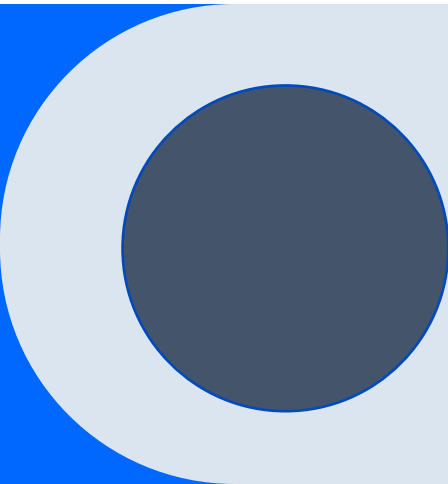





Understanding Withdrawal



Nicole Rodin, PharmD, MBA
Clinical Assistant Professor
Washington State University CPPS

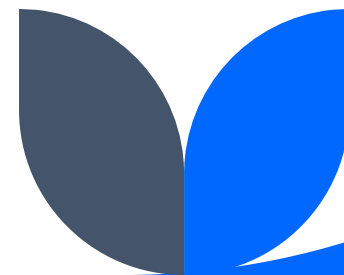


Session Objectives

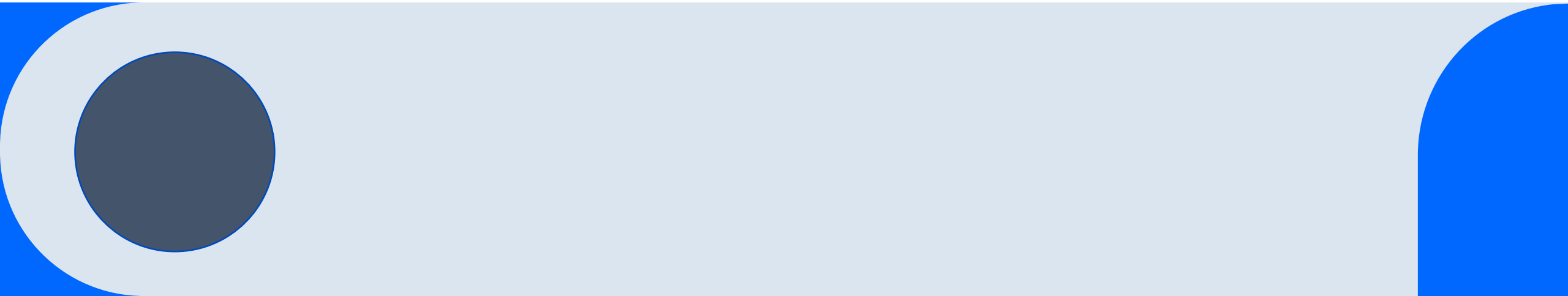
1. Describe how withdrawal occurs in the body
2. Identify life threatening symptoms of various withdrawal processes
3. Explain what typical withdrawal symptoms are experienced in withdrawal from alcohol, opioids, stimulants, cannabis, and benzodiazepines.

Prevalence of Withdrawal Syndromes

- Approximately half of patients with an alcohol use disorder (28.9 million Americans) experience alcohol withdrawal when reducing or stopping their consumption
- About 10% of patients who abuse benzodiazepines reported withdrawal symptoms
- 47% of patients who use cannabis regularly experience cannabis withdrawal syndrome
- Most patients who chronically use opioids and/or stimulants will report withdrawal symptoms at discontinuation

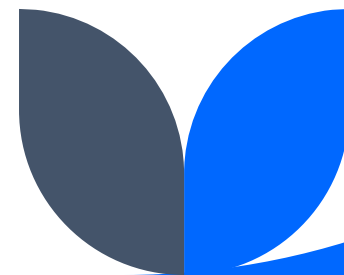


**What is
withdrawal?**



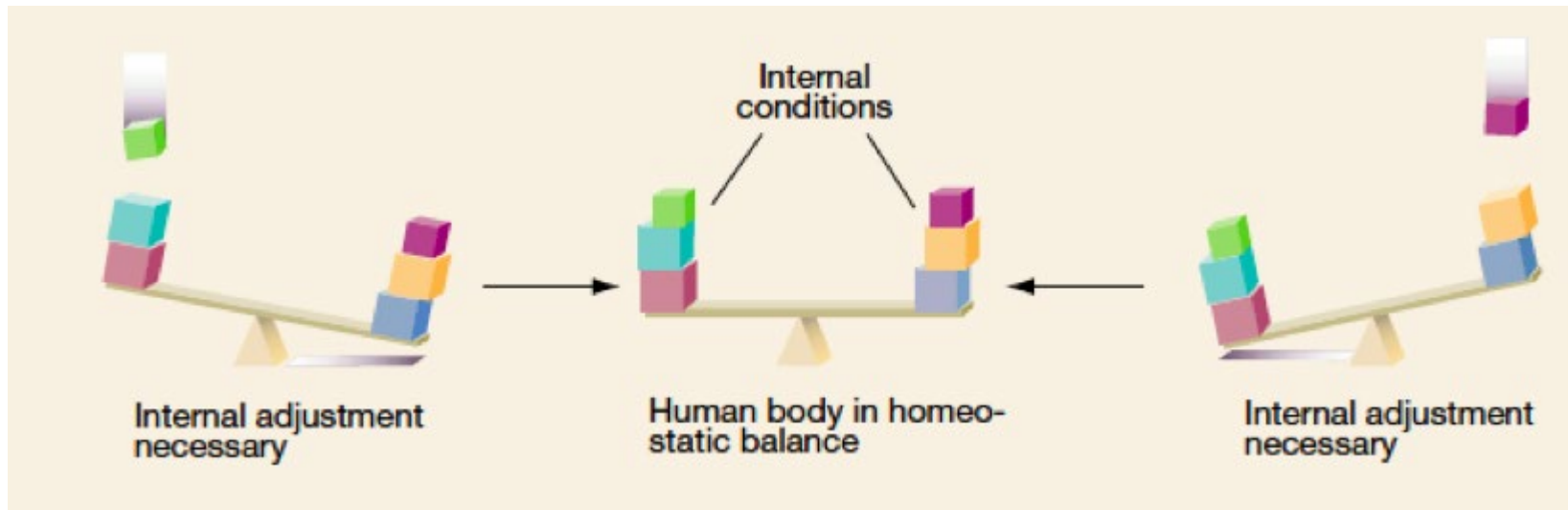
Withdrawal Defined

- Physiological response to the sudden stopping or slowing of the use of a substance to which the body has become dependent on.
- Can include various physical, mental, and emotional symptoms.
- Can be painful and life threatening
- Not exclusive to the abuse of substances



What is the basis for withdrawal?

