DATB: Addiction

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2016-10-04

These slides are available online, along with fun 5-minute quizzes and other materials:

http://datb.mit.edu/

About This File

This file was created on 2016-10-04 at 2.44a by copying the file “ESP Class - Addiction.pptx”, converting it into .PPT format, and then modifying it.

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Reminder: Stellar Website

We have a Stellar website, and I've been updating it:

datb.mit.edu/stellar

What Is Addiction?

Addiction is continued use of a substance despite harms that outweigh the benefits, with a lack of control over substance use.

Types of Harm

Physical: Infection, injury, brain damage

Psychological: Anxiety, depression, guilt, shame

Social: Prison, loss of employment, disowned by friends and family

Monetary: Bankruptcy, forced to work in prostitution or drug dealing

Evidence of Lack of Control

Broken promises to oneself: “I will only have two beers tonight.”

Broken promises to others: “I will not be late to work again.”

Feeling helpless: “I could not possibly go a week without cocaine.”

Evidence of Lack of Control

Lying, including lying to doctors, to family, or to oneself.

Lying about substance use, about level of control, about level of harm, or about level of benefit from the substance.

Recap: What Is Addiction?

Addiction is continued use of a substance:

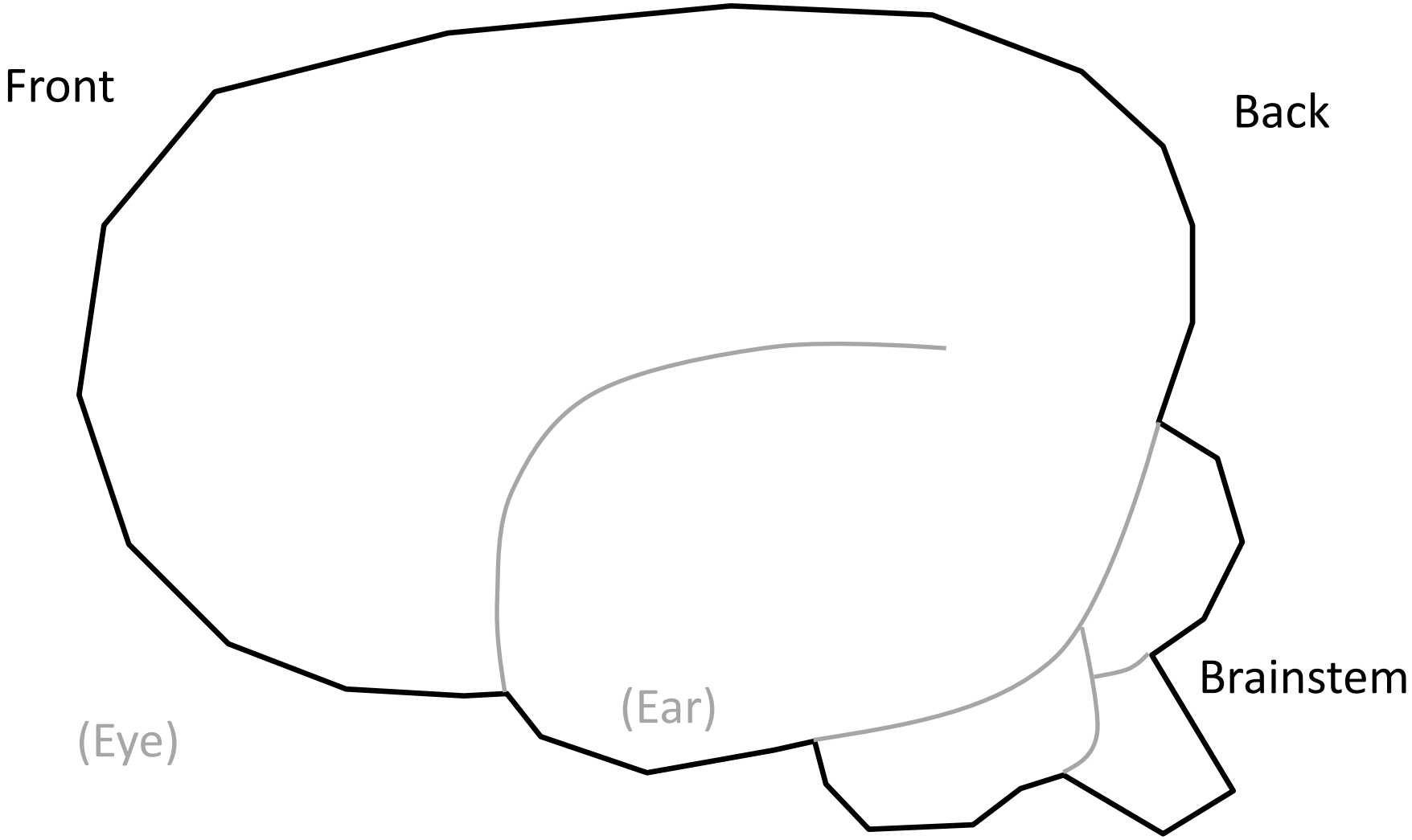
(1) Despite harms that outweigh the benefits

