

Control Vs. Choice In Addiction



HOW DO PEOPLE CHOOSE AND WHAT GOES
WRONG WHEN ADDICTIONS HAPPEN?

ADI JAFFE, PH.D.
ALL ABOUT ADDICTION

Talk summary



- What is addiction?
- Understanding choice
- How does control factor in?
- What happens when drugs enter the picture?
- And when they leave? Is there hope?

What is addiction?



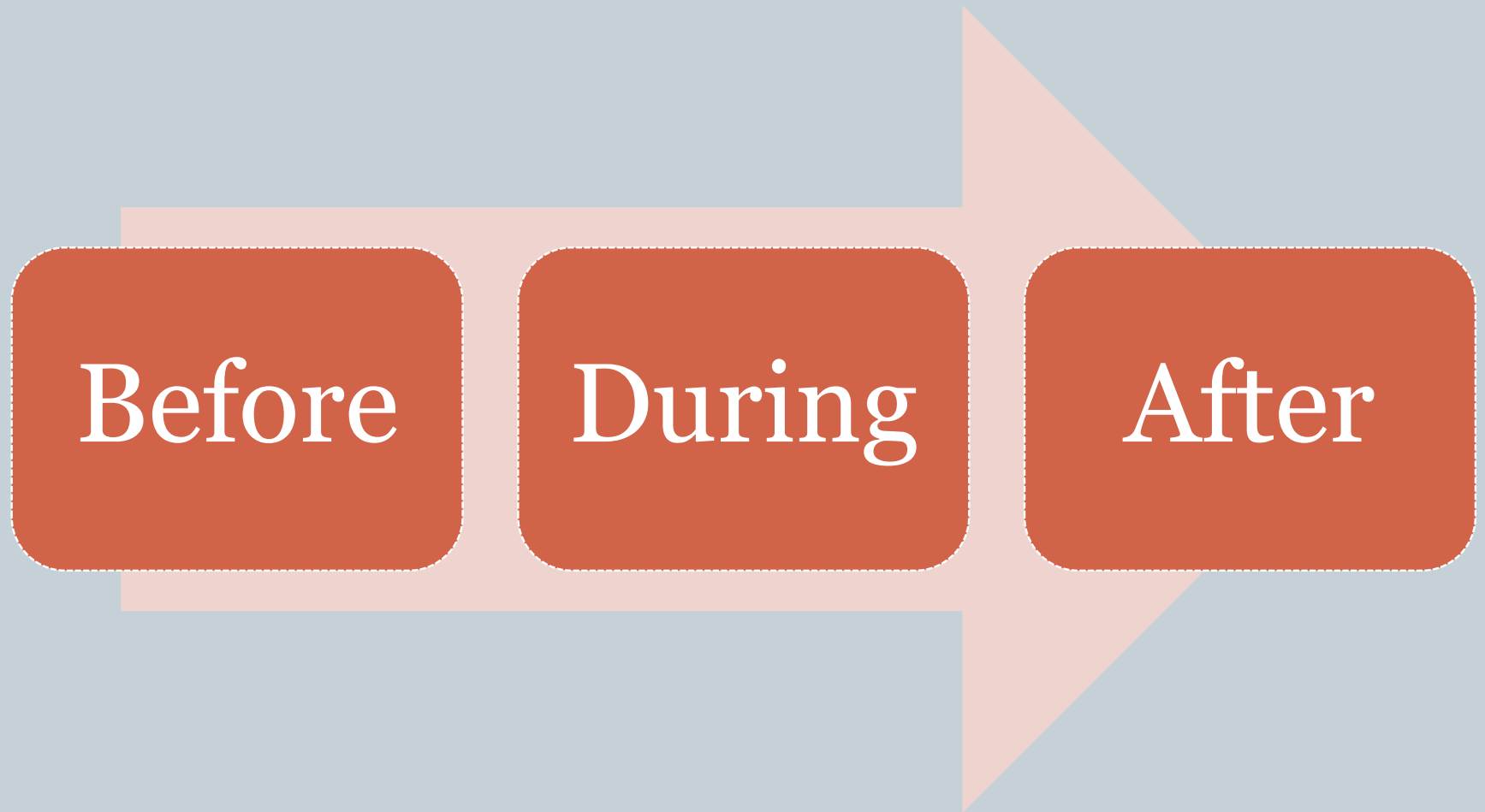
- **Addiction is a complex condition that involves biology, psychology, and the environment**
 - Call it a disease or not – the issue is a semantic one that has more to do with stigma than anything else
 - Regardless, many aspects of addiction are out of a person's individual control, and that's what truly matters
 - ✦ Genetics, the environment one is born into, injuries (and resultant pain medication)
 - The notion of choice in addiction is true, as long as one can truly understand what “choice” really means
 - ✦ The book by dr heyman from harvard

What is addiction?



- Throughout this talk it's important that we understand that addiction is not really all that different from other chronic diseases:
 - Diabetes – Especially type II, whereby genetic predisposition interacts with behavior, causing a final syndrome.
 - Hypertension – again, a combination of vulnerability (estimated at 40%-50%) combined with environmental and behavioral influences (stress, diet, etc.)
 - Addiction is (50%-60% heritable) and sees compliance rates with treatment that are very similar to these other two conditions (around 30%) and very similar relapse rates (around 60%)
- The only difference seems to be the stigma about addiction relapse!