Homeostasis



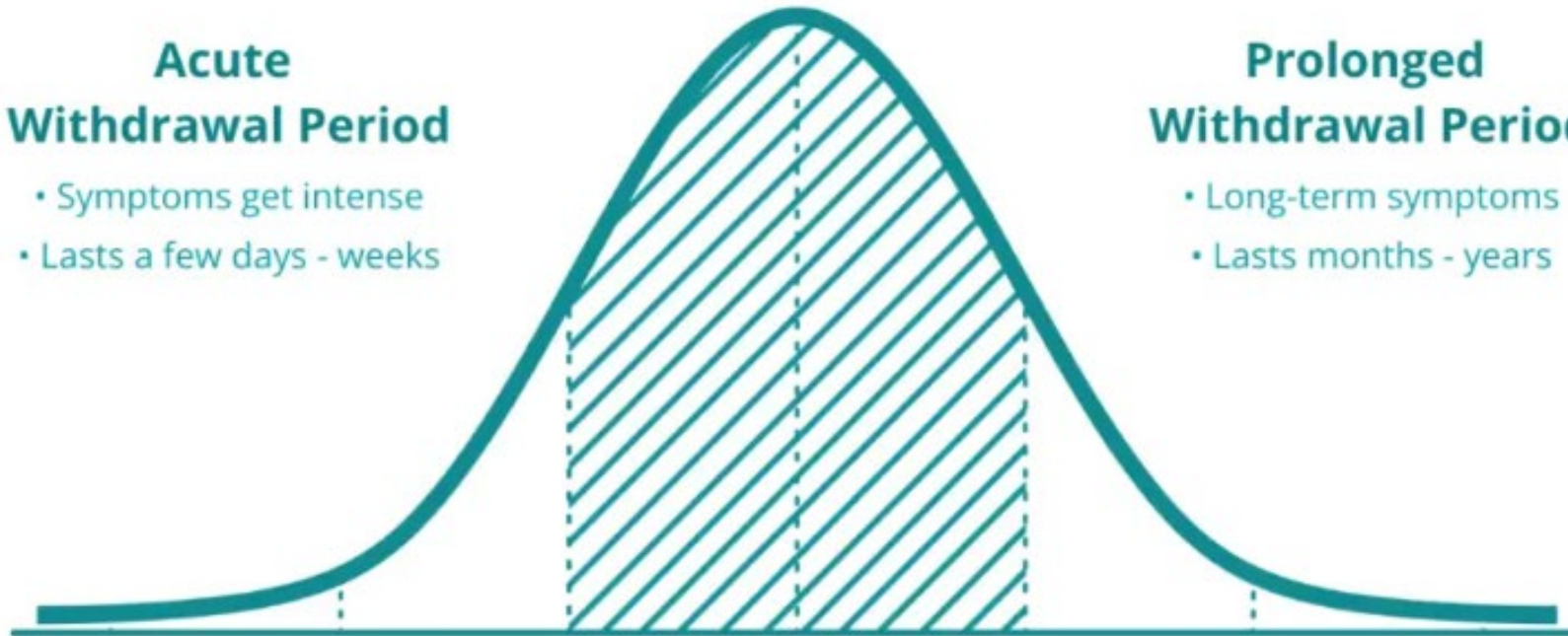
Stages of Withdrawal

Acute Withdrawal Period

- Symptoms get intense
- Lasts a few days - weeks

Prolonged Withdrawal Period

- Long-term symptoms
- Lasts months - years

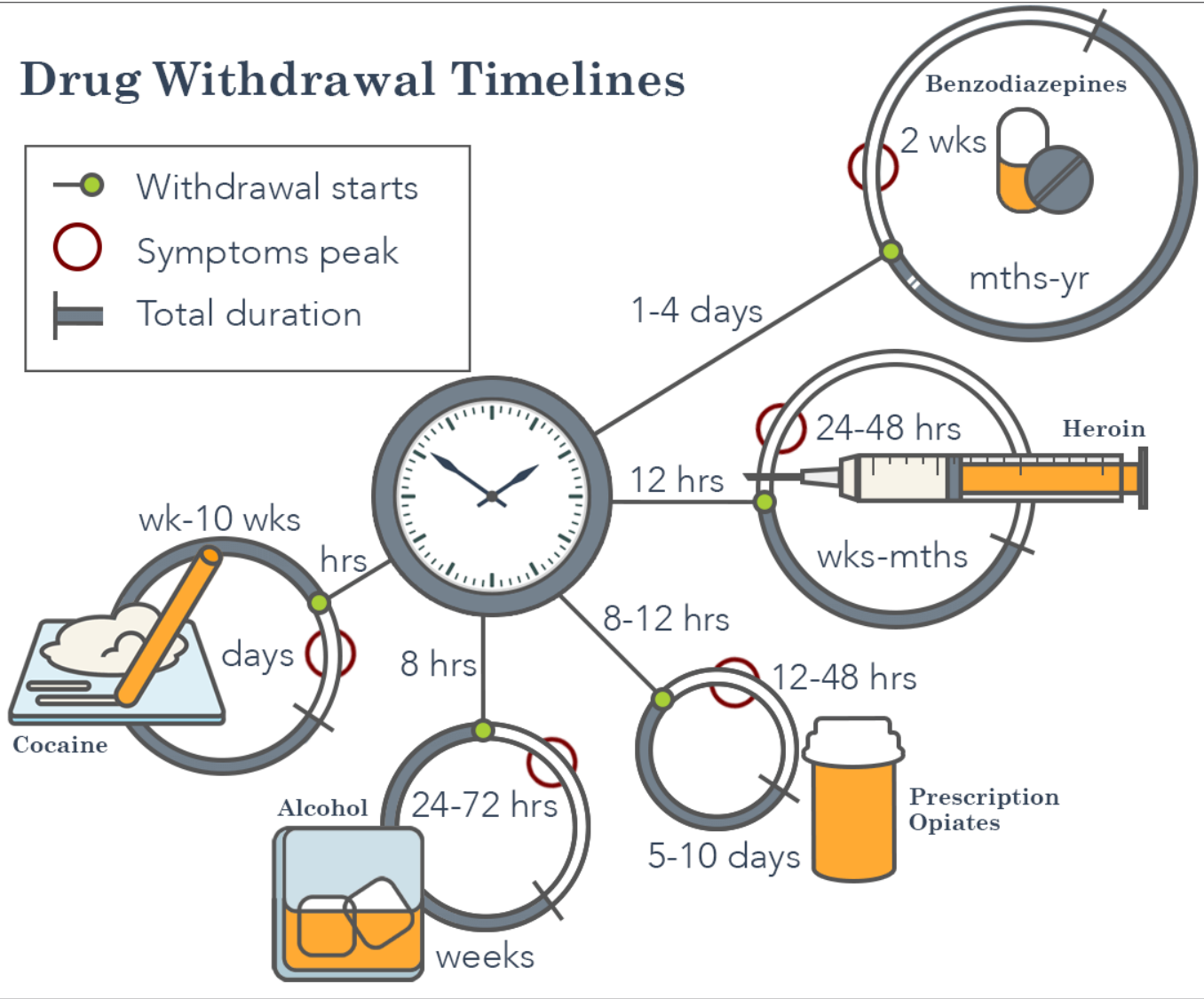


Protracted Withdrawal Period

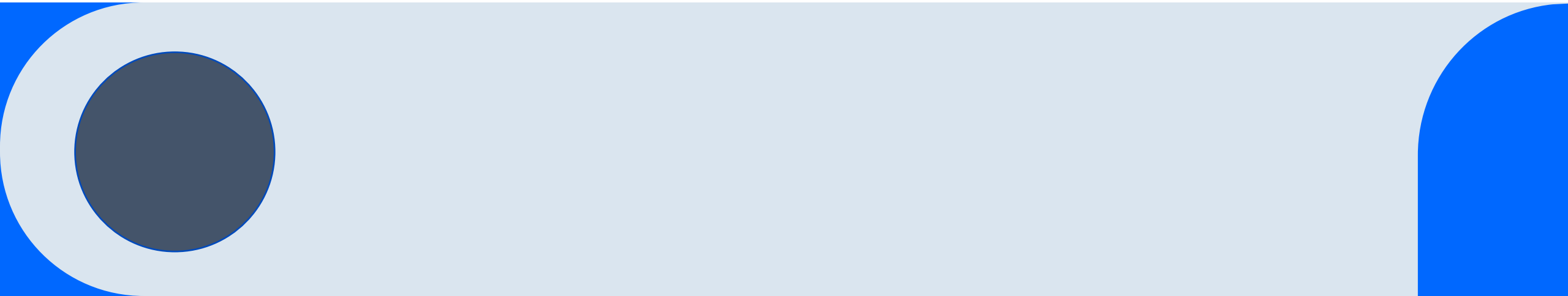
- Symptoms at worst
- Intensity begins to decrease

