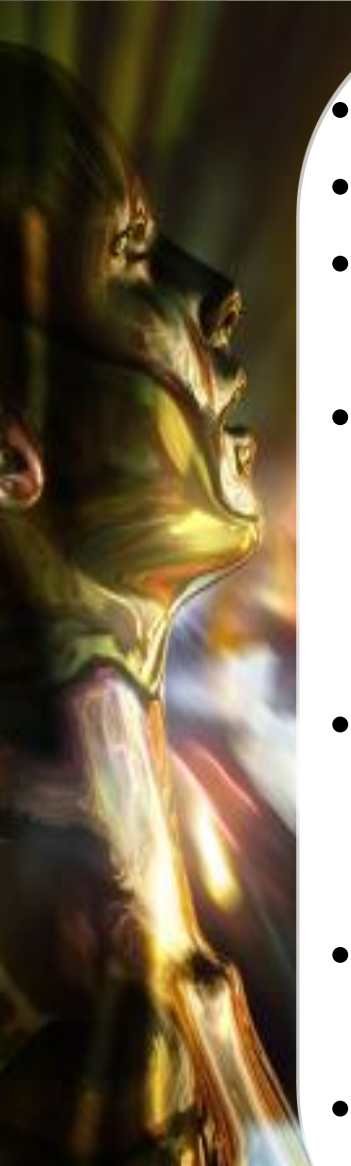
- Impairs dopaminergic and serotonergic function in animal studies; human relevance unclear
- Impairs executive function, inhibitory control, and decision making (as shown by cortex and limbic functional brain scan abnormalities)

Opiates: Heroin and Morphine

- **Opium: dried form of sap exuded by the seed pods of opium poppy**
 - Has several psychoactive ingredients, but most notable are morphine & codeine.
 - Which along with other drugs of a similar structure are referred to as opiates.
- **Medicinal uses**
 - Analgesics (painkillers)
 - Treatment of cough and diarrhea
- **High risk of addiction**



Opiate Addiction



- Addicts enjoy feeling rush after IV injection.
- But Tolerance and physical dependence develop.
- Desire to avoid withdrawal adds to motivation to use & tolerance encourages use of higher doses.
- Withdrawal symptoms begin 6-12 hours after last dose & include restlessness, pacing, fidgeting, eyes watering, runny nose, yawning, sweating, which is followed by fitful sleep
- Once awake they experience chills, shivering, nausea, vomiting, diarrhea, cramps, dilated pupils, tremor, muscle pains and spasms.
- Many health hazards related to use of dirty needles & poorly processed “street” versions.
- Death from overdose by suppressing breathing