Addiction's progression

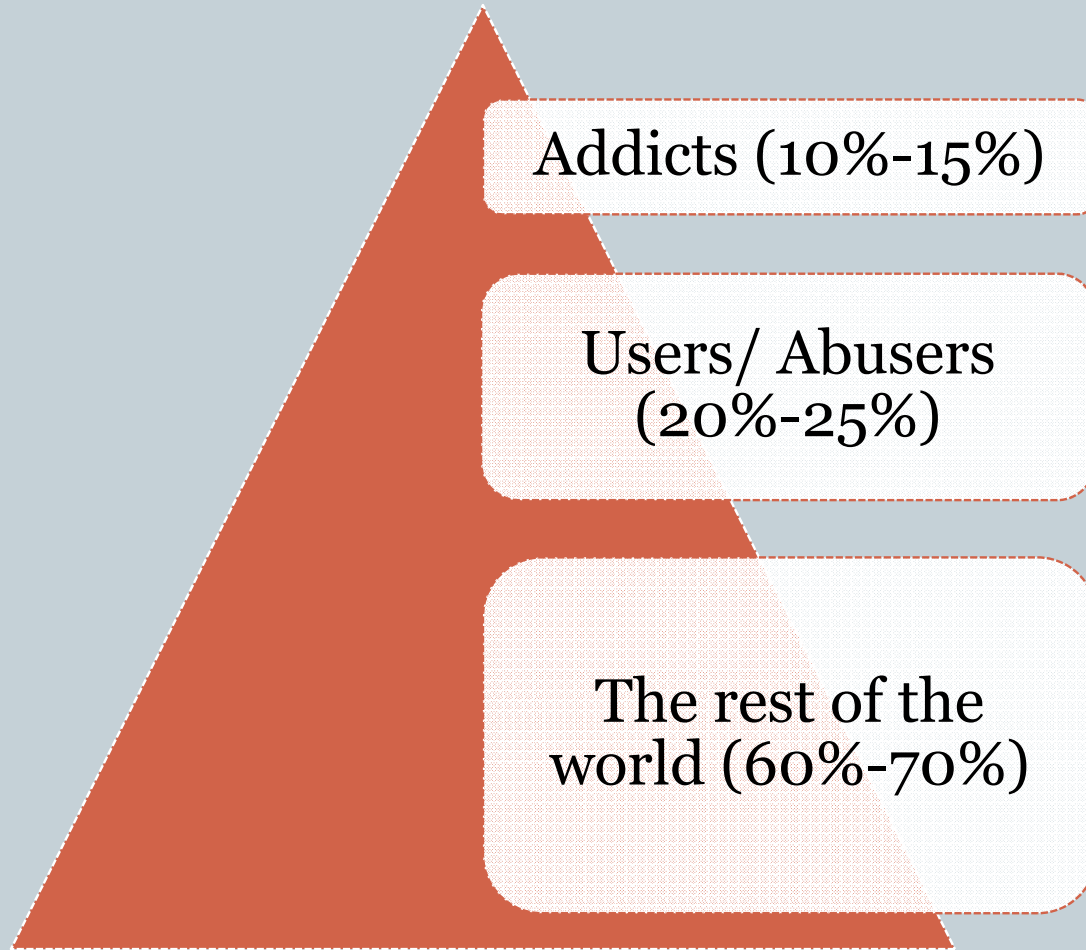


Before

During

After

Keeping Things in Perspective



Understanding Choice

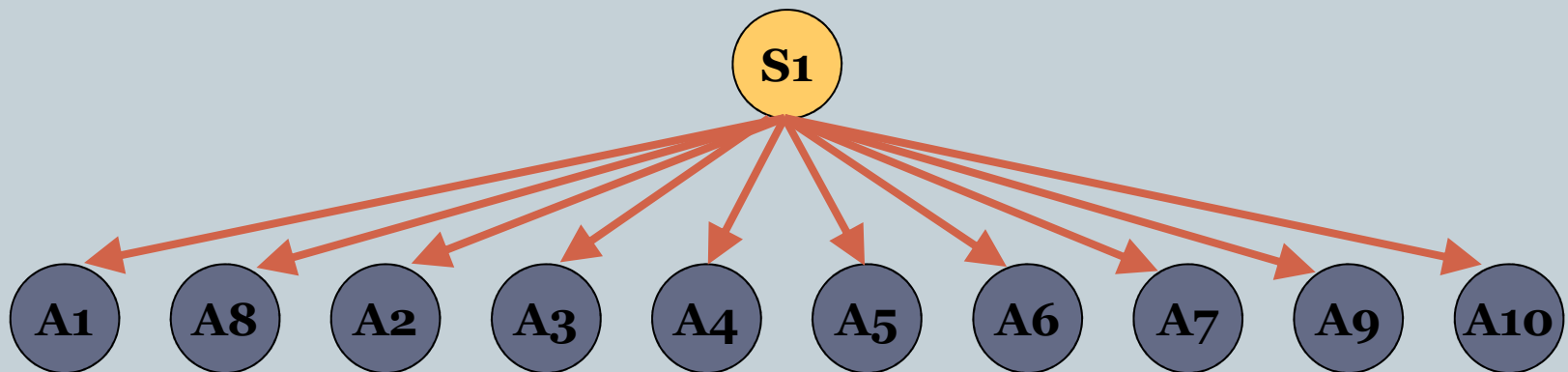


- We normally think of choice as being straight forward
 - You choose to pick up a phone, close a door, light a cigarette, or do a line of coke
- The reality is that there are incredibly complex brain circuits involved in making choices
 - Those circuits can function differently for genetic (pre-existing), environmental (pre existing or not), or behavioral (like drug taking) reasons

Understanding Choice - Options



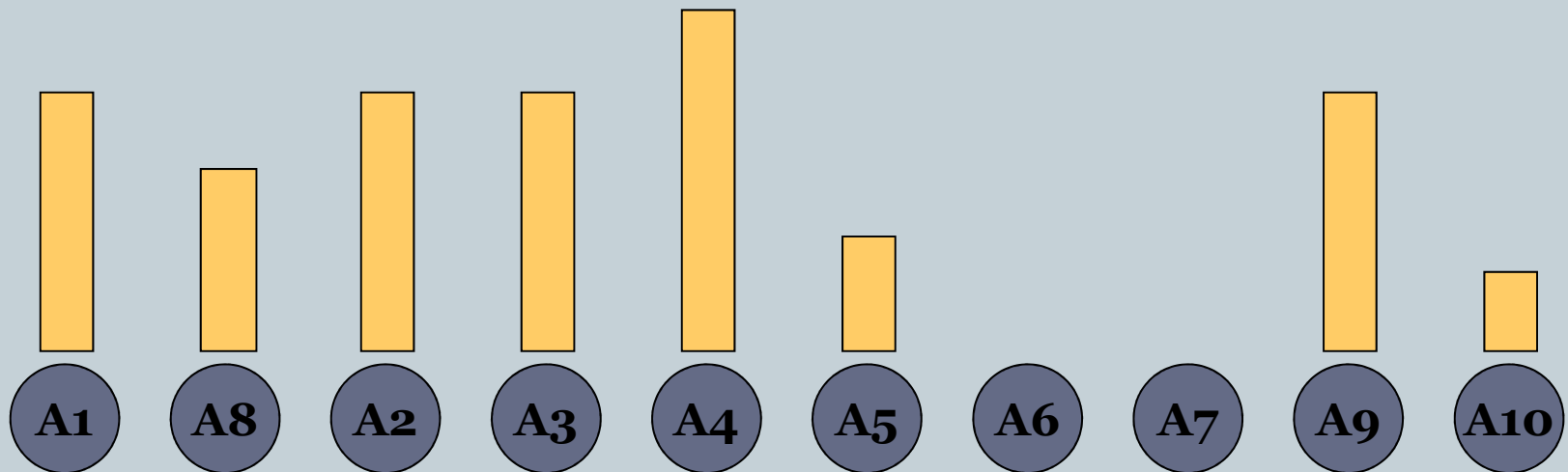
- At every point in time, an individual can be thought of as having a number of possible action to perform – the brain is there to help us make the best choice possible, but how?
- Let's think about the goal...