Drug Withdrawal Timelines

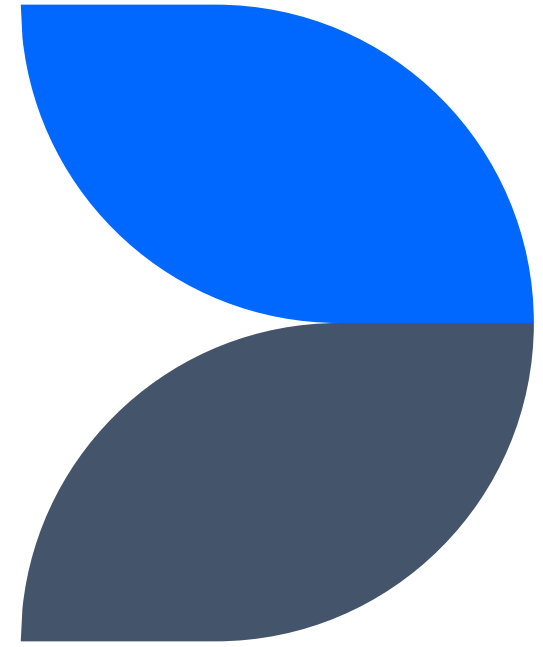
- Withdrawal starts
- Symptoms peak
- Total duration



Life Threatening Withdrawal



Is withdrawal life threatening and does that make it dangerous to reverse an overdose?



Deadly Withdrawal Syndromes



- Severe alcohol withdrawal can be associated with alcohol withdrawal delirium (delirium tremens)
 - If unmanaged, this can result in severe seizures and death
 - <5% of alcohol withdrawal cases

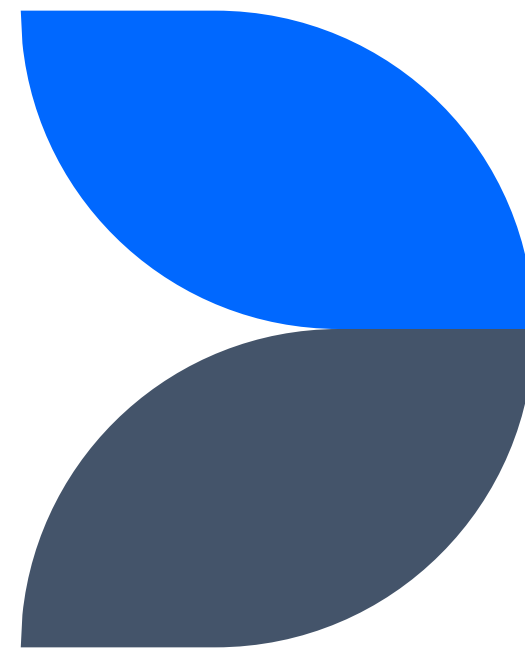


- Benzodiazepine withdrawal can result in seizures that can be life threatening
 - High doses and chronic use increases the risk
 - More prevalent when the drug is quickly reversed



- Other withdrawal syndromes rarely result in death
 - Of note: any prolonged situation where the body is deprived of a necessary element can result in death (i.e. prolonged dehydration)

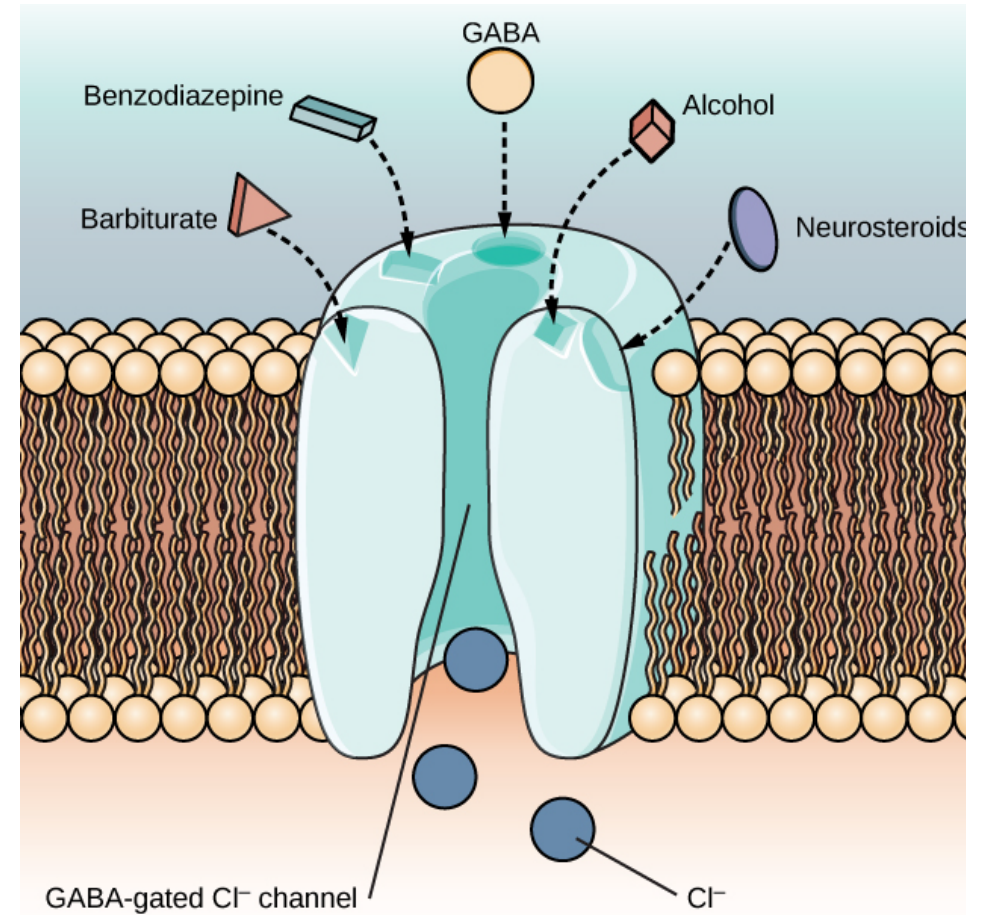
**Yes, it is safe to
reverse an opioid
overdose.**