Treatment for Heroin Addiction

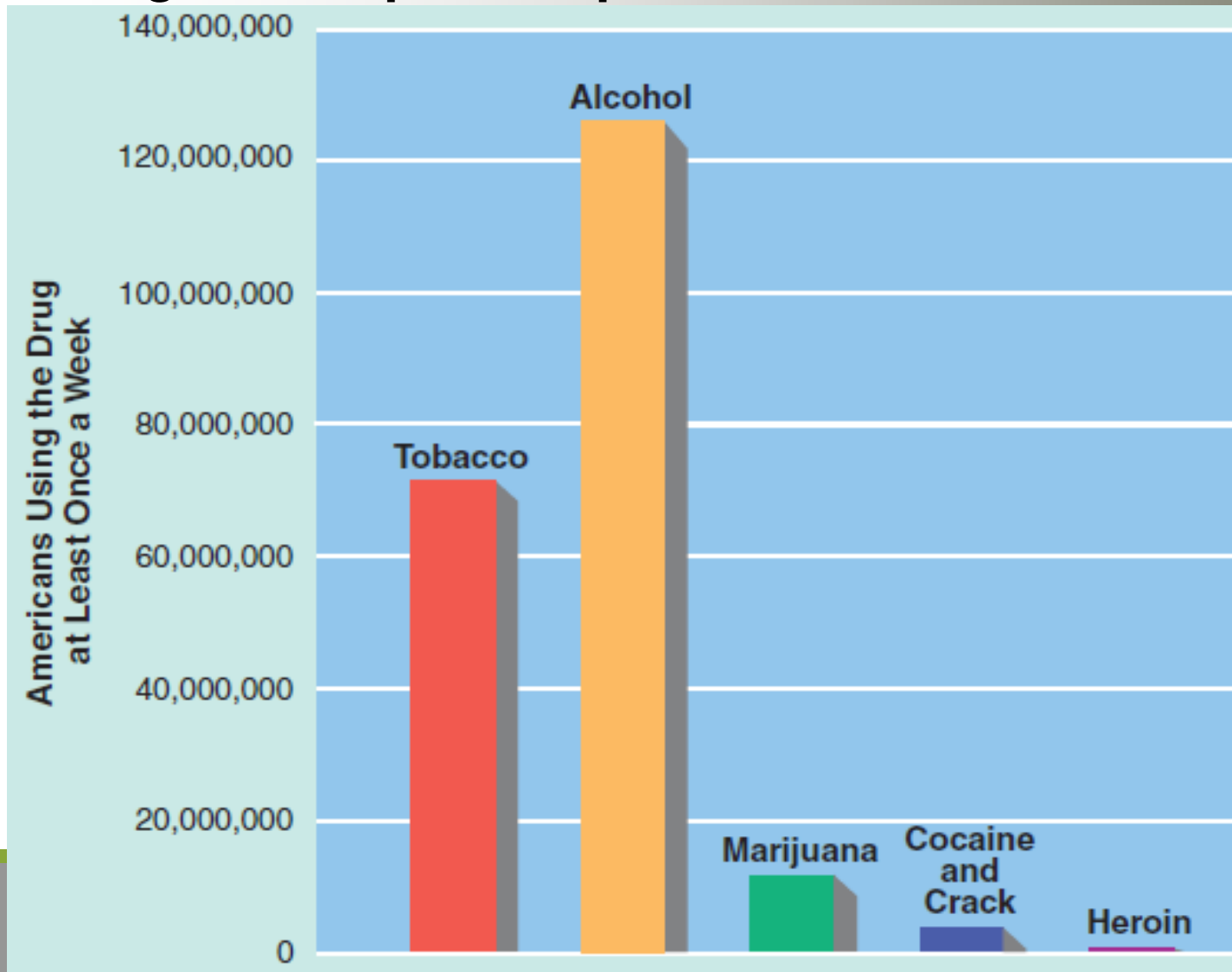


- Main treatment is with Methadone (ironically an opiate itself).
- It binds to opiate receptors, but....
 - Produces less pleasure than heroin
 - Administered orally
 - Prevents withdrawal
- Buprenorphine – similar to methadone but longer lasting
- Substituting a less dangerous drug for the abused drug.
- Some countries have heroin clinics.

Comparison of the Hazards of Tobacco, Alcohol, Marijuana, Cocaine, and Heroin



Alcohol and tobacco are associated with the greatest negative impact on public health



Prevalence of drug use in US. Figures based on survey of people age 12+ who live in households and used the drug in question at least once in the last month. (Based on National Survey on Drug Use and Health, 2005.)

Any issues with this type of research?

Biopsychological Theories of Addiction

- Dependence due to pain of withdrawal
- But doesn't explain relapse

Physical-dependence theories

Positive-incentive theories

Must explain:

- Difference between hedonic value & positive incentive value of drug
- How a drug user becomes an addict

Biopsychological Theories of Addiction

- Positive-incentive value (wanting) – anticipated pleasure associated with taking the drug
- Hedonic value (liking) – actual pleasure experienced
- With drug use, positive-incentive value increases due to memory of the pleasure of early drug experience; the hedonic value decreases due to drug tolerance
- Result: addicts crave drugs more and enjoy them less

Incentive-sensitization theory

Relapse and Its Causes

Understanding cause of relapse, could help with treatment.....