Understanding Choice - Options



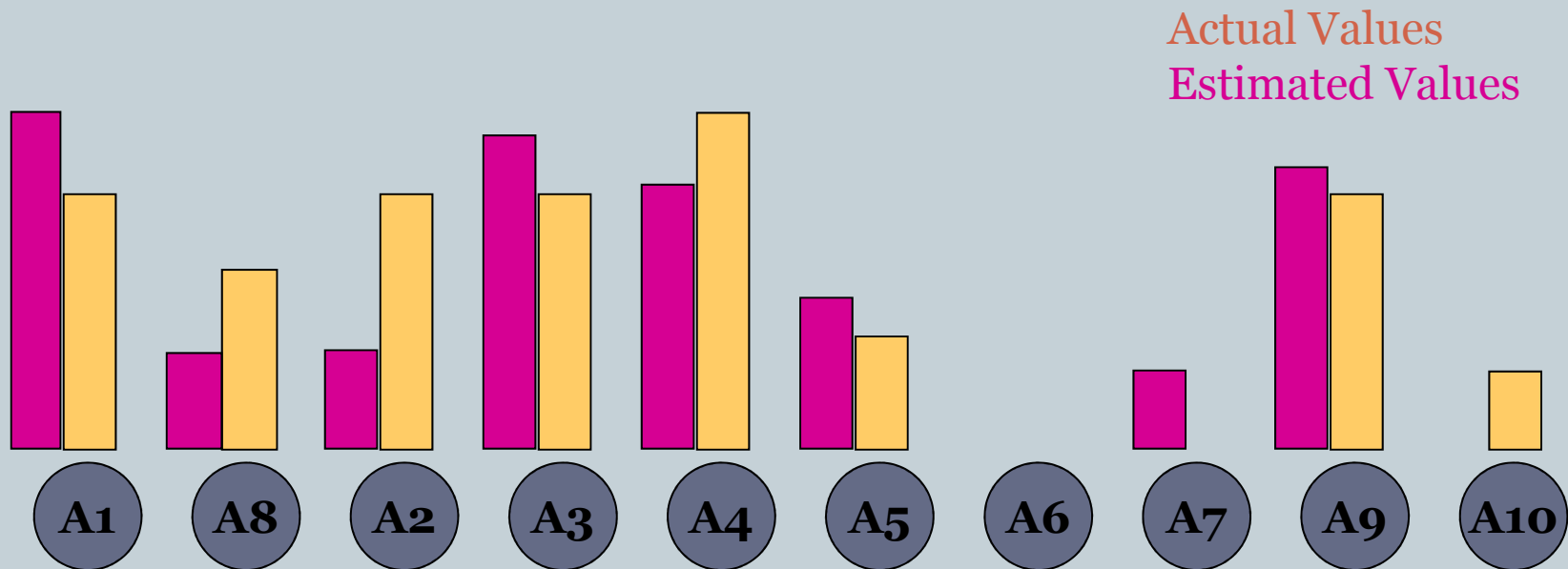
- In order to choose, we have to know something about how valuable, or rewarding, each selection would be, right?
- So we start out by estimating



Understanding Choice - Options



- And we probably end up being a little off (if we have enough experience with these actions, if we don't, we may have no estimate or really bad ones)



We need to learn the real values



- Without getting too far into the equations for this, learning (about rewards) is the process of adjusting our expectations to match reality so that we can make better choices for the long term...
- Right???