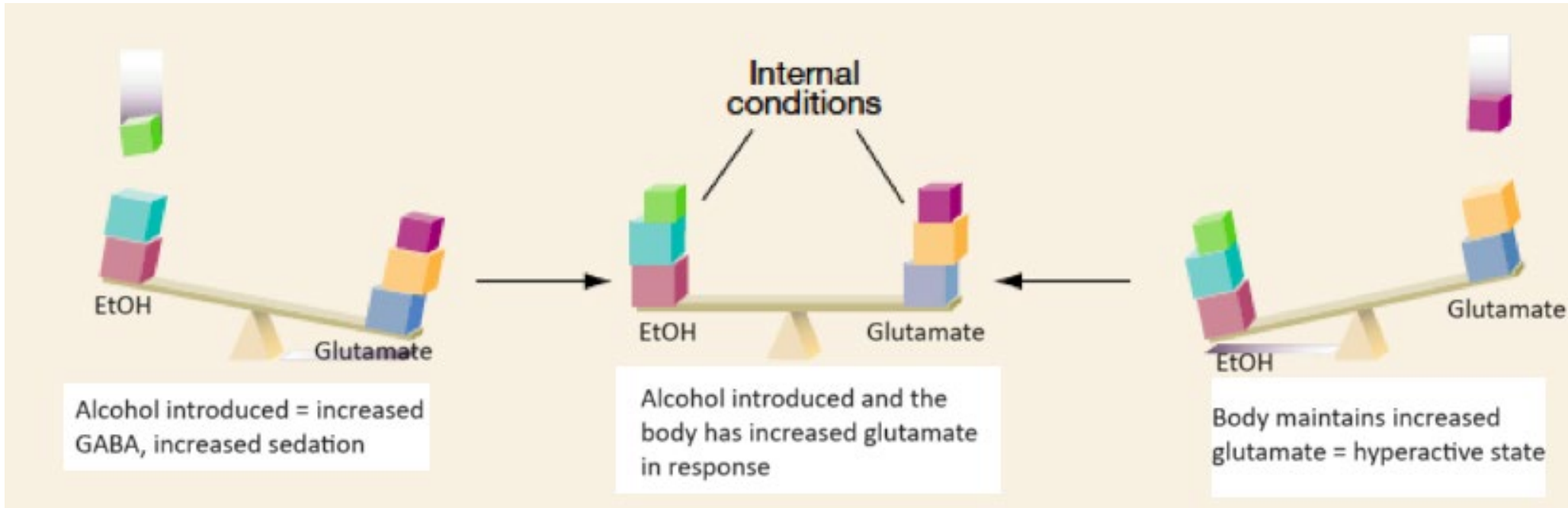


Alcohol Withdrawal

Alcohol's Mechanism



Homeostasis with Alcohol



Alcohol Withdrawal Syndrome is Unique

Kindling or sensitization

- Consecutive withdrawal experiences can lead to an increase in the severity of the withdrawal over time
- Increases the risk of seizures
 - Due to the lowered seizure threshold after repeated episodes of alcohol withdrawal syndrome



When does withdrawal occur?

Risky
Drinkers

Alcohol Use
Disorder



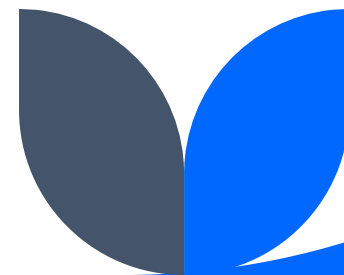
Symptoms of Alcohol Withdrawal

- Can start within hours and can peak ~72hours
- Tremors
- Insomnia
- Sweating
- High Blood Pressure
- High Heart Rate
- Agitation, Anxiety, Depression

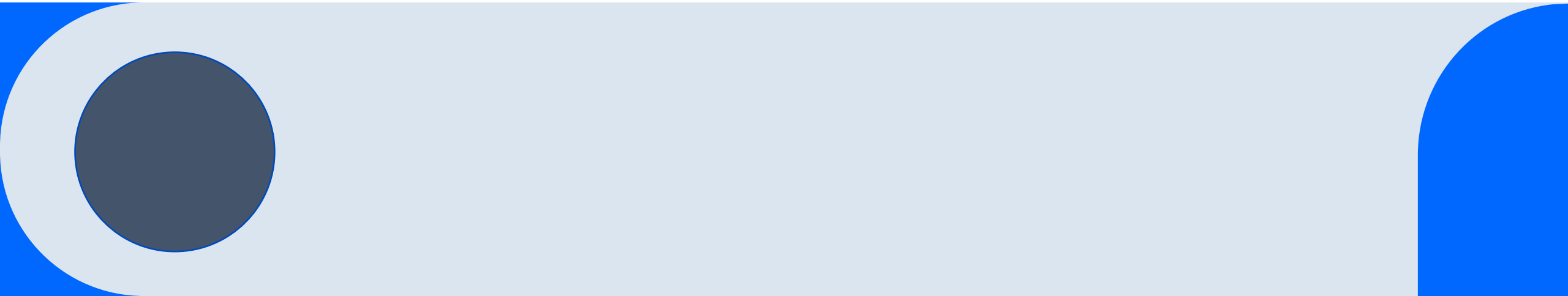


Complications of Alcohol Withdrawal

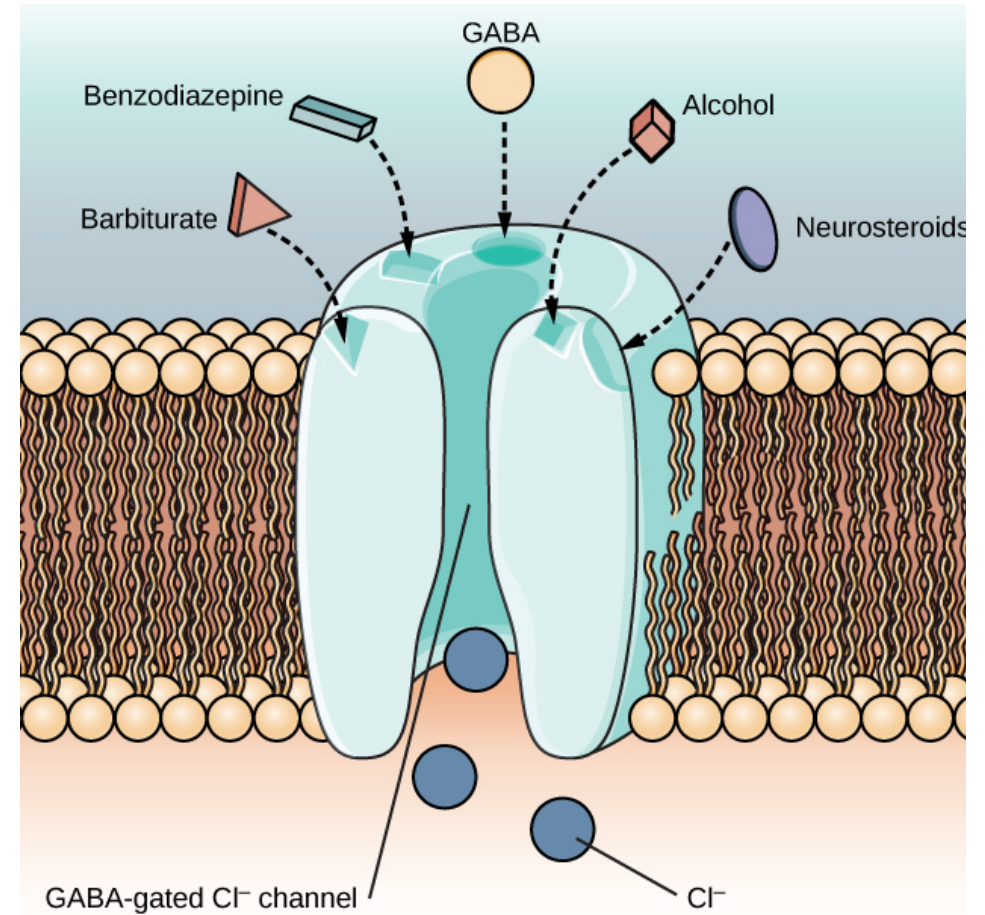
- More severe symptoms
 - Auditory, visual, tactile hallucinations- ~2%, typically resolve within 72 hours
 - Wernicke Encephalopathy- thiamine deficiency
 - Withdrawal Seizures- 8-48 hours post cessation
 - alcohol withdrawal delirium (delirium tremens)- can occur 3-8 days after cessation or reduction