(2) With a **lack of control** over substance use

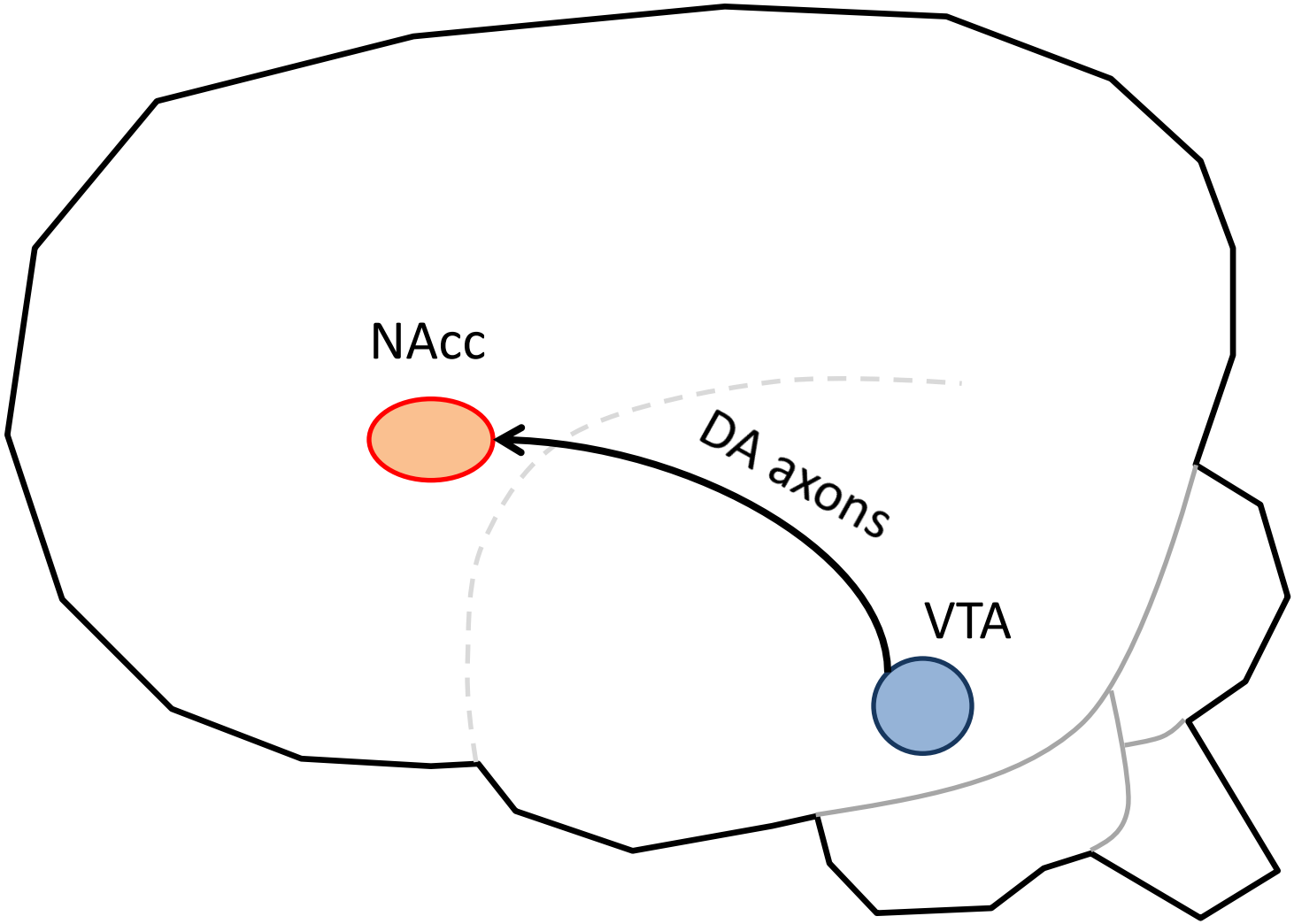
The Addiction Pathway

The addiction pathway, also called the mesolimbic dopamine pathway, is a collection of **dopaminergic** neurons (brain cells that **release DA**) that project axons from the **ventral tegmental area (VTA)** to the **nucleus accumbens (NAcc)**. The NAcc is in a larger region called the septum (anatomic name) or the ventral striatum (functional name).

This Is a Brain (trust me)



The Addiction Pathway



Purpose of the Addiction Pathway

Why did we evolve this addiction pathway (i.e. the mesolimbic dopamine pathway)?

- Food
- Sex
- Reward-based learning of sequential tasks, a simple type of learning

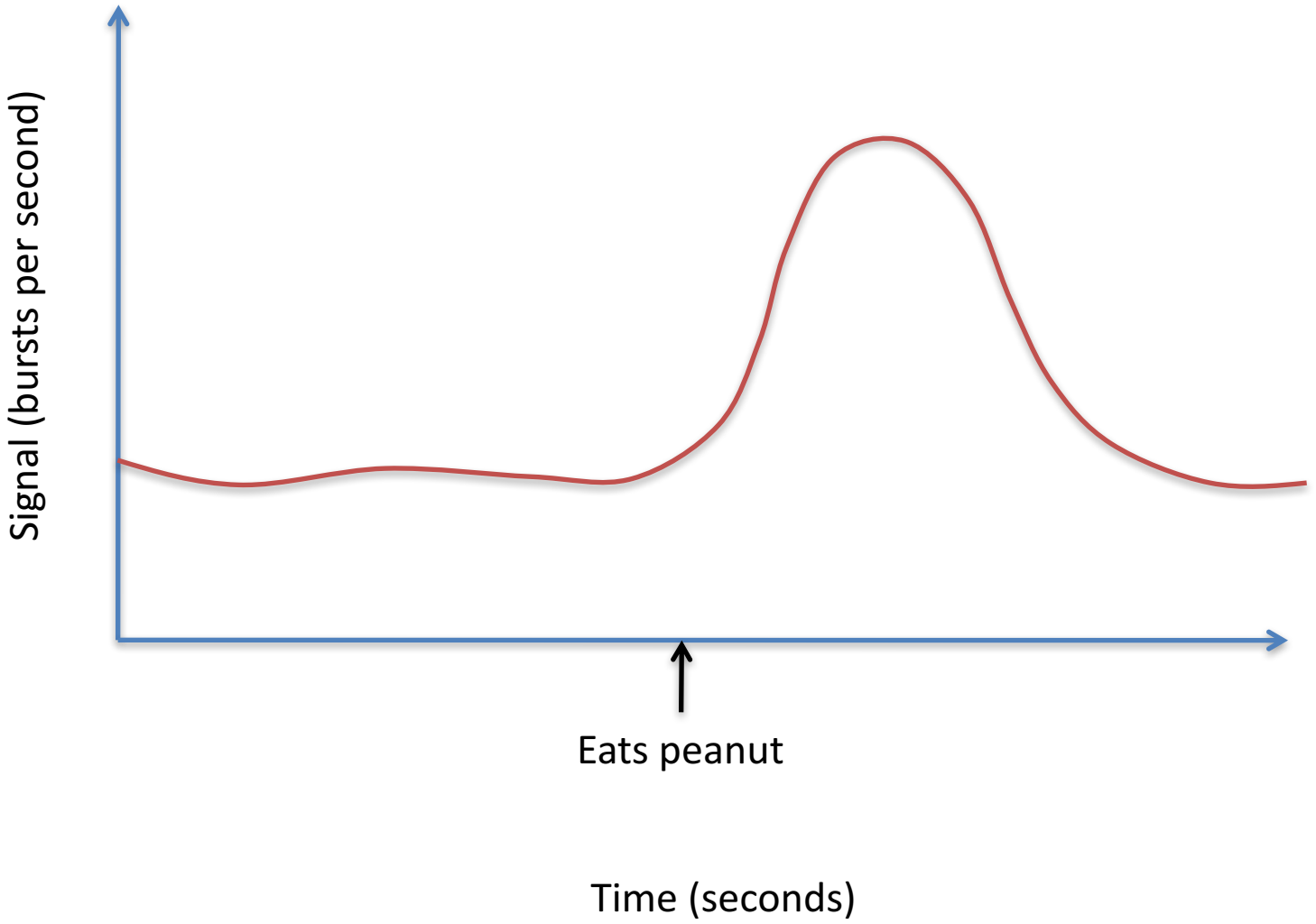
Purpose of the Addiction Pathway

Food and **sex** are the **original addictive stimuli,** in an evolutionary sense.