- **Stress** – drug use as a coping mechanism
- **Priming** – a single exposure leads to a relapse
- **Environmental cues** – certain people, times, places, objects previously associated with the drug
 - Conditioned drug tolerance
 - Returning to place where drugs once taken (or even thinking about drug) causes conditioned compensatory responses (tolerance/withdrawal), craving, and relapse



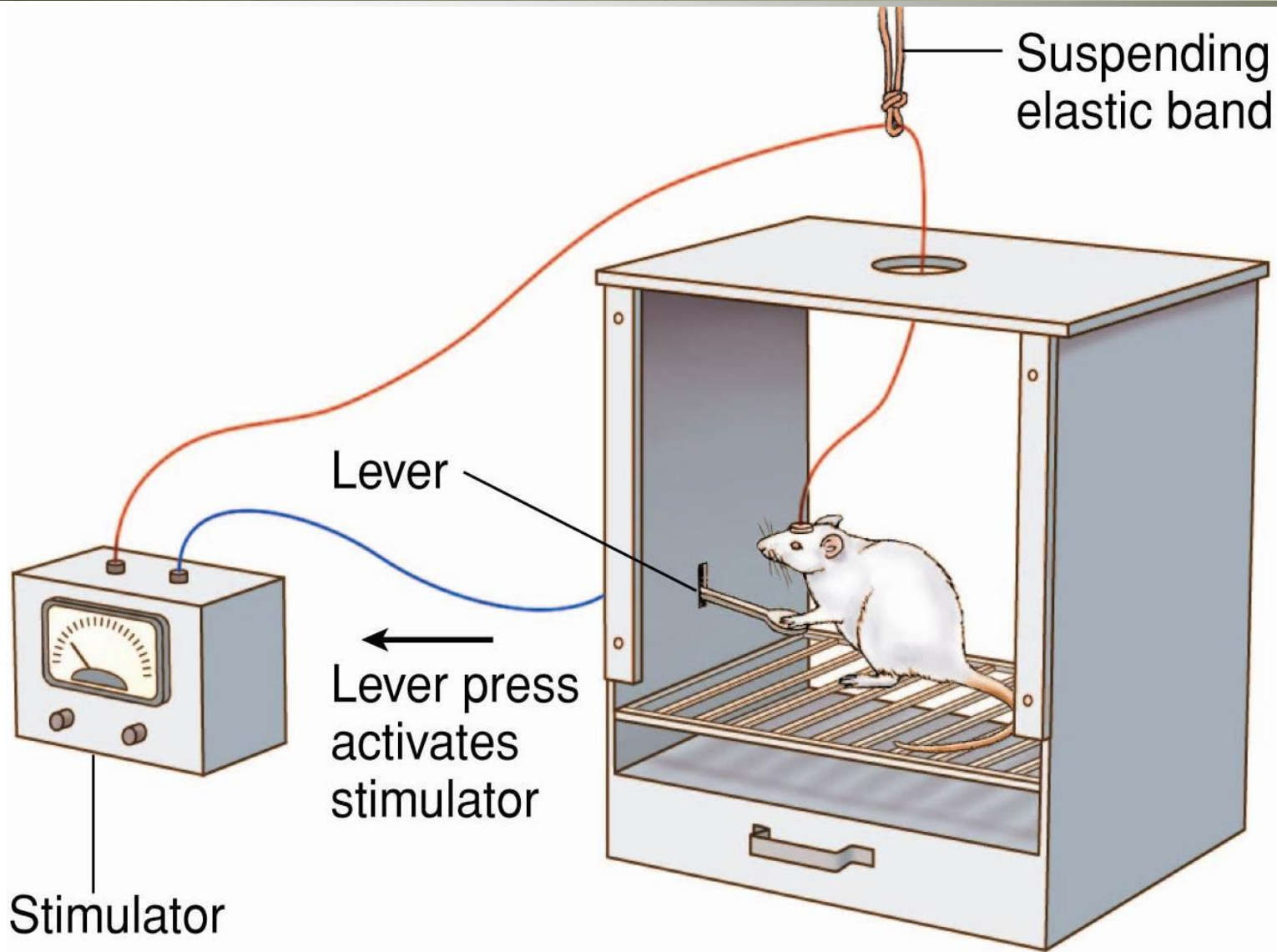
Intracranial Self-Stimulation and Brain “Pleasure Centers”



- There exists in the brain circuitry that reinforce behavior & species (inc. humans) will administer brief bursts of weak electrical stimulation to these area.
- Known as intracranial self stimulation - brain sites involved are known as pleasure centers.
- Olds and Milner (1954), who discovered intracranial self stimulation, argued that specific brain sites that mediate self-stimulation are those that normally mediate the pleasurable effects of natural rewards (such as food and water).