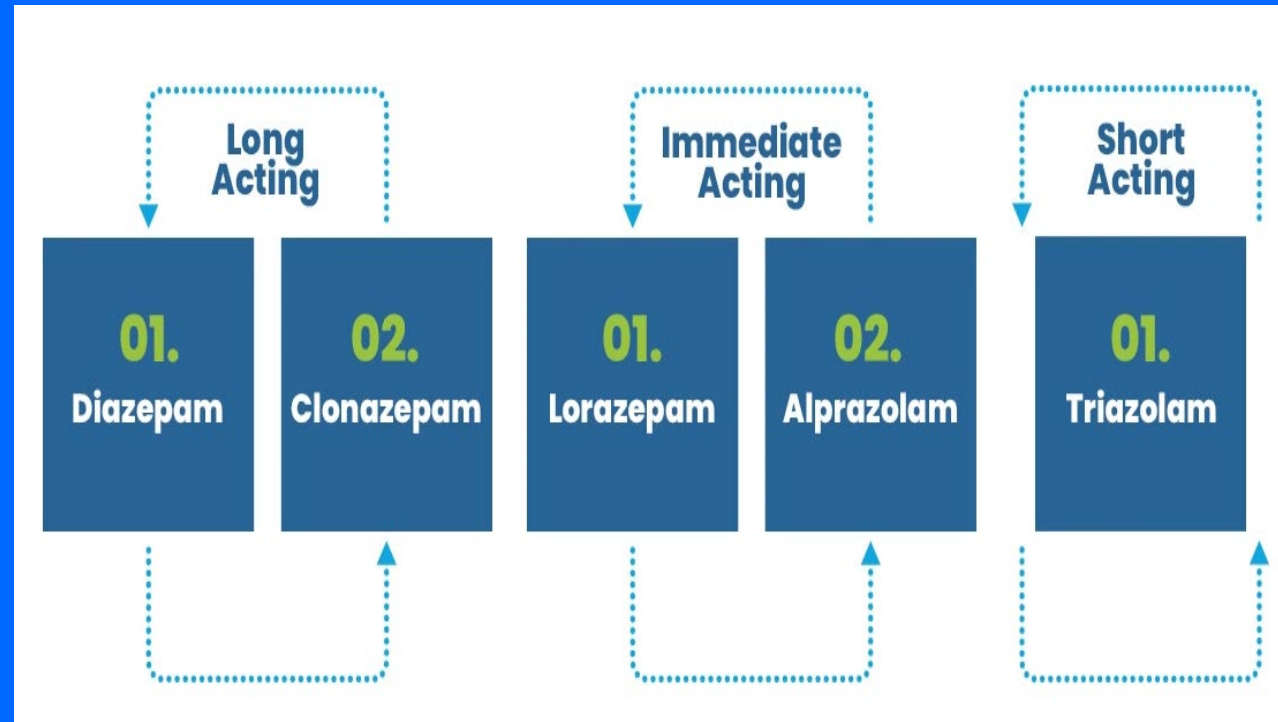
Benzodiazepine Withdrawal



Benzodiazepines and GABA



Types of Benzodiazepines

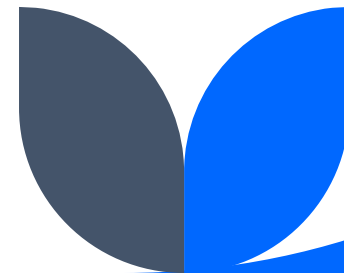


Benzodiazepine Withdrawal Risks

- More variable, depends on
 - How long someone has been using them
 - How much they have been using
 - What type of benzodiazepine is typically used
 - Underlying physical conditions
 - Other substance use

Benzodiazepine Withdrawal Symptoms

- Nausea
- Panic attacks
- Tremors
- Anxiety
- Agitation
- Sweating
- Headaches
- Twitching
- Heart palpitations
- Muscle pain
- Short term memory loss
- Brain fog
- Depression (suicidal ideation)
- Mood swings
- Seizures



Benzodiazepine Withdrawal Timeline

- Depends on the benzo used
 - Shorter acting benzos- begin 10 hours after last use
 - Longer acting benzos- begin 24+ hours after last use
- How long withdrawal lasts is very patient dependent
 - Some symptoms can last years if untreated
 - Only in a small percentage of patients





Opioid Withdrawal

Opioid Receptor Activity

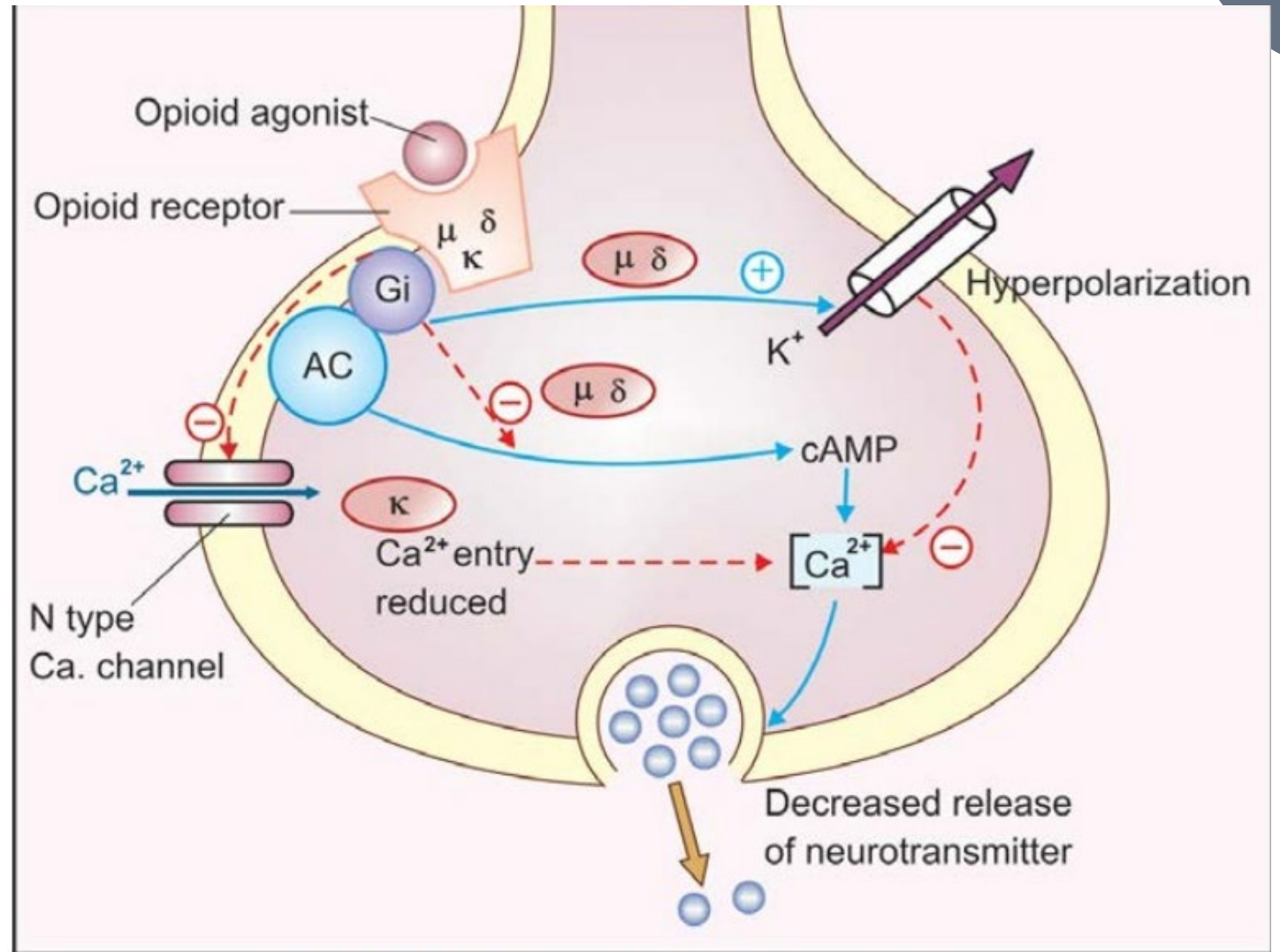
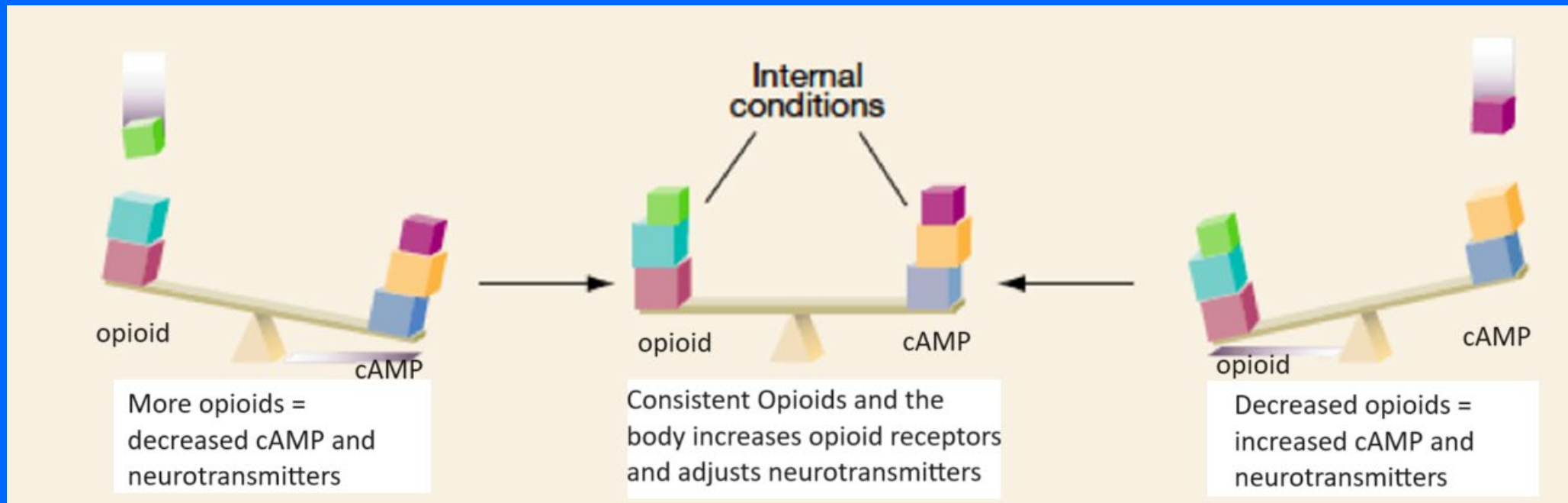