$$Q_{k+1} = Q_k + \frac{1}{k+1} [r_{k+1} - Q_k]$$

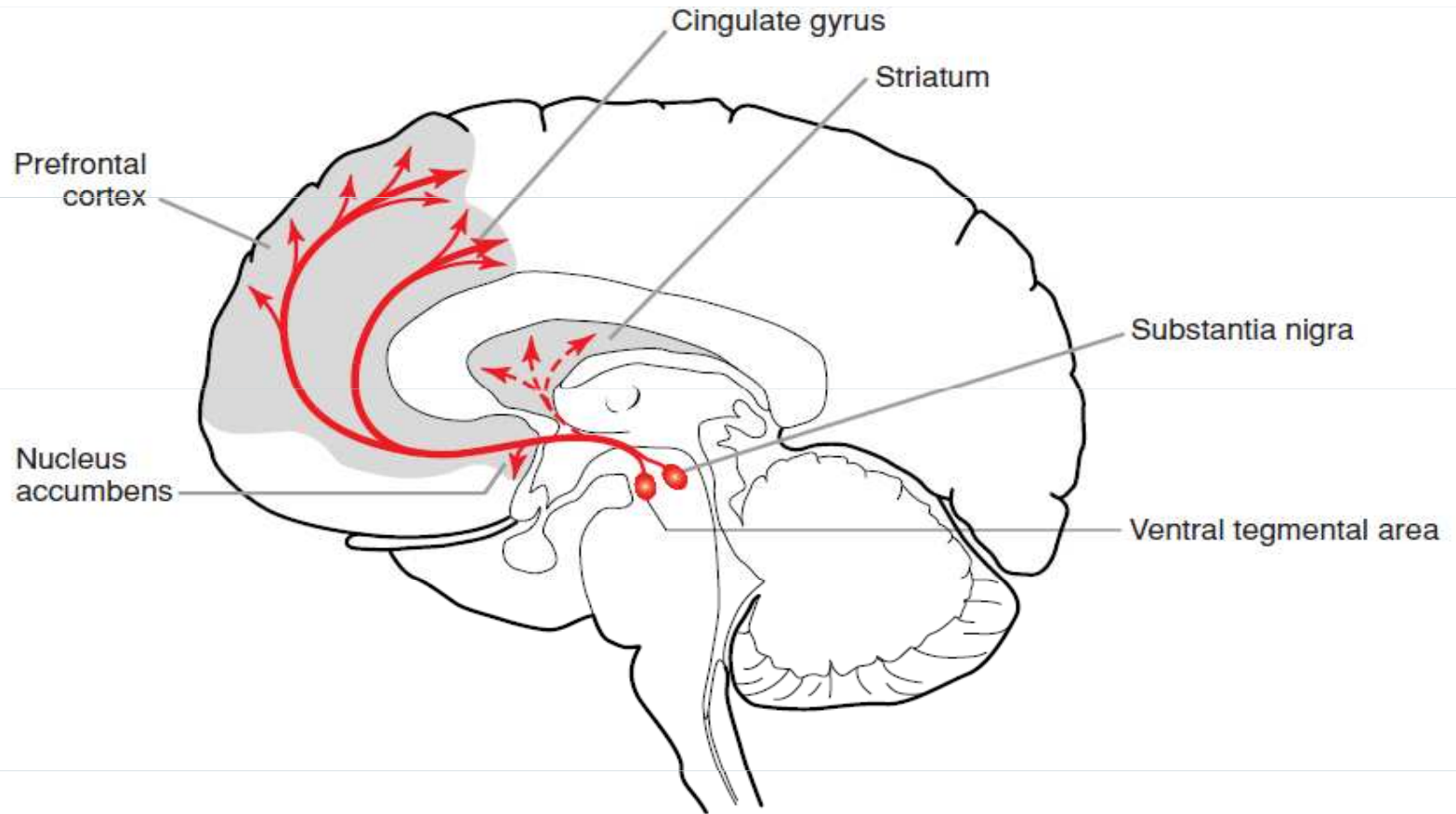
NewEstimate = OldEstimate + StepSize [Target – OldEstimate]

Understanding Choice - Calculating

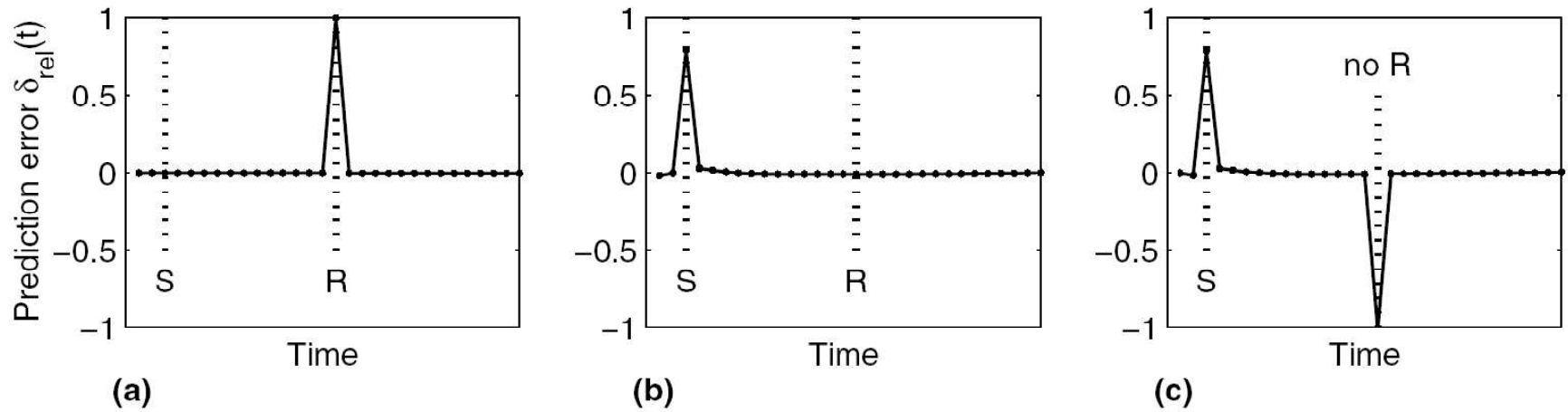


- All of the calculations take place in the brain
 - likely within a system known as the mesolimbic dopamine pathway, which some people call our “Reward System” although that is quite the simplification.
- Regardless of where it happens, it’s pretty clear that a large portion of our learning is dedicated to improving future choices
 - On tests (in class)
 - At meetings (in work)
 - In conversation (with loved ones or acquaintances)

The brain system for reward learning

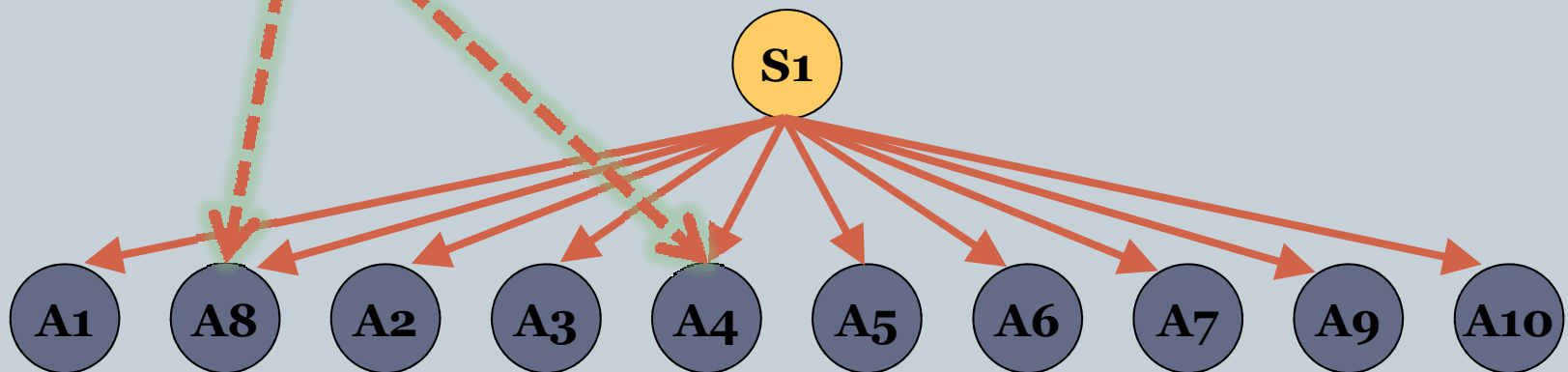
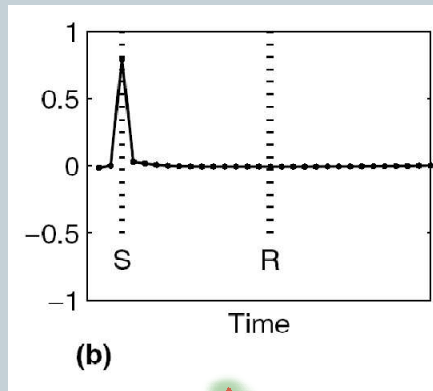