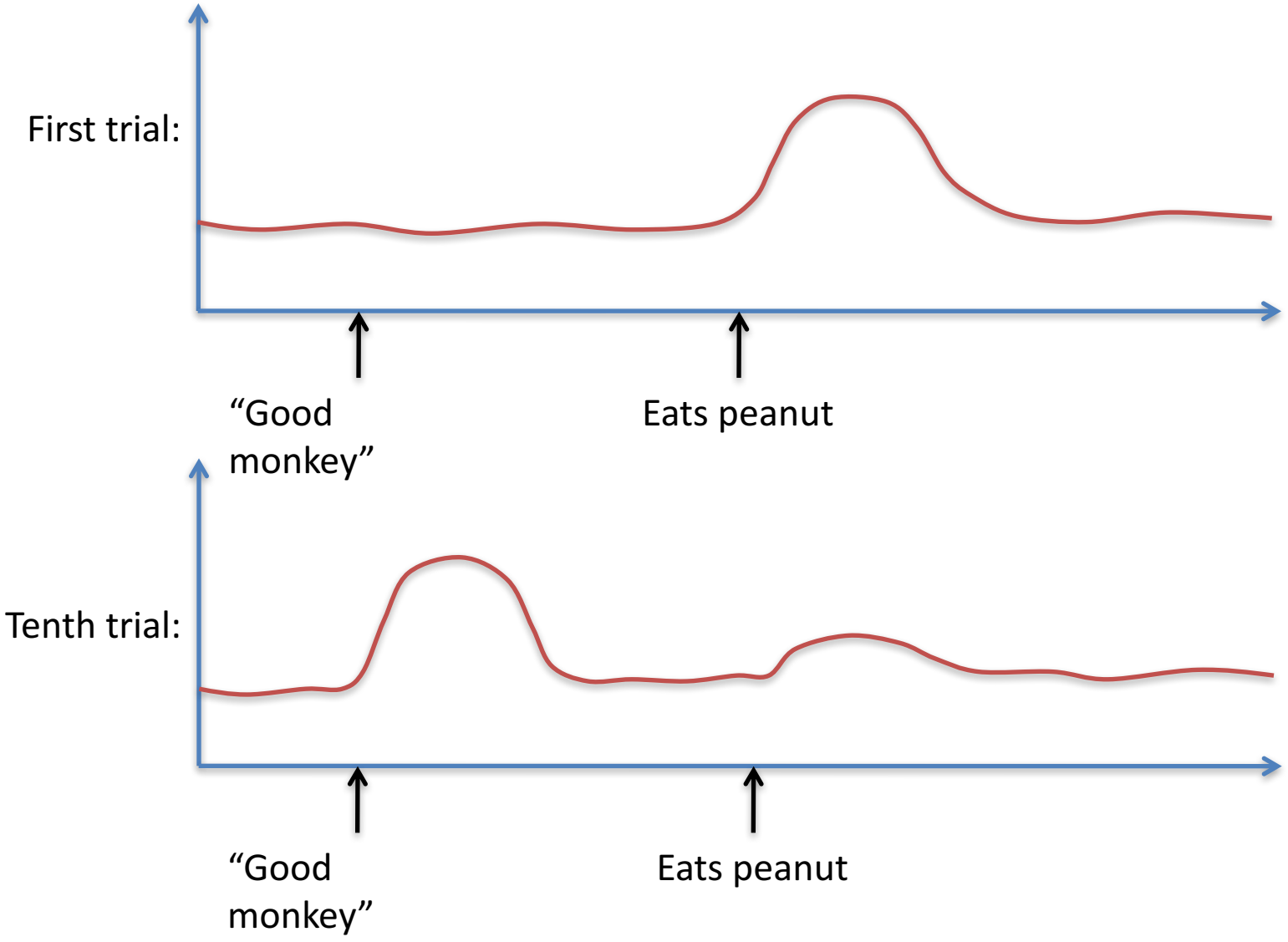
Addictive drugs, e.g. cocaine, simply mimic the brain signals of natural rewards such as food and sex.

Obesity is very similar to addiction, but sadly the two core anti-addiction techniques do not work: (1) avoiding the drug completely and (2) replacing the drug with something less harmful.