Fig. 34.1: Opioid receptor transducer mechanisms
AC-Adenylate cyclase; Gi-coupling protein; cAMP-Cyclic AMP



Opioids and Homeostasis



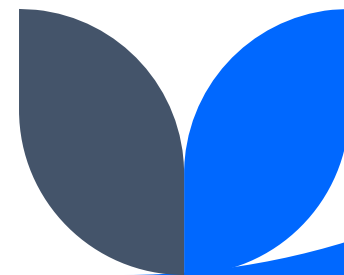
Two Types of Opioid Withdrawal

Withdrawal
from
decreased use

Precipitated
withdrawal

Opioid Receptors are Responsible for:

- Mediate our response to a lot of hormones
- Perception of taste, vision, smell
- Perception of pain
- Gut motility and thirst
- Mood stabilization
- Etc.



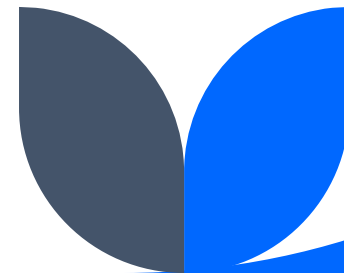
Symptoms of Opioid Withdrawal

- Watery eyes
- Sneezing
- Goose bumps/ chills
- Muscle/bone pain
- Diarrhea
- High blood pressure
- Temperature regulation
- Yawning
- Nausea
- Vomiting
- Pupils dilating
- Light sensitivity
- Increased heart rate
- Sweating
- Anxiety, agitation, depression



Fentanyl Withdrawal

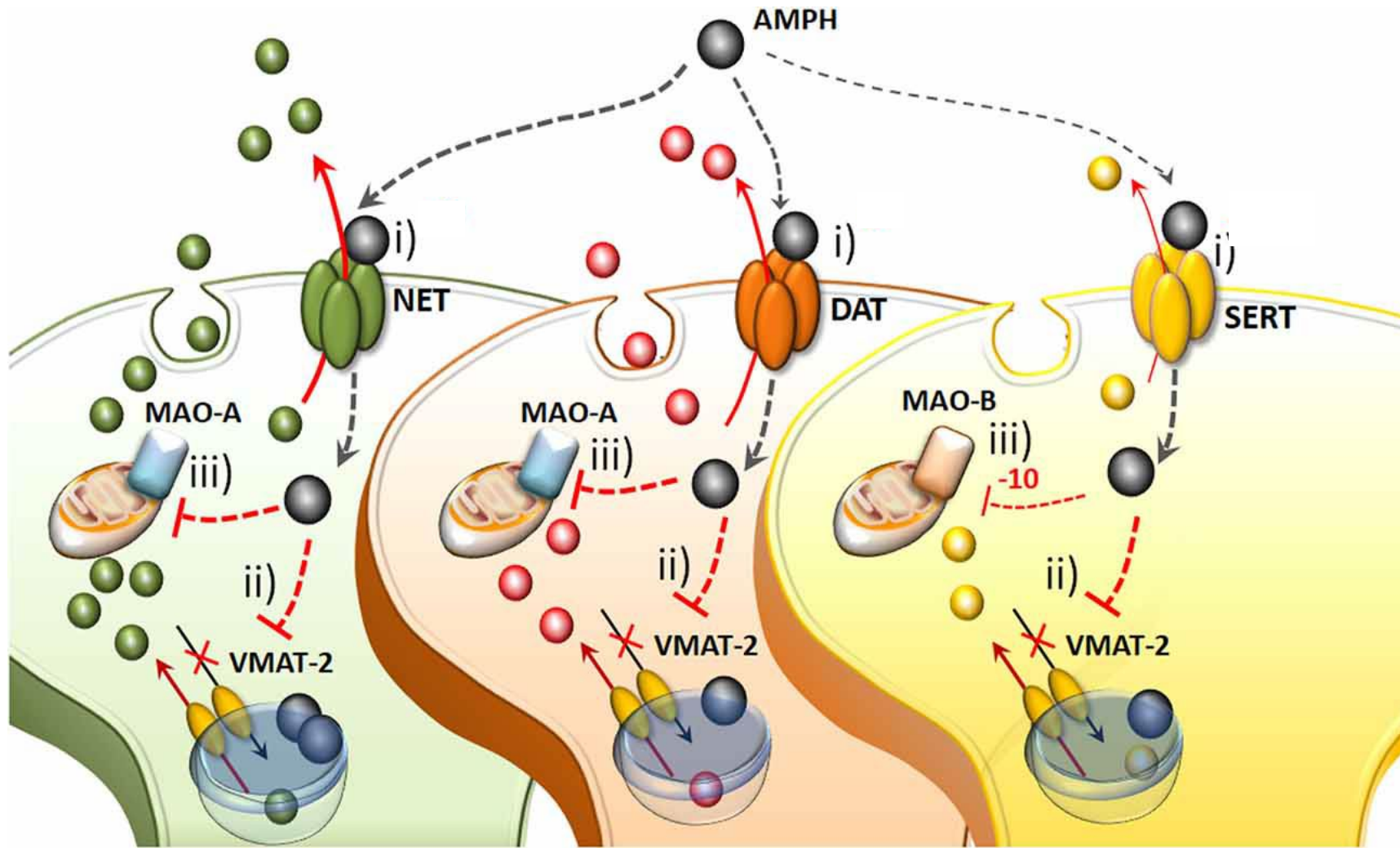
- Acts quickly, but for a short amount of time
- Potent
- Very available
- Tolerance develops
- Withdrawal has been described as more severe than other opioids
- More variable withdrawal timelines
- Fear for precipitated withdrawal
- But treatment options are still available!!