Intracranial Self-Stimulation and Brain “Pleasure Centers”



A rat pressing a lever to obtain rewarding brain stimulation

Intracranial Self-Stimulation and Brain “Pleasure Centers”



- Initially it was thought that intracranial self-stimulation was the same regardless the site of stimulation.
- Early studies found rats would press lever 1,000 times an hour for stimulation to septal and lateral hypothalamus areas.
- This suggested lever pressing for brain stimulation was different from lever pressing for natural reinforcers (food), with 2 observations contributing to this view.
 1. Despite high response rates, many rats stopped pressing lever immediately when electrical current delivery mechanism was shut off
 2. Experienced self-stimulators did not re-start lever pressing when returned to apparatus after being briefly removed from it and in these cases the rats had to be primed to start again.

Intracranial Self-Stimulation and Brain “Pleasure Centers”



- These differences seemed to discredit Olds and Milner's theory but there is research to suggest the circuits mediating intracranial self-stimulation are natural reward circuits.
- 1. Brain stimulation through electrodes that mediate self-stimulation often elicits a natural motivated behaviour, e.g., eating/drinking in the presence of the appropriate goal object.
- 2. Producing increases in natural motivation for example by food often increases self-stimulation rates.
- 3. Difference may have been seen because the 2 types of motivation are different:
 - Lever pressing for food means pressing the lever, waiting for food & then having to approach & consume it to experience reward
 - Whereas with self-stimulation to brain the reward is instant and direct.

Mesotelencephalic Dopamine System and Intracranial Self-Stimulation



- The Mesotelencephalic Dopamine System plays a major role in Intracranial Self-Stimulation.
- It is a system of dopaminergic neurons that project from the mesencephalon into various regions of the telencephalon.
- Neurons that compose the system have cell bodies in 2 midbrain nuclei – the substantia nigra & ventral tegmental area.
- Their axons project to a variety of telencephalic sites including specific regions of the prefrontal neocortex, limbic cortex, olfactory tubercle, amygdala, septum, dorsal striatum, and in particular the nucleus accumbens.
- Most axons of the dopaminergic neurons that have their cell bodies in the substantia nigra project to the dorsal striatum and this component is called the nigrostriatal pathway

Mesotelencephalic Dopamine System and Intracranial Self-Stimulation



- Most axons of the dopaminergic neurons that have their cell bodies in the ventral tegmental area project to various cortical and limbic sites and this component is called the mesocorticolimbic pathway.
- Although there is intermingling of neurons between these 2 pathways, it is the particular neurons that project from the ventral tegmental area to the nucleus accumbens that have been most frequently implicated in the reward effects of brain stimulation, natural reward, and drug addiction.