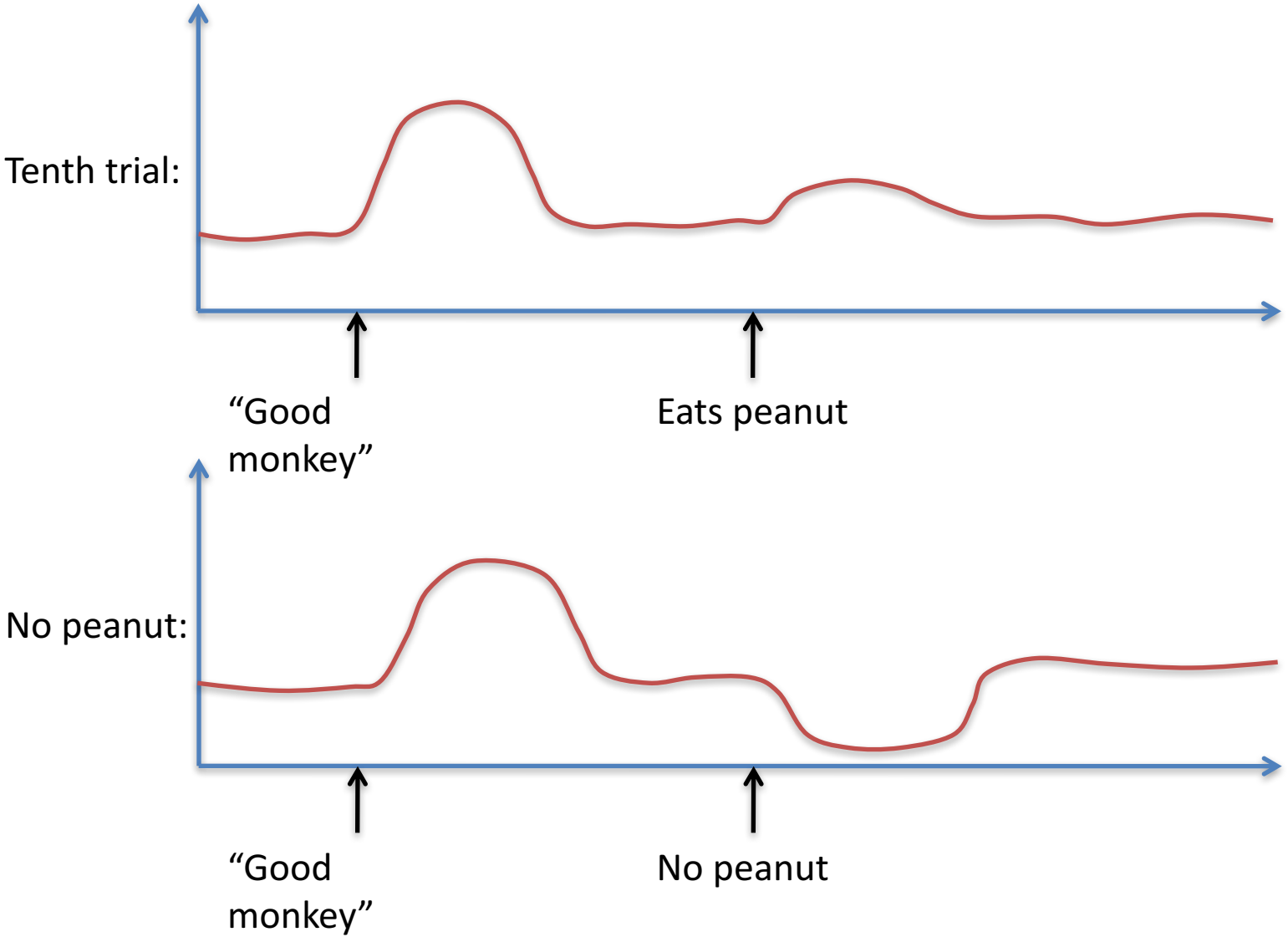
Dopamine signals unexpected rewards



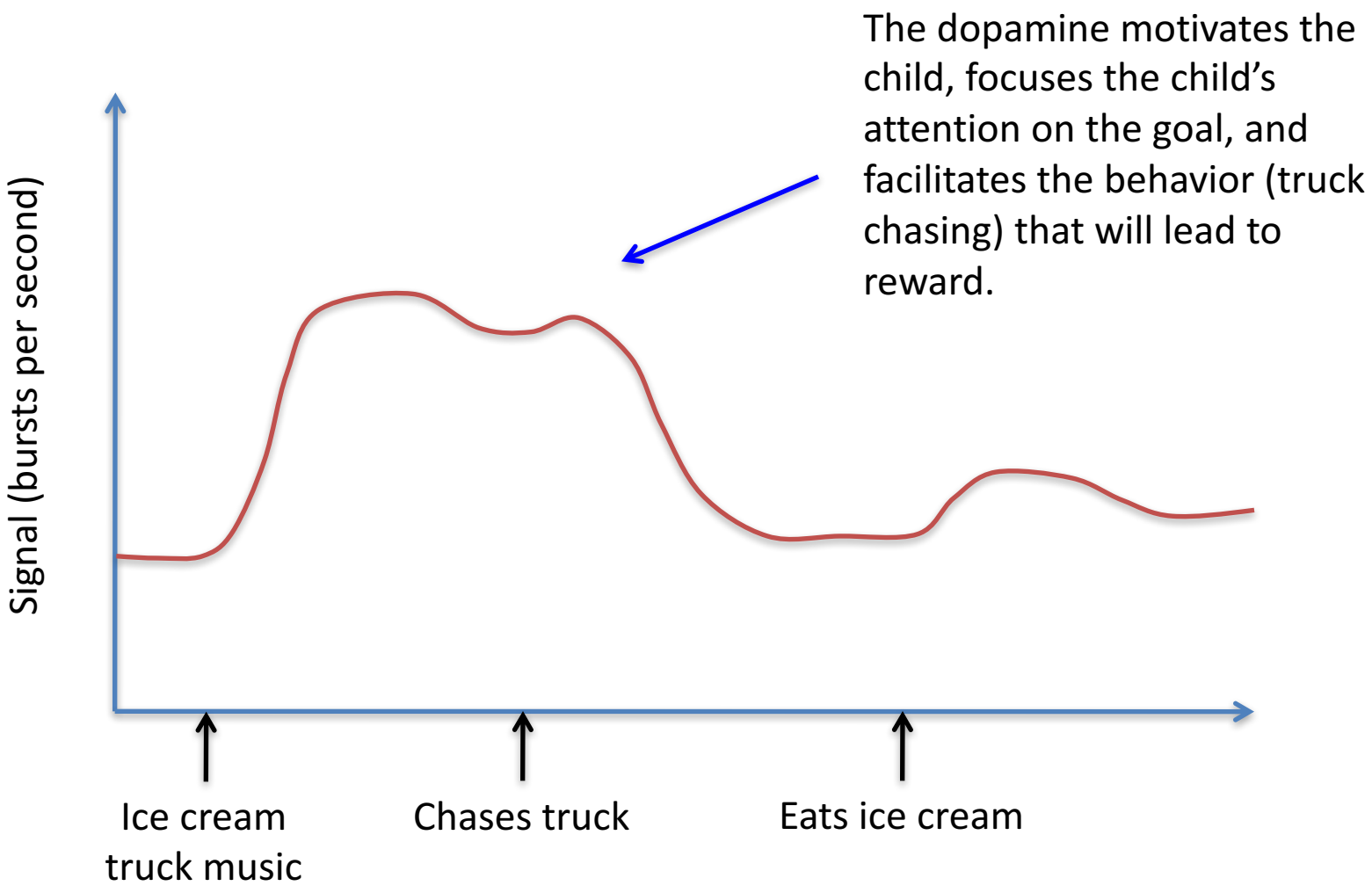
Dopamine signals predicted/expected rewards