A possible mechanism using dopamine



Taken from Redish (2004)

How learning helps us choose



How does control factor in?



- The learning system for choices is obviously quite complex
 - Neurotransmitters
 - ✦ Dopamine
 - ✦ Glutamate
 - ✦ GABA
 - ✦ And likely more
 - Brain area
 - ✦ Neucleus Accumbens
 - ✦ Ventral Tagmental Area
 - ✦ Prefrontal Cortex
 - ✦ Hippocampus
 - ✦ Amygdala

How does control factor in?



- Each of those neurotransmitters, and each of the brain regions rely on a whole set of factors to support their function:
 - Neurotransmitters
 - ✦ Manufacturing (Dopamine needs Tyrosine)
 - ✦ Packaging (molecules put neurotransmitters into packages for release)
 - ✦ Release (needs Calcium and proper signaling)
 - ✦ Recycling and breakdown (DAT, the cocaine target blocks DA recycling)
 - Brain regions
 - ✦ Construction of neurons
 - ✦ Their maintenance

How does control factor in?

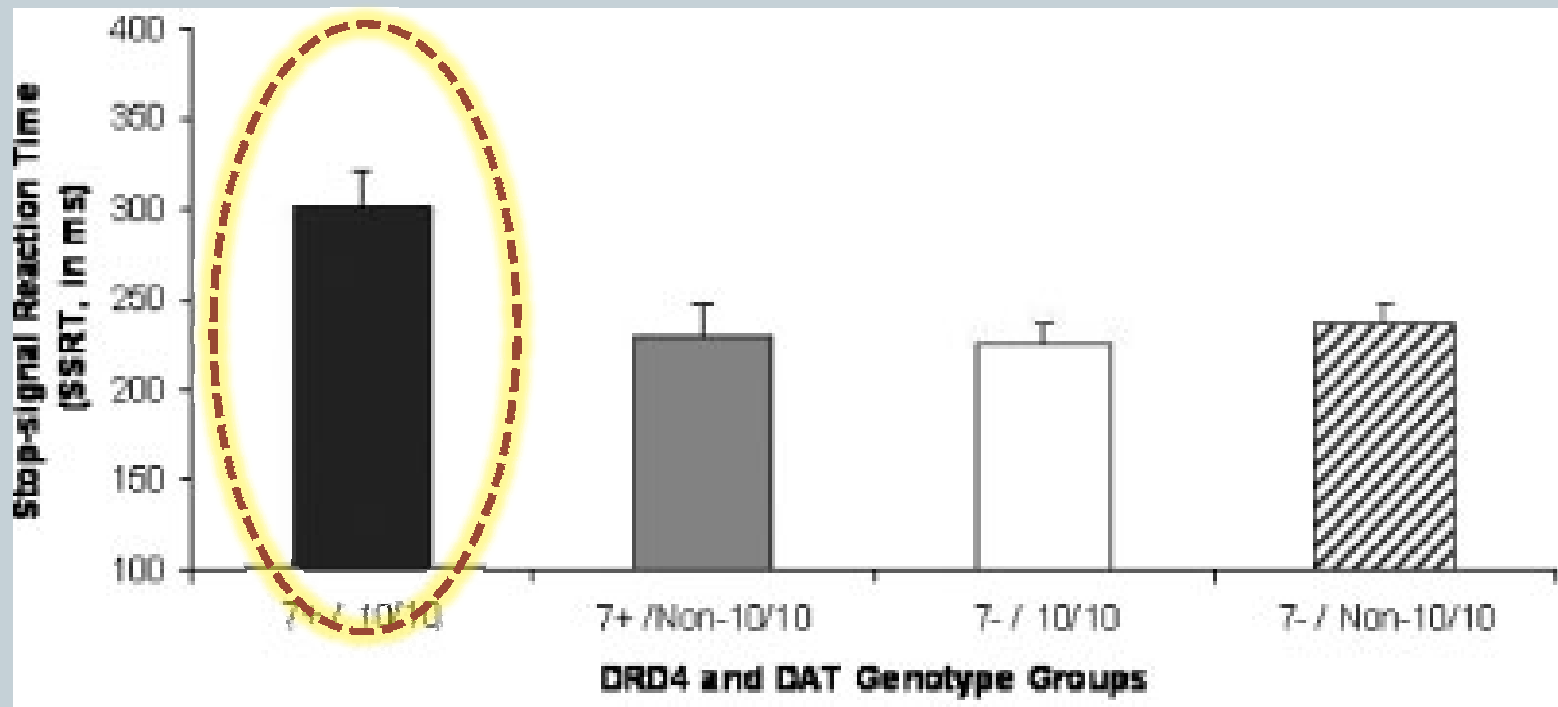


- Problems in any of these areas lead to issues in the functioning of the system that can have terrible impacts on its precision and effectiveness
 - Non-addiction related areas (where you can see the result of brain dysfunction)
 - ✦ Parkinson's Disease - death of DA producing neurons in the substantia nigra.
 - ✦ Huntington's disease – Problems in the striatum make it impossible to choose proper motor function and patients end up with flailing limbs (known as the Huntington's Dance).
 - In addiction relevant instances (where we can't "see" the effect and people have problems believing)
 - ✦ Attention deficit and impulsivity
 - DA receptor (D4 –7 repeat version which is less active) and faster recycling of DA by DAT. All leading to a reduction in some functioning of the DA system.
 - Noradrenaline (alpha 2) receptor
 - PFC – Likely a DA → NE balance issue

How does control factor in?