Mesotelencephalic Dopamine System and Intracranial Self-Stimulation

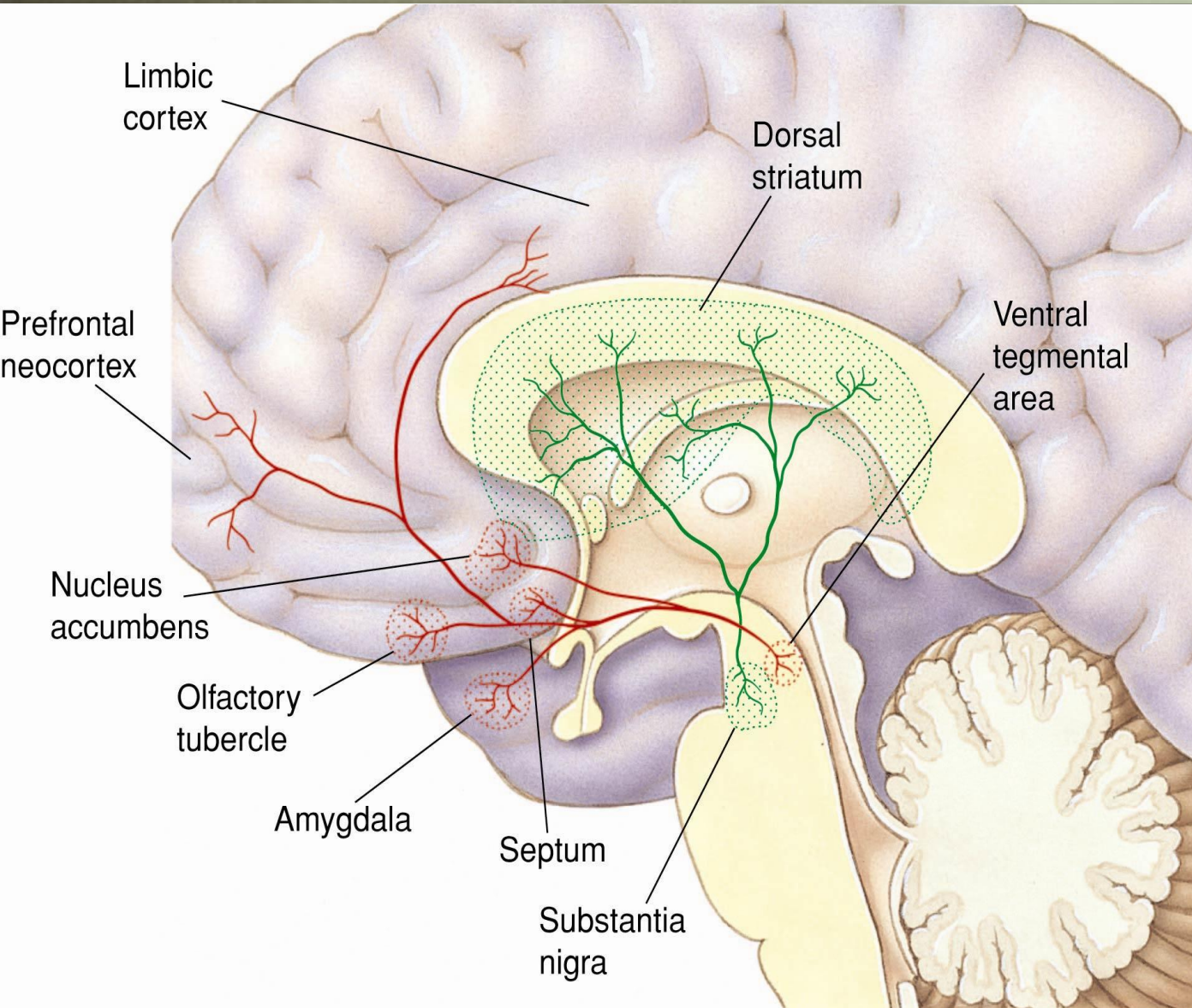


Diagram to show the 2 pathways – ventral tegmental area in red projecting to its various areas and the substantia nigra in green projecting to its various areas.



Mesocorticolimbic Pathway & Reward

- Evidence supports view that mesocorticolimbic pathway of mesotelencephalic dopamine system plays role in mediating intracranial self-stimulation.....
1. Many of the brain sites where self-stimulation occurs are part of the mesotelencephalic dopamine system.
 2. Intracranial self-stimulation is often associated with an increase in dopamine release in the mesocorticolimbic pathway.
 3. Dopamine agonists tend to increase intracranial self-stimulation, while dopamine antagonists tend to decrease it.
 4. Lesions of the mesocorticolimbic pathway tend to disrupt intracranial self-stimulation.

Two Key Methods for Measuring Drug-Produced Reinforcement in Laboratory Animals



Research on neural mechanisms of addiction with non-humans has used 2 methods:

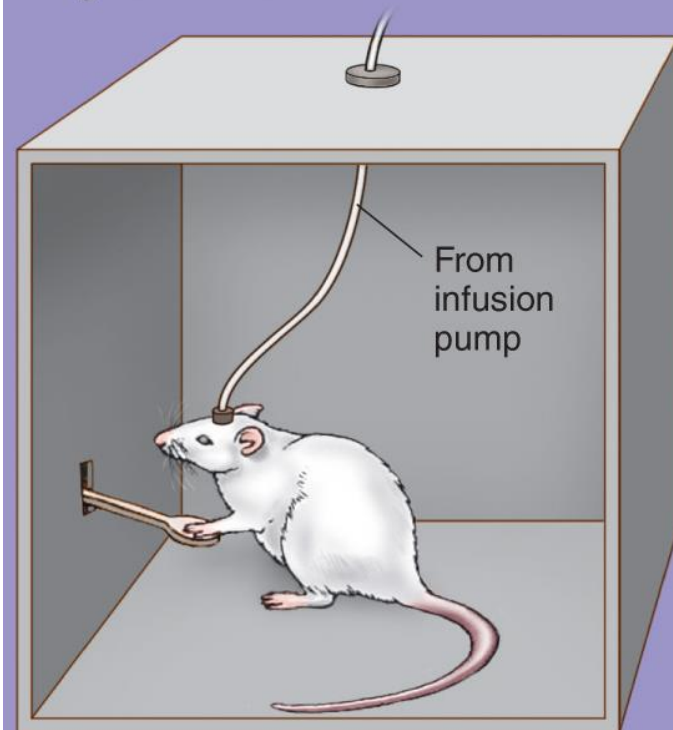
1. Drug self-administration paradigm: e.g., rats press lever to inject themselves with drugs that humans are addicted to.
2. Conditioned place-preference paradigm: rats repeatedly receive drug in one compartment of a 2 compartment box
 - When placed back in box, they choose to spend most of their time in compartment where drug was administered
- Advantage: rats can be tested when they are drug free, which means the measure of the incentive value of a drug is not confounded by the effects the drug may have on behavior.



Two Key Methods for Measuring Drug-Produced Reinforcement in Laboratory Animals



Drug Self-Administration



The rat presses the lever to self-inject a drug, either into an area of its brain or into general circulation.

Conditioned Place Preference



A rat repeatedly receives a drug in one of two distinctive compartments. Then, on the test, the tendency of the rat, now drug-free, to prefer the drug compartment is assessed.

Two behavioral paradigms that are used extensively in the study of the neural mechanisms of addiction: the drug self-administration paradigm and the conditioned place-preference paradigm.

Dopamine and Drug Addiction



- **Following research on role of dopamine in intracranial self-stimulation, studies implicated dopamine in the rewarding effects of neural reinforcers and addictive drugs.**
- **E.g., in rats dopamine antagonists blocked self-administration of, or the conditioned preference for several types of addictive drugs & reduced reinforcing effects of food.**
- **Findings from research suggest dopamine signals something similar to reward value or pleasure and the nucleus accumbens appears to play a key role in this.**

Nucleus Accumbens (NA) & Drug Addiction



- Once evidence suggested link between dopamine with natural reinforcers and drug-induced reward, research on animals examined particular sites in the mesocorticolimbic dopamine pathway.
- Events in the nucleus accumbens & dopaminergic input to it from the ventral tegmental area appeared to be related to the experience of reward/pleasure and 4 main findings emerged.....



Nucleus Accumbens (NA) & Drug Addiction



1. Lab animals would self-administer microinjections of addictive drugs directly into nucleus accumbens.
2. Microinjection of drugs into nucleus accumbens produced conditioned place preference for compartment where they were administered.
3. Lesions to either nucleus accumbens or ventral tegmental area blocked self-administration of drugs into general circulation or the development of drug-associated conditioned place preferences.
4. Both self-administration of addictive drugs & experience of natural reinforcers were found to be associated with elevated levels of extracellular dopamine in the nucleus accumbens.



Support for the Involvement of Dopamine in Addiction: Evidence from Imaging Human Brains



- Support for role of dopamine comes from brain imaging
- Volkow et al. administered various doses of radioactively labelled cocaine to addicts and asked them to rate the resulting high.
 - Also used PET to measure degree to which the labelled cocaine bound to dopamine transporters.
 - Intensity of high experienced correlated with degree to which cocaine bound to dopamine receptors
 - No high was experienced unless the drug bound to 50% of the dopamine transporters.