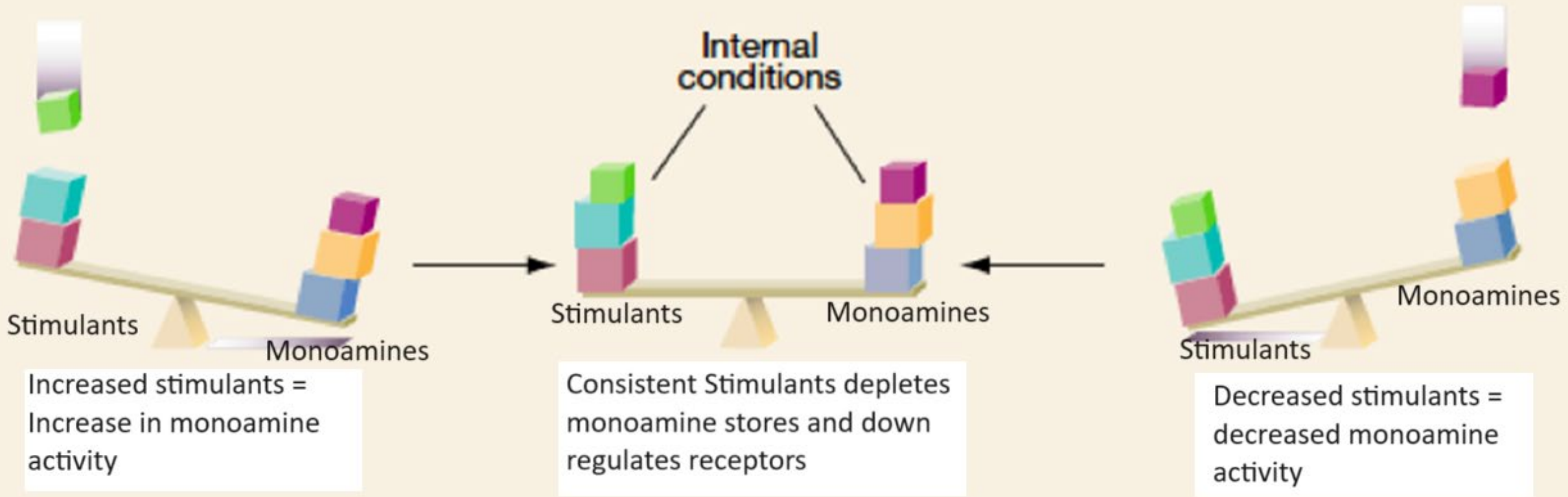
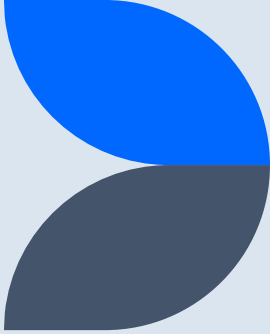
Stimulant Withdrawal



Stimulants on Receptors



Stimulant Withdrawal



Symptoms of Stimulant Withdrawal

- Depression (suicidal ideation), anxiety, agitation
- Low energy
- Weight gain
- Dehydration
- Chills/goose bumps
- Insomnia and/or too much sleep
- Brain fog
- Loss of pleasure
- Paranoia