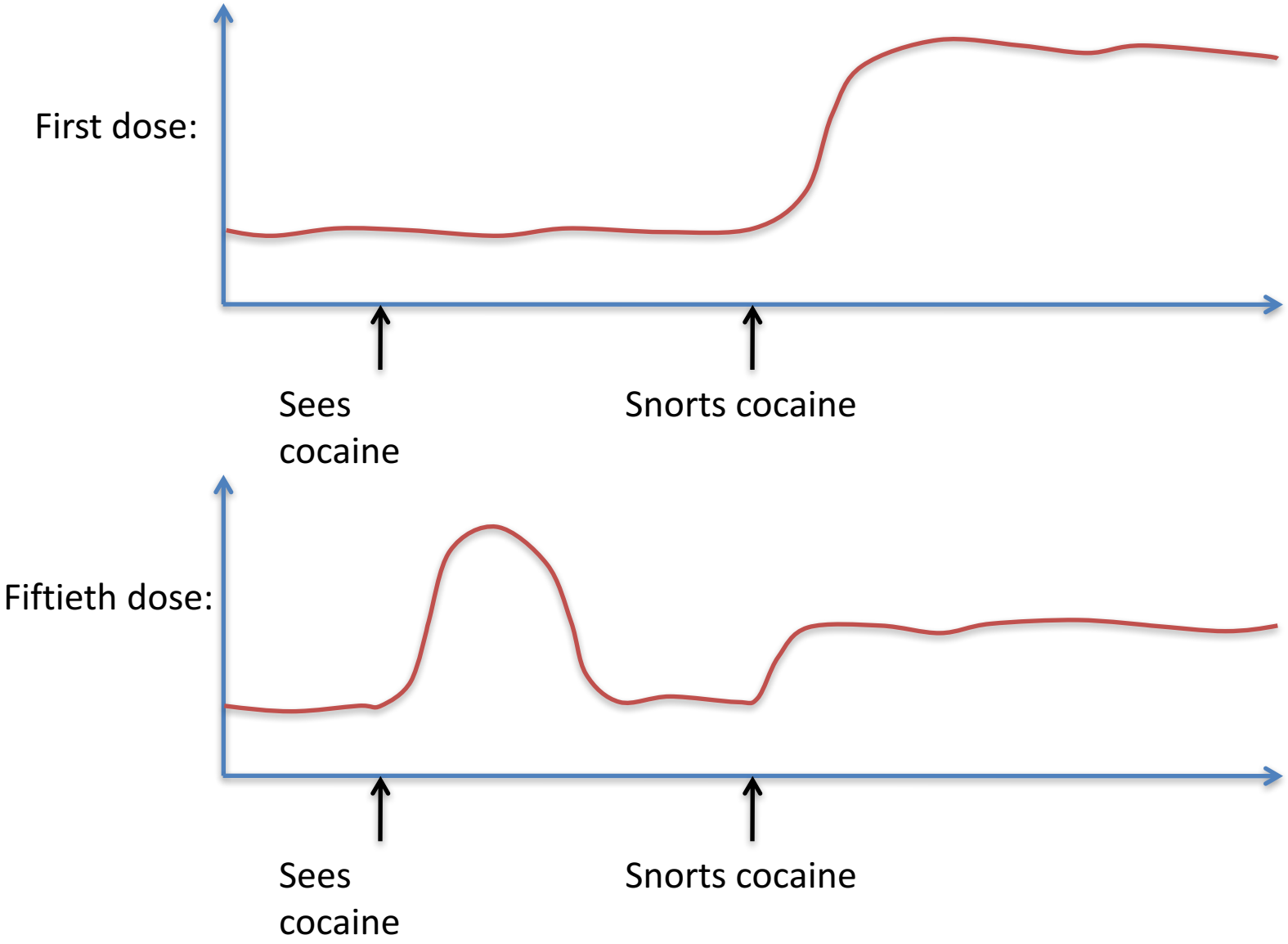
Dopamine signals error in prediction



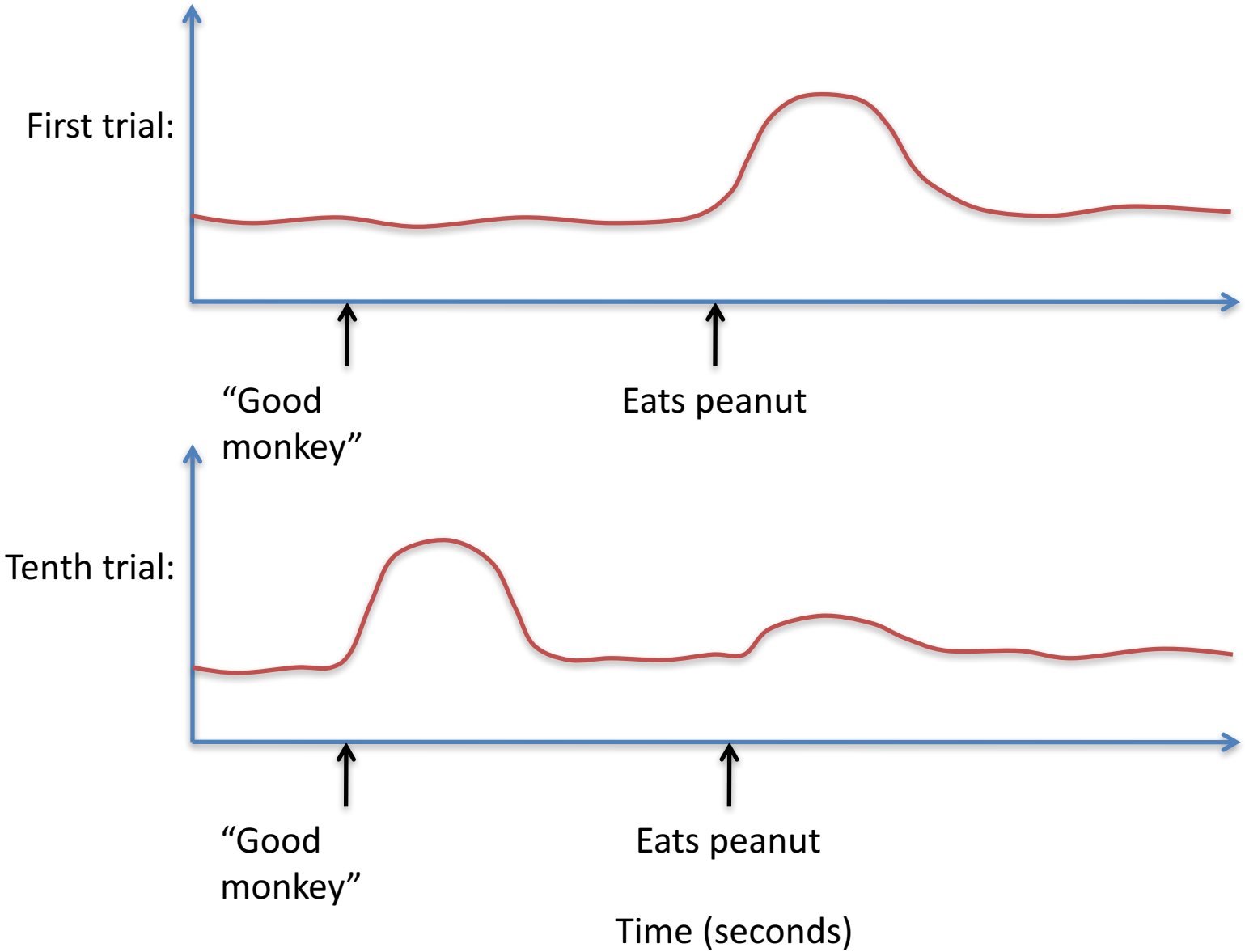
The dopamine burst motivates the animal