Support for the Involvement of Dopamine in Addiction: Evidence from Imaging Human Brains



- Brain-imaging also suggests nucleus accumbens plays role in mediating reward effect of addictive behavior
- E.g., healthy non-addicted humans given amphetamine injection.
 - As dopamine levels in nucleus accumbens increased in response to injection, Ps reported increase in euphoria.
- Brain-imaging studies show that dopamine function is diminished in human addicts.
- But when addicts are exposed to their drug or stimuli associated with the drug, their nucleus accumbens and other parts of the mesocorticolimbic pathway tend to become hyperactive.

Dopamine Release in the NA: What Is Its Function?



- But reward is a complex process with many psychological components – so what exactly is the role in reward of dopamine release in the nucleus accumbens.
- Studies have found increases in the extracellular dopamine levels in the nucleus accumbens following the presentation of a natural reward such as food or an addictive drug.
- Further evidence also comes from the finding that the ventral tegmental neurons, which release their dopamine into the nucleus accumbens, fire in response to a stimulus at a rate proportional to its reward value.
- Some studies have also suggested that dopamine released in the nucleus accumbens is related to the expectation of reward rather than to the experience itself.



Dopamine Release in the NA: What Is Its Function?

- Tobler et al. found that dopaminergic neurons with their cell bodies in the ventral tegmental area fire at a rate related to the value of the reward.
- When expected reward is delivered, there is no change in firing rate, but when greater than expected reward is given firing increased (and vice versa).
- Dopamine release in nucleus accumbens reflected both experience and expectation of reward
- But it seemed to reflect discrepancy between expected and actual reward.



Current Approaches to Brain Mechanisms of Addiction



Current approach takes into account historical theories regarding reward and drug conditioning

Current Issues in Modern Addiction Research



- Addiction is psychologically complex
- Addicts show poor decision making & lack of self control, suggestive of prefrontal cortex role
- Drug addiction may be related to other non-adaptive behaviors, e.g., compulsive eating, gambling, sexual behavior, klepto-mania, etc.
- Other neurotransmitters also involved: glutamate, endogenous opioids, norepinephrine, GABA, and endocannabinoids

Brain Structures That Mediate Addiction: The Current View



- **Current research not in complete agreement but there is consensus other areas are involved in....**
1. Initial drug taking: mediated in same way as pleasure activity, with the mesocorticolimbic pathway (particularly nucleus accumbens playing a key role).
 - But it does not act alone
 - Instead it interacts with 3 other areas:
 - Prefrontal lobes (role in decision making);
 - Hippocampus: provides info about previous experiences;
 - Amygdala: coordinates positive and negative reactions.

Brain Structures That Mediate Addiction: The Current View



2. Craving & compulsive drug use: repeated consumption brings major changes in motivation as addict develops habit & compulsion despite adverse effects.
 - Due to direct neural response to repeated exposure of drug-induced pleasure and as product of conditioned response to drug-associated cues.
 - Several changes in brain's response contribute to development of addiction:
 - Change in how striatum reacts to drugs, which spreads from the nucleus accumbens to the dorsal striatum, which is known to play a role in habit formation.
 - At same time the prefrontal cortex in controlling behavior declines & stress circuits in hypothalamus begin to interact with dorsal striatum.
 - Development of addiction is a pathological neuro-plastic response.

Brain Structures That Mediate Addiction: The Current View



3. Relapse – thought to be triggered by 3 factors:
 - Priming doses,
 - Associated cues,
 - Stress.
- Evidence from animal studies shows:
 - Prefrontal cortex mediates priming-induced relapse,
 - Amygdala mediates condition cue induced relapse,
 - Hypothalamus mediates stress-induced relapse.



Case Study

A Noteworthy Case of Addiction

Subject:
Sigmund Freud

- Famous essay “Song of Praise” (July, 1884), created a wave of interest in using cocaine
- After 3 years, Freud stopped using the drug
- 7 years later, his physician ordered him to stop smoking due to a heart condition
- Despite having no difficulty ceasing all use of cocaine, Freud could not stop smoking and died from cancer in 1939

Next Week....



Biopsychology of psychiatric disorders

Essential Reading....

Pinel, J. P. J. *Biopsychology* – Chapter 18