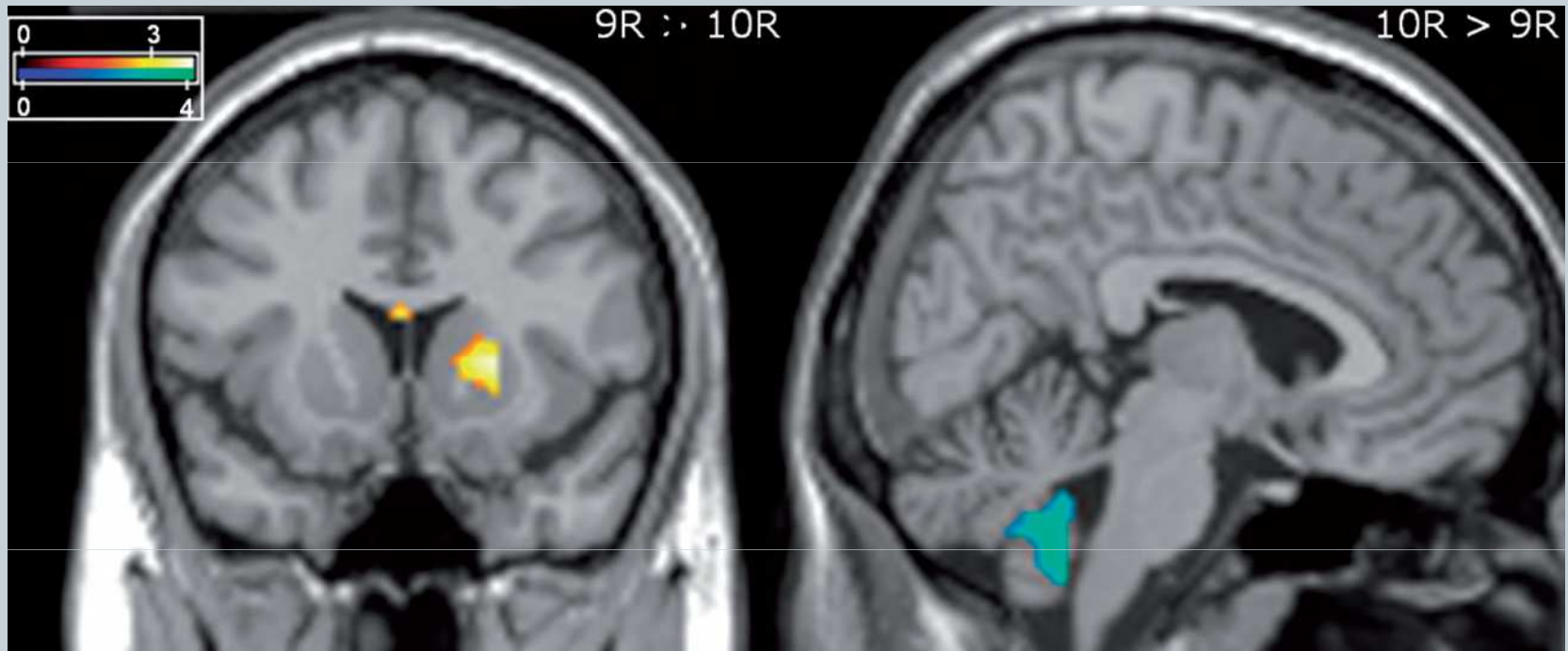
- But here's some proof we can "see" (stop-signal reaction task)



Taken from Congdon, Lesch, and Canli, 2007



- More evidence you can see:
 - Differential activation of brain regions based on DAT genotype (during go-no-go trials, the 9 allele provided more activation in the striatum)