Drugs of abuse mimic natural reward



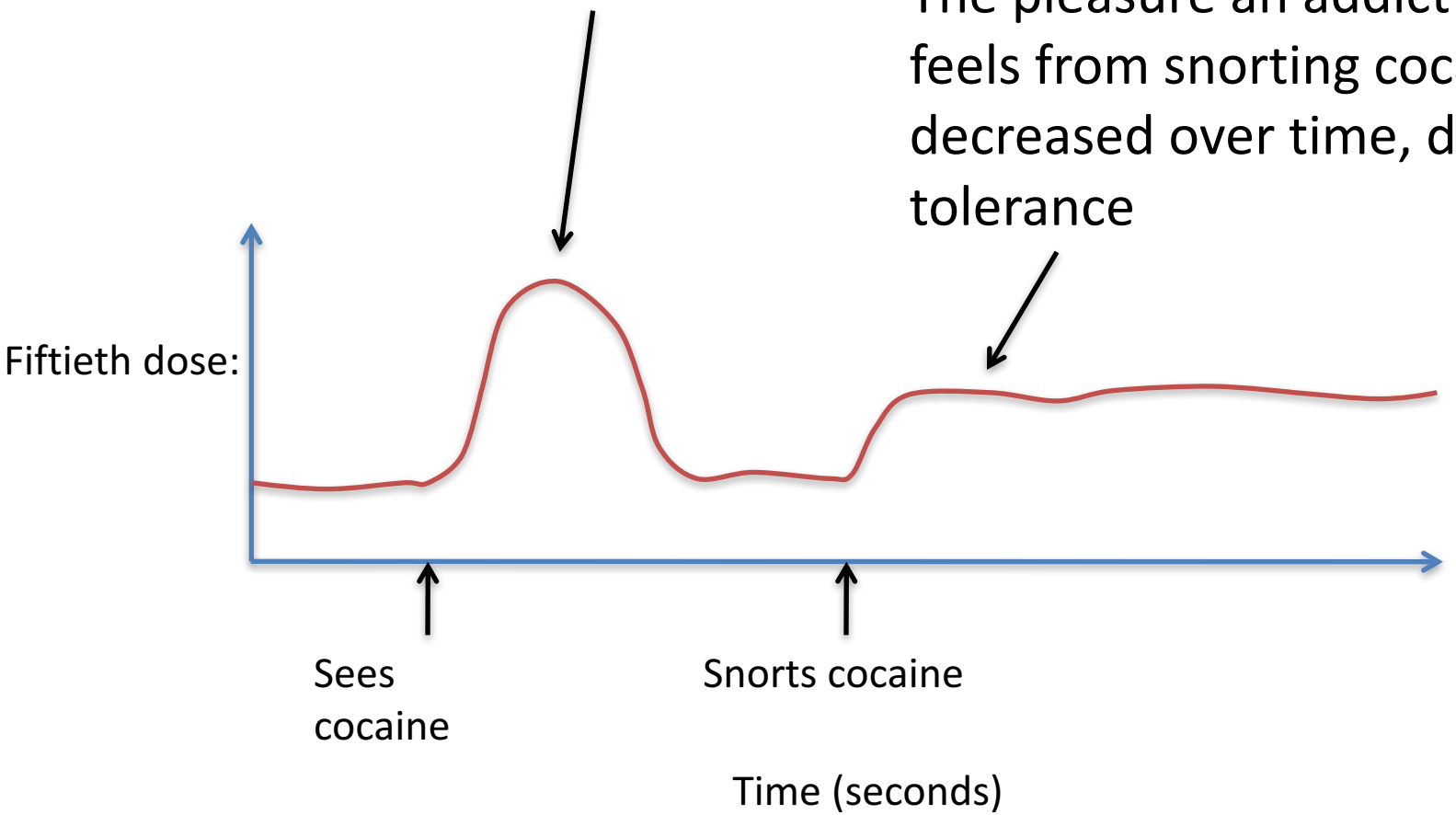
Why does seeing cocaine cause dopamine release?
Remember how conditioning normally works:



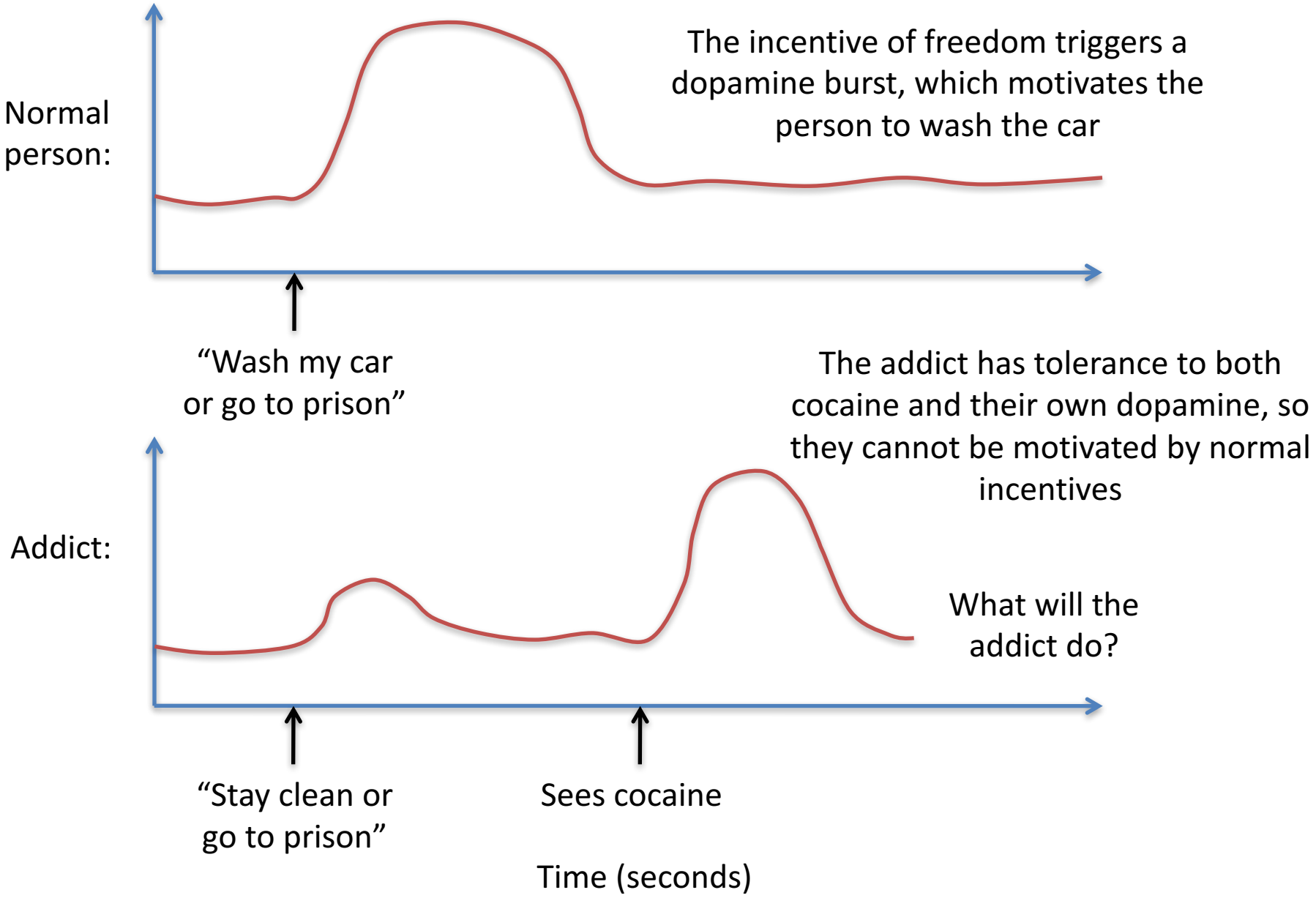
Drugs of abuse mimic natural reward

When an addict sees cocaine, the dopamine burst *produced by his own cells* motivates him to get cocaine and snort it.

The pleasure an addict actually feels from snorting cocaine is decreased over time, due to tolerance



Drug addicts are insensitive to non-drug motivators



Addictive Drugs Are Supramaximal Stimuli

Addictive drugs mimic **food** and **sex,** but addictive drugs stimulate the mesolimbic pathway **far more strongly.**

Drugs are **supramaximal** in that they produce a response higher than anything in nature.

McDonald's food is arguably **supramaximal** as well, because it tastes better than any natural food, and it is coupled with stereotyped associative cues like maroon counters and a logo.

What Was the *y*-axis?

In the prior graphs, what was the *y*-axis, the level of signal?

A. Electrical activity (action potentials), measured by a wire in a rat or monkey brain. (Resolution of 1 millisecond.)

B. Dopamine (DA) release, measured by a very small tube sucking fluid out of a rat or monkey brain. (Resolution of 1 second.)

C. PET scan of a human with radioactive D_2 receptor ligand. (Resolution of 5 to 30 minutes.)

D. fMRI of a human, measures blood flow. (Resolution of 5 seconds.)

Liking versus wanting

Addicts don’t like doing drugs as much as they used to.

Addicts want to do drugs.

Addicts don’t want to do anything else.

Speed of onset and addiction

Drugs which take effect quickly are more addictive, because a fast spike in dopamine more closely mimics natural rewards and the drug-taking behavior is more closely associated with the reward if they come close together

Speed of onset and addiction

Faster onset, more addictive:

Crack cocaine

Injected heroin

Smoked meth (ice)

Slower onset, less addictive:

Powder cocaine (snorted, has an 11 minute absorption half-time)

Snorted heroin (absorbed faster than snorted cocaine. Why?)

Snorted meth (even less addictive: swallowed meth)

Speed of onset and addiction

Faster onset, more addictive:

Xanax (the fast elimination and need for more doses also increases addiction potential. Why do frequent doses lead to stronger addiction? Discuss.)

Slower onset, less addictive:

Klonopin, Librium

Speed of onset and addiction

Faster onset, more addictive:

Snorted Ritalin

Vicodin

Abused (chewed, crushed and snorted) OxyContin

Slower onset, less addictive:

Oral Ritalin

OxyContin

Properly used (intact time-release tablets) OxyContin

ADHD

ADHD is treated with stimulants that boost dopamine (and norepinephrine), why does this work?

Dopamine normally facilitates goal-directed behavior by:

- Increasing motivation
- Focusing attention on the goal
- Providing energy to work towards the goal
- Speeding learning and reinforcing memory

ADHD

Why does dopamine speed learning and reinforce memory?

Discuss

Common Confusion

The following factors are ***not*** part of the definition of addiction:

Tolerance

Withdrawal

Dependence

Tolerance

Drug tolerance is the need for increasingly large doses to reach the same effect.

Many non-addictive drugs cause tolerance, for example diphenhydramine (Benadryl).

Tolerance

Addiction can exist without tolerance. In fact, many addictive drugs cause the opposite of tolerance, which is called **sensitization.**

Classical stimulants are most noted for causing sensitization, including cocaine and methamphetamine.

Tolerance

Tolerance does *not* increase forever, there is a ceiling.

Opioids such as heroin and morphine probably display the most dramatic tolerance. In opioid addicts, **50-fold tolerance** is sometimes observed. In sick people with extreme pain, opioid tolerance can grow even higher.

Tolerance

Tolerance to stimulants is much more limited and harder to gauge. Stimulant addicts may display **5- to 10-fold tolerance.**

Stimulant users may display **2-fold sensitization,** meaning that the drug is twice as potent as it was when they first used it. They only need a half dose. More commonly, they take a full dose and get twice as high.

Tolerance is ***not*** part of addiction

Withdrawal

Withdrawal is the name for unpleasant symptoms that arise when you reduce the dose or discontinue drug use.

Many non-addictive drugs cause withdrawal, including glucocorticoid steroids such as dexamethasone and blood pressure medications. In fact, dexamethasone withdrawal can be fatal.

Withdrawal

Drug addiction can exist without withdrawal. Crack cocaine addicts almost universally can abstain from drug use for a whole day without bothersome withdrawal.

Withdrawal is ***not*** part of addiction

Dependence

Dependence means that you would experience withdrawal if you tried to stop. Thus, dependence is almost a synonym for withdrawal, and as such it is orthogonal to addiction.

Unfortunately, many people use the word dependence as a synonym for addiction, which is just awful in my opinion.

Dependence is ***not*** part of addiction

What Is Addiction?

Addiction is continued use of a substance despite harms that outweigh the benefits, with a lack of control over substance use.

What Is **NOT** Addiction?

A type I diabetic taking insulin. They do have **dependence** and they would have **fatal withdrawal.** Why is this not addiction?

A type II diabetic taking insulin. They do have **tolerance** (called insulin resistance).

What Is **NOT** Addiction?

A recovering addict taking methadone or buprenorphine as prescribed by a competent physician. They do have tolerance and withdrawal. Why is this not addiction?

What Is **NOT** Addiction?