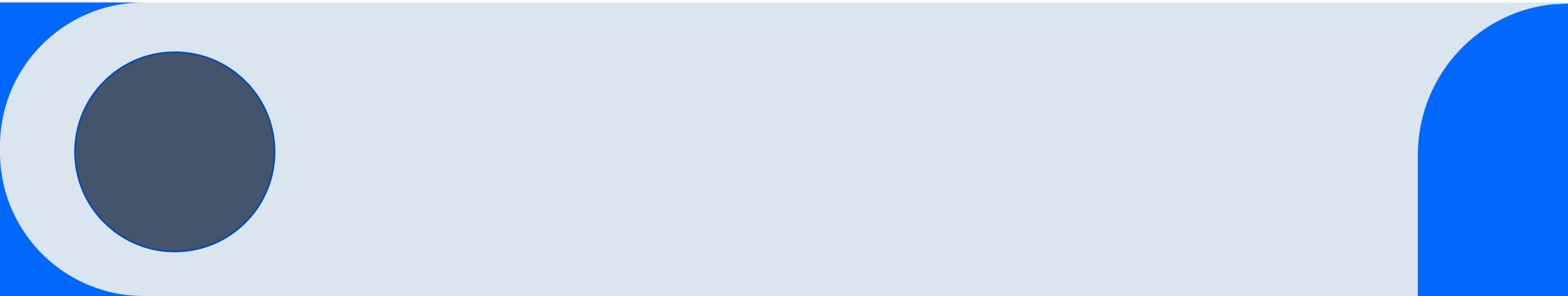


Timeline of Stimulant Withdrawal

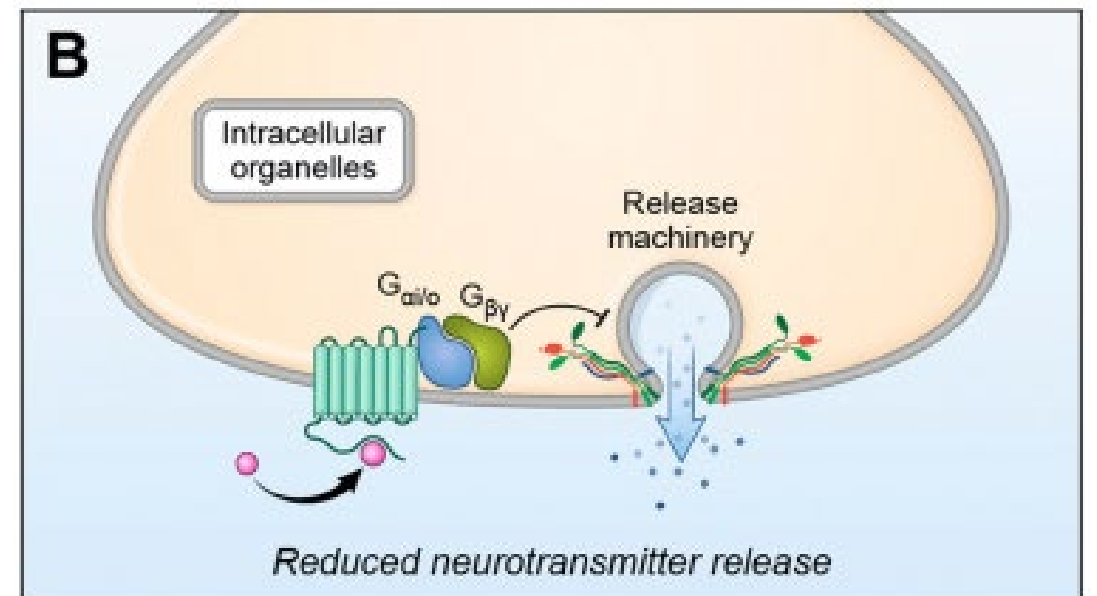
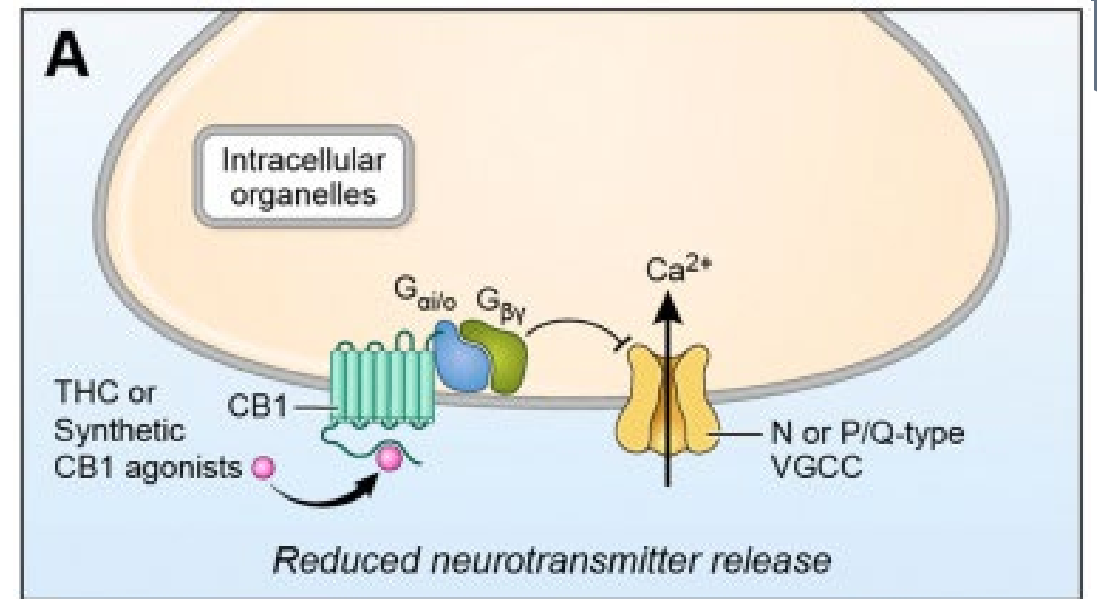
- Varies greatly on:
 - Type of stimulant
 - Duration of use
 - Personal make-up
 - Tolerance developed
 - Cravings can last longer than other withdrawal symptoms
- Averages:
 - Cocaine: lasts 3-4 days
 - Ecstasy/MDMA: 3-5 days
 - Methamphetamine:
 - Acute: 7-10 days
 - Protracted: 2-3 weeks



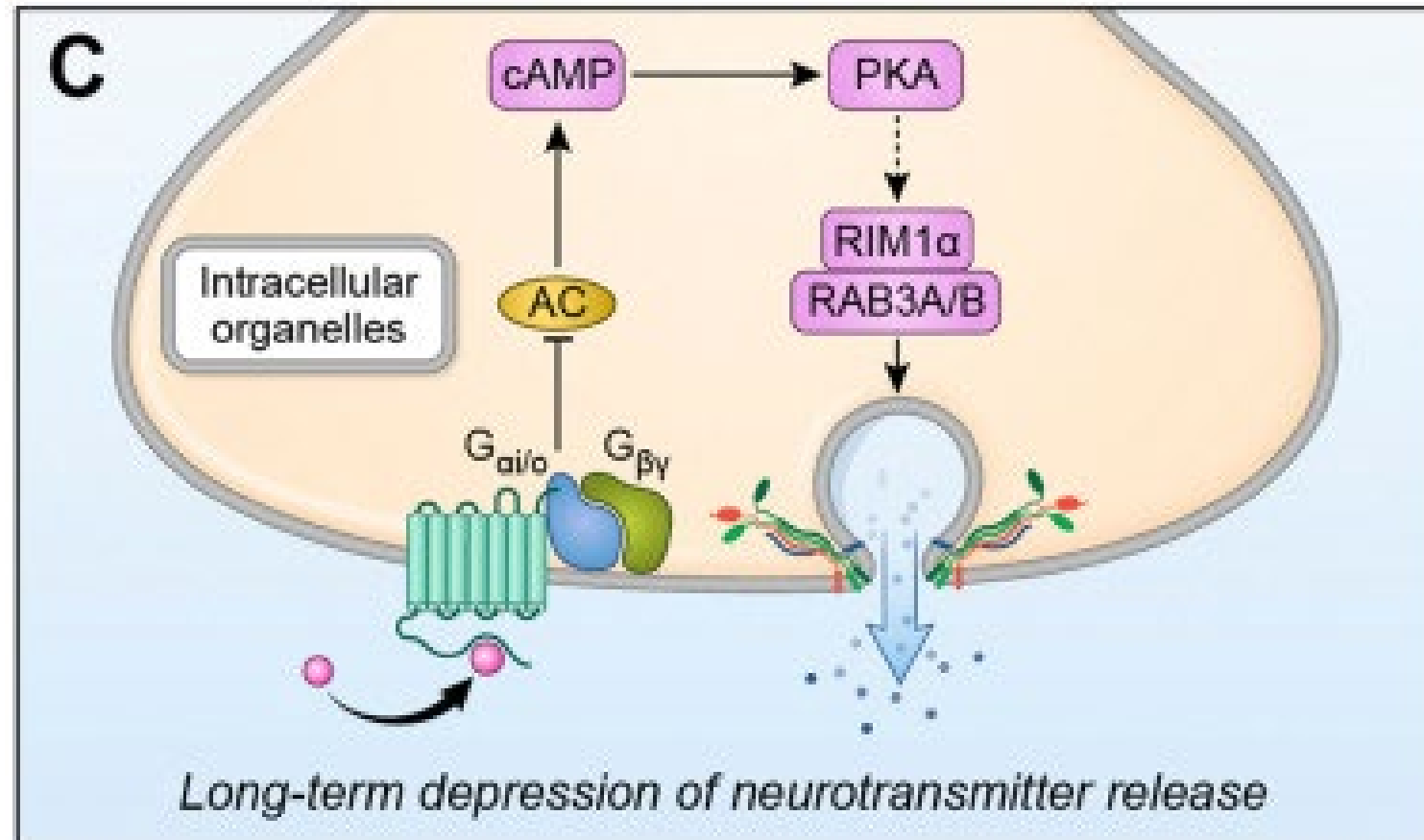
Cannabis Withdrawal



THC and Cannabinoids



Cannabis and Homeostasis



Marijuana Withdrawal Symptoms & Timeline

- Depression, anxiety, agitation, irritability
- Restlessness
- Insomnia
- Appetite changes (decrease)
- Sleep disturbances
- Headache
- Nausea and vomiting
- Sweating
- tremors
- Timing can vary on use and duration
- On average:
 - Symptoms usually start ~24-48 hours
 - Symptoms peak at 2-6 weeks
 - Most will resolve in 3-4 weeks



Questions?

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