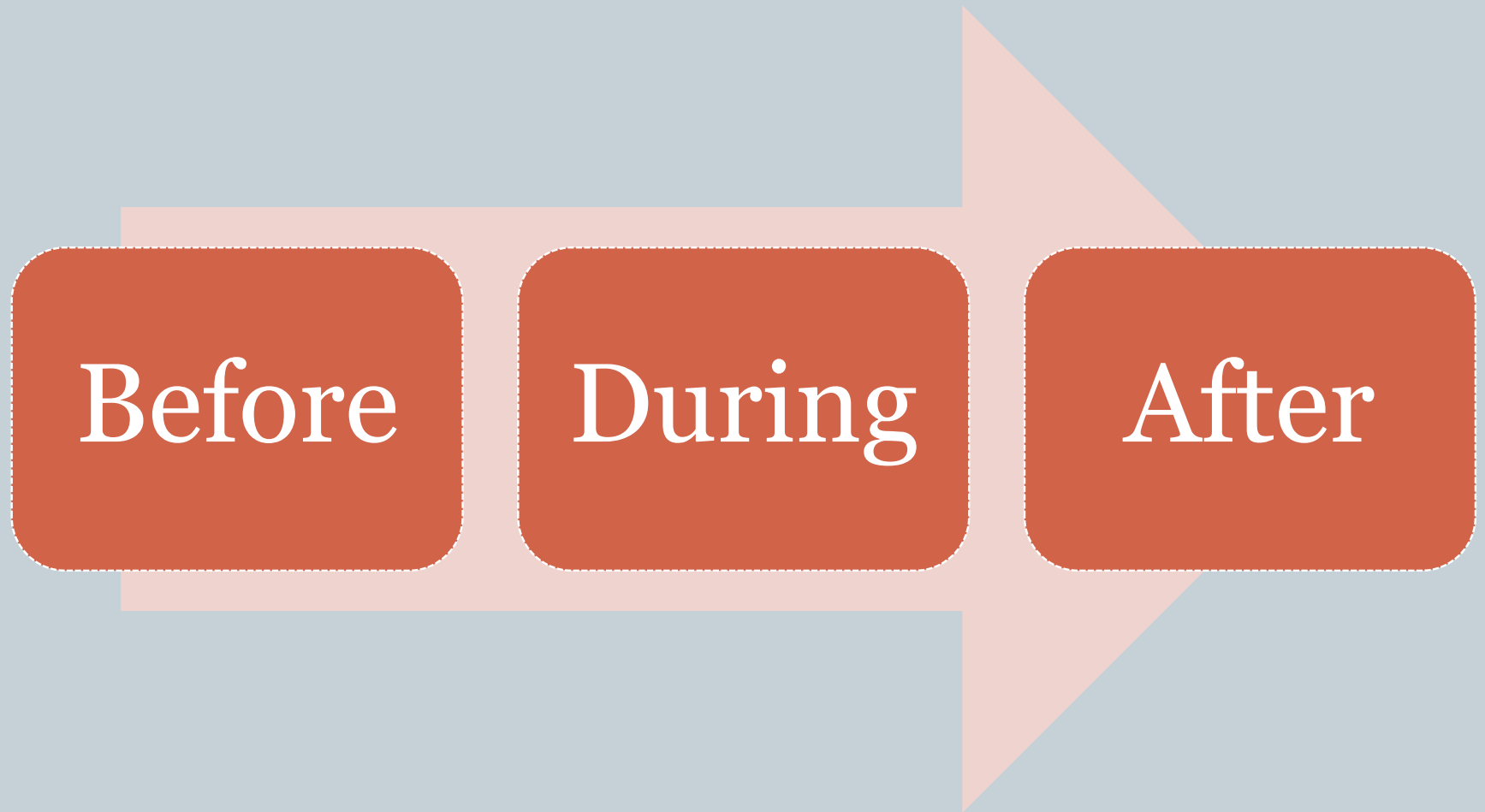


Planned Vs. Automatic processing



- As if all of this wasn't complicated enough, there's evidence that choice mechanisms are biased towards automatic, instinctual, choices when aroused or anxious:
 - Amygdala function normally combines with PFC control to affect NAc firing
 - When amygdala function is high (either because of transient arousal or in conditions like schizophrenia and addiction) it likely trumps PFC inputs to bias activation towards emotionally charged events (McGinty & Grace, 2009).

Addiction's progression



Before

During

After

Control and Choice in Addiction



- When you throw drugs into the mix, the entire equation we've been discussing gets distorted
 - Drugs directly change the release of many neurotransmitters
 - ✦ Dopamine (essentially all drug of abuse)
 - ✦ GABA (benzodiazapines, alcohol)
 - ✦ Opioids (opiates, alcohol)
 - ✦ Serotonin (alcohol, mdma)
 - ✦ Norpinephrine (methamphetamine, cocaine)
 - Chronic drug use can create long, if not permanent changes in the ways some brain regions function
 - ✦ Neurotoxicity, reductions in neurotransmitter production, receptor density, and more
 - ✦ Very unique alterations in learning (enhanced associative learning that is inflexible to changing environmental needs)
 - ✦ Semi-permanent enhancement of learning about drug-related cues (triggers)

Control and Choice in Addiction



- It doesn't make it any easier that individuals who develop drug-dependence (addiction) are also more likely to suffer from:
 - ADHD
 - ✦ 30%-50% in substance abusers – 1%-6% in general population
 - Depression
 - ✦ 30%-60% in substance abusers – 7%-10% in general population
 - Anxiety disorders
 - ✦ 20%-45% in substance abusers – 5%-10% in general population
 - Schizophrenia
 - ✦ 4.5 times more likely to have a substance abuse or dependence disorder compared to the general population

Estimates drawn from Chan, Dennis, and Funk (2007) and Meyer & Nasrallah (2009).

Control and Choice in Addiction

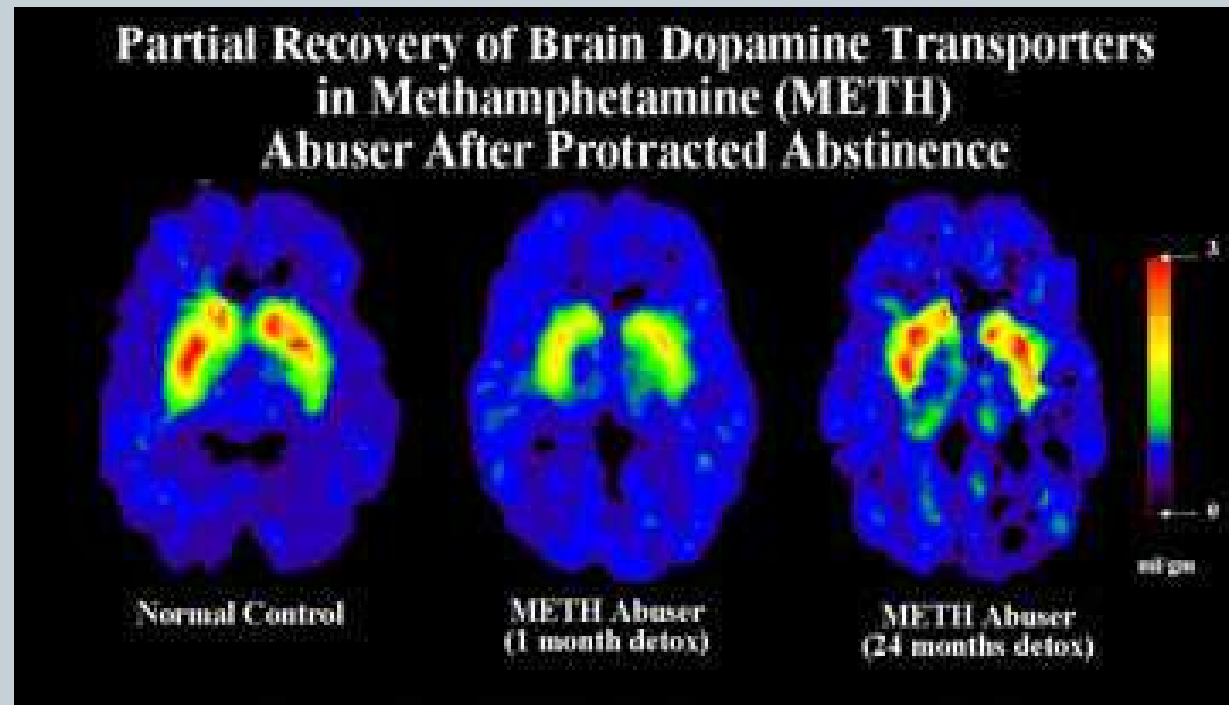


- But genes can also be protective against addiction
 - Obviously the reverse of the genetic variations we already talked about have lower drug dependence and addiction rates (and also lower adhd, depression, and so on).
 - But some people are protected specifically from use of some drugs based on their genetic makeup
 - ✦ ALDH2-2, common in Asian populations, is protective against alcoholism because individuals can't process aldehyde very well which leads to extreme flushing (almost no alcoholism found in individuals with 2 copies of this version)
 - ✦ Nicotine metabolism – individuals who break down nicotine slowly smoke less cigarettes, are less likely to become addicted, and are twice as successful at quitting smoking with nicotine replacement alone