A 60-year-old woman who says “I was addicted to Valium for 20 years, I will never take Valium again. I still have permanent withdrawal symptoms. I was addicted, Valium is very addictive.”

Why is this **NOT** addiction?

What Is **NOT** Addiction?

Everyone who claims to be “addicted” to SSRI antidepressants. Here is why they are **not** addicted:

1. They have full control over their drug-taking behavior. If they take a pill to avoid withdrawal, then it was their choice. If you don’t understand how this is different than cocaine addiction, please ask a cocaine addict about their “decision making process”.

2. They can taper off with no supervision.

What Is **NOT** Addiction?

Everyone who claims to be “addicted” to SSRI antidepressants. Here is why they are **not** addicted:

3. Hopefully, the benefits outweigh the harms. If they do not, then the patient and doctor should change the plan. The patient and doctor may **disagree** about the cost-benefit balance, especially if the patient is blaming things on the SSRI that are not plausibly related.

4. SSRIs do not cause DA release in the NAcc. This is a *sine qua non* feature of true addiction. SSRIs are simply non-addictive drugs. Not ever.

Physical vs. Psychological

The idea of “physical addiction” and “psychological addiction” is **horse crap.** Addiction is a disease, and like all diseases it is based on **physical changes** in the brain. The physical basis of addiction can be seen at autopsy or with PET scans. You can take a picture of it. Addiction is also psychological and behavioral.

Physical vs. Psychological

People often talk about “physical withdrawal” and “psychological withdrawal”, which is **horse crap** because withdrawal is **not** part of the definition of addiction.

Different drugs cause different withdrawal symptoms in different people. This has very little to do with addiction. The severity of symptoms will impact treatment choices, but the physical vs. psychological distinction is useless.

Physical vs. Psychological

People often talk about **“psychological dependence”**, such as “Johnny cannot board an airplane without Valium.” This is not addiction and this is not even dependence. Johnny doesn’t have withdrawal without Valium, he has a panic attack. The panic attack is induced by the airplane, not by the lack of Valium (which he only takes a few times per year, when he flies).

What Causes Addiction?

Simple answer: Repeatedly taking an addictive drug, but **only** with the right circumstances.

Risk factor: Family history of addiction.

Risk factor: Age 10 to 25.

Risk factor: Taking the drug for fun.

Risk factor: Faster-onset drug.

What Causes Addiction?

Protective: Taking the drug exactly as prescribed by a competent physician.

Protective: Taking the drug in the context of an illness, e.g. a recent surgery.

Protective: Taking the drug on a regular schedule, **not** as needed.

Protective: Being given the drug, e.g. by a robotic pump or a nurse with a pill.

What Causes Addiction?

Risk factor: **Environmental stress,** anxiety, depression, any kind of hardship. Heroin use in Vietnam soldiers was very high.

Risk factor: Drug availability – easy access, low price.

Risk factor: Social acceptance of the drug.

Nora Volkow MD

She is the director of the National Institute on Drug Abuse (NIDA). She is the granddaughter of Leon Trotsky. She is one of my heroes.

She has done some great experiments and written some great quotes.

Nora Volkow Quotes

All quotes are from the NEJM paper where she was lead author, the topic was opioid addiction.

“Unlike tolerance and physical dependence, addiction is not a predictable result of opioid prescribing. Addiction occurs in only a small percentage of persons who are exposed to opioids - even among those with preexisting vulnerabilities.”

Nora Volkow Quotes

“The identification of these risks* does not automatically rule out opioids as part of effective pain management.”

* She is referring to risks like a past history of opioid overdose, marijuana in the urine, methamphetamine in the urine, and other things that often result in untreated pain due to prejudice on the part of the doctors. Nobody deserves pain, and that includes people who have made mistakes.

Opioid Prescribing vs. Addiction

Increased opioid prescribing **correlates** with more addiction and more overdoses.

Correlation does not imply causation, and reverse-causation is definitely at play. Existing drug addicts **ask for drugs** and that causes prescriptions, cf. pill mills. Drug addicts make great customers, and that is true for licensed doctors as well as crack dealers.

Opioid Prescribing vs. Addiction

Increased opioid prescribing pours gasoline on the fire of existing addiction. More pills in more medicine cabinets means more pills to steal or buy. It means more temptation for relapse. Being able to easily convince a doctor to write you a scrip also makes it easier to relapse, **if you lie to the doctor.**

Unethical OxyContin marketing **definitely** helped to fuel the opioid epidemic. The pills are large, the target (PCPs) were uneducated.

Legitimate Prescriptions Rarely Cause Addiction

Legitimate prescriptions from a **competent** physician given to an **honest** patient and **used in accord with directions** will almost never cause addiction.

Tolerance and withdrawal are predictable and inevitable.

Tolerance and withdrawal *per se* are not bad and should not be avoided.

Legitimate Prescriptions Rarely Cause Addiction

About 99% of people who use opioids as directed for surgery, cancer, or other organic pain **do not become addicted.** It may be more like 99.9%.

100% of people who use stimulants as directed for ADHD do not become addicted. The doses used for ADHD are insufficient to cause addiction, it is necessary to violate the physician's orders in order to cause new-onset addiction.

What Caused the Opioid Epidemic?

The US is honestly in an opioid addiction epidemic. What caused it?

1. The War in Afghanistan and very cheap heroin.

2. The economic recession. (Heroin is cheap, it makes you happy, and it fits your schedule nicely if you are unemployed.)

3. Unethical OxyContin marketing.

4. Easy-to-scam doctors who wrote too many prescriptions **to lying drug addicts.**

What Caused the Opioid Epidemic?

5. Drug use is a **social phenomenon,** and drug addiction is socially contagious. It spreads within communities. This actually caused the **end** of the crack cocaine epidemic.

6. Doctors running pill mills to make money.

7. Poor education of doctors and pain patients.

8. **Cheap heroin.** This really cannot be over-emphasized. Afghanistan's heroin production exceeded global demand by a wide margin, which inspired drug dealers to find new customers.

Addiction Can Be Hard to Diagnose

The following factors can make it hard to diagnose addiction:

Lying

Uncertain harms from the substance

Uncertain benefits from the substance

Preexisting problems, which are not due to the substance

However, addiction is often *very easy* to diagnose.

Most of the people who use heroin or cocaine every day are clearly and unquestionably addicts.

Despite all this uncertainty about diagnosis, it is important to keep two things in mind:

First, full-blown addicts cannot plausibly remain in denial or fool their doctors and family.

Second, borderline addicts or near-addicts should be careful. They are walking a fine line, and they need to be watched, guided, and cautioned.

Slide Title

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More space-filling text here, this time in English. Yes, this is dummy text for typesetting purposes.

A third paragraph of junk.