Control and Choice in Addiction

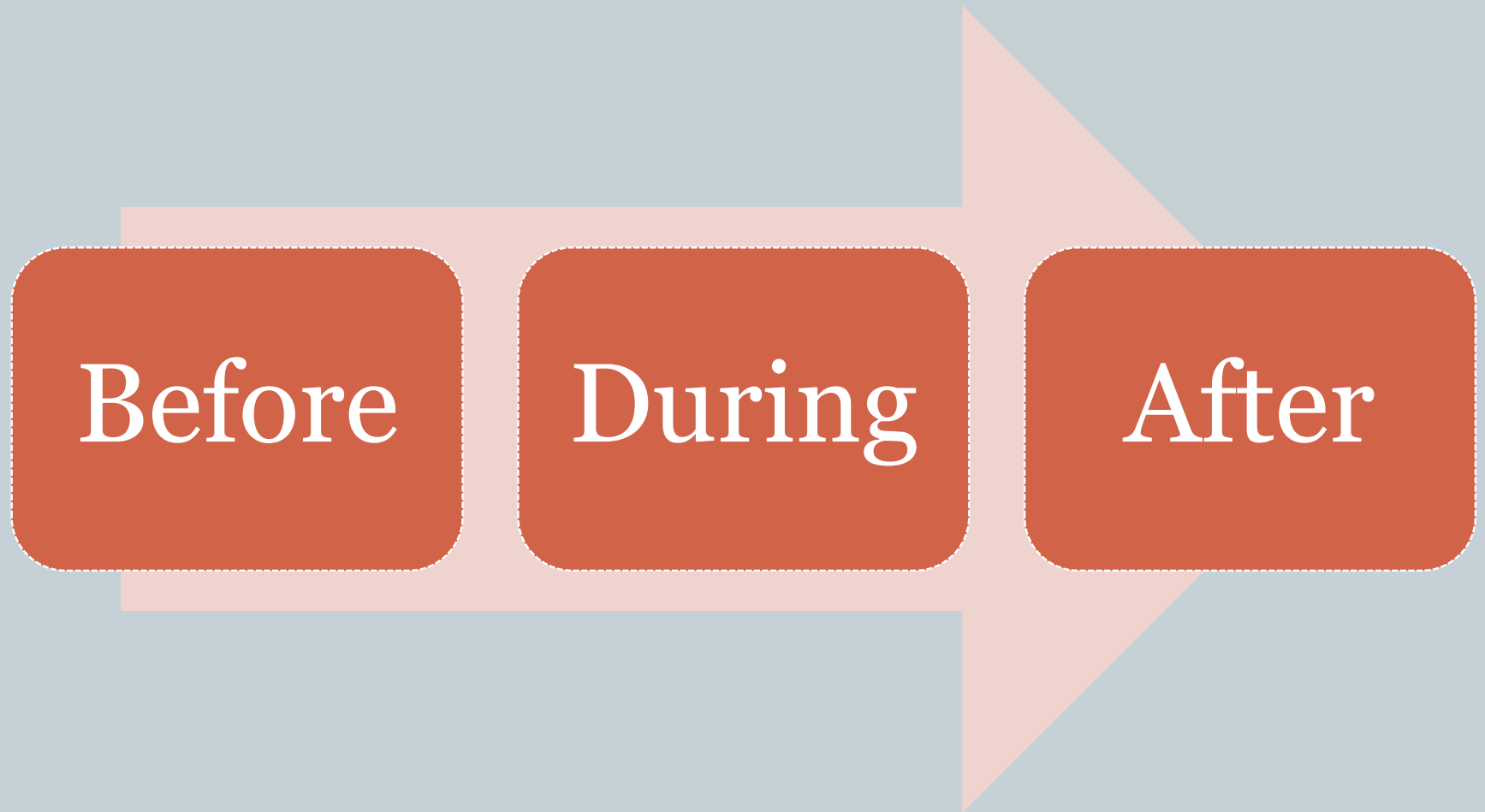


- When you combine all of the drug effects with systems that are more often than not compromised from the get-go...



Volkow et. al (2005)

Addiction's progression



Before

During

After

Can addiction treatment help?!



- As the previous figure showed, there appears to be some recovery of brain function after long abstinence from drug abuse.
 - Without actual experiments using randomized subjects, it's hard to know how much of what's missing is due to pre-existing factors and how much is due to drug use.
- Nevertheless, it obvious that we're fighting an uphill battle when dealing with addiction
 - But remember that this isn't different from other chronic conditions!
 - So what do we do?

Can addiction treatment help?!



- We come up with tricks and methods that make it more likely that people will:
 - Go into treatment (MI, medications)
 - ✦ Motivational enhancement therapy, antidepressants, modafinil.
 - Stay in (CM, medications)
 - ✦ Reward positive behaviors, buprenorphine and vivitrol to reduce relapses and their consequences (vaccines?)
 - To get our evidence based practices (CBT, talk therapy, social-support, 12-step facilitation, medication)
 - ✦ Manuals for standardization, social-support is important, and medication for those still struggling can really help
 - Prevention of relapse
 - ✦ CBT is good for this, hopefully the new medications, and maybe some future pharmacotherapies (propranolol??) can help here, but it's hard
- Triggers serve as very strong re-igniters of drug-seeking behavior, possibly permanently, which makes it very difficult for recovering addicts.
 - This goes right back to the issue of control versus choice



- **We do our best to tailor treatment to the individual**
 - Medication + Nicotine replacement for individuals that metabolize nicotine quickly
 - Outpatient versus residential based on severity, treatment experience, and more
 - One day, we will hopefully be able to really tailor treatment (genetics, imaging tests, drug experience, and more)
- **When all is said and done, individuals often need to make significant life changes AFTER treatment to reduce their chances of reinstatement of the problems**
 - For many, this means complete abstinence is the best course
 - Does it have to mean that thought for everyone?