

MEDICAL ASPECTS OF ADDICTION

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From Use to Addiction

Brief Use and
Experimentation

How? Why?
Who?

Addiction:
A Chronic,
Medical Illness

What are the
medical
interventions for
this disease?

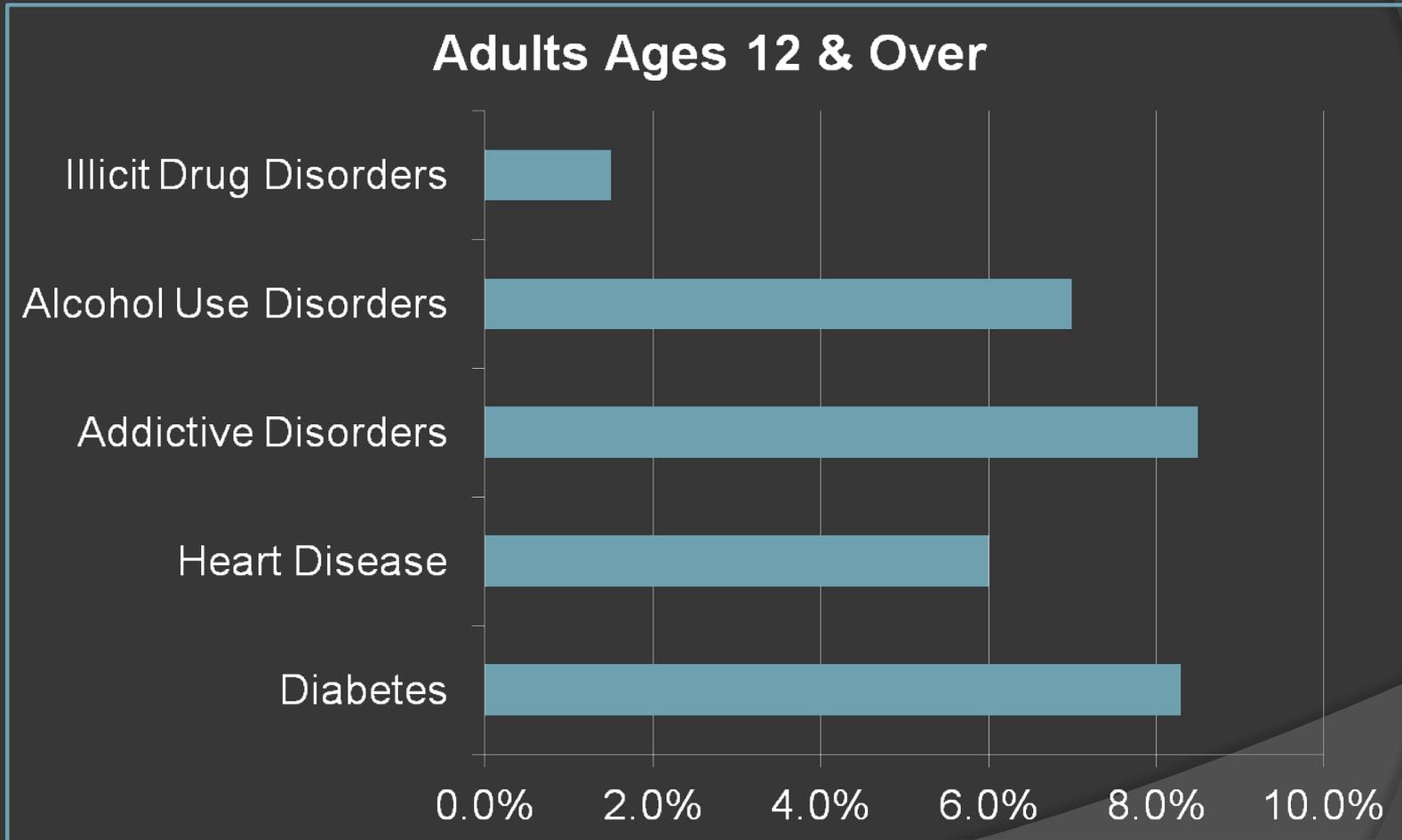
Overview

- ① Who
 - Epidemiology of Addiction
- ② Why
 - Genetics of Addiction
- ③ How
 - Neurobiology of Addiction
- ④ Medical Interventions
 - Medications for Craving & Withdrawal

Epidemiology of Addiction

- Psychiatric Diagnoses increase risk:
 - Bipolar – especially mania, esp. males
 - Antisocial personality disorder
 - Conduct Disorder
 - Untreated ADHD
 - Schizophrenia
- 2.5% of the population drinks 1/3 of the alcohol

Prevalence in General Population



NSDUH, 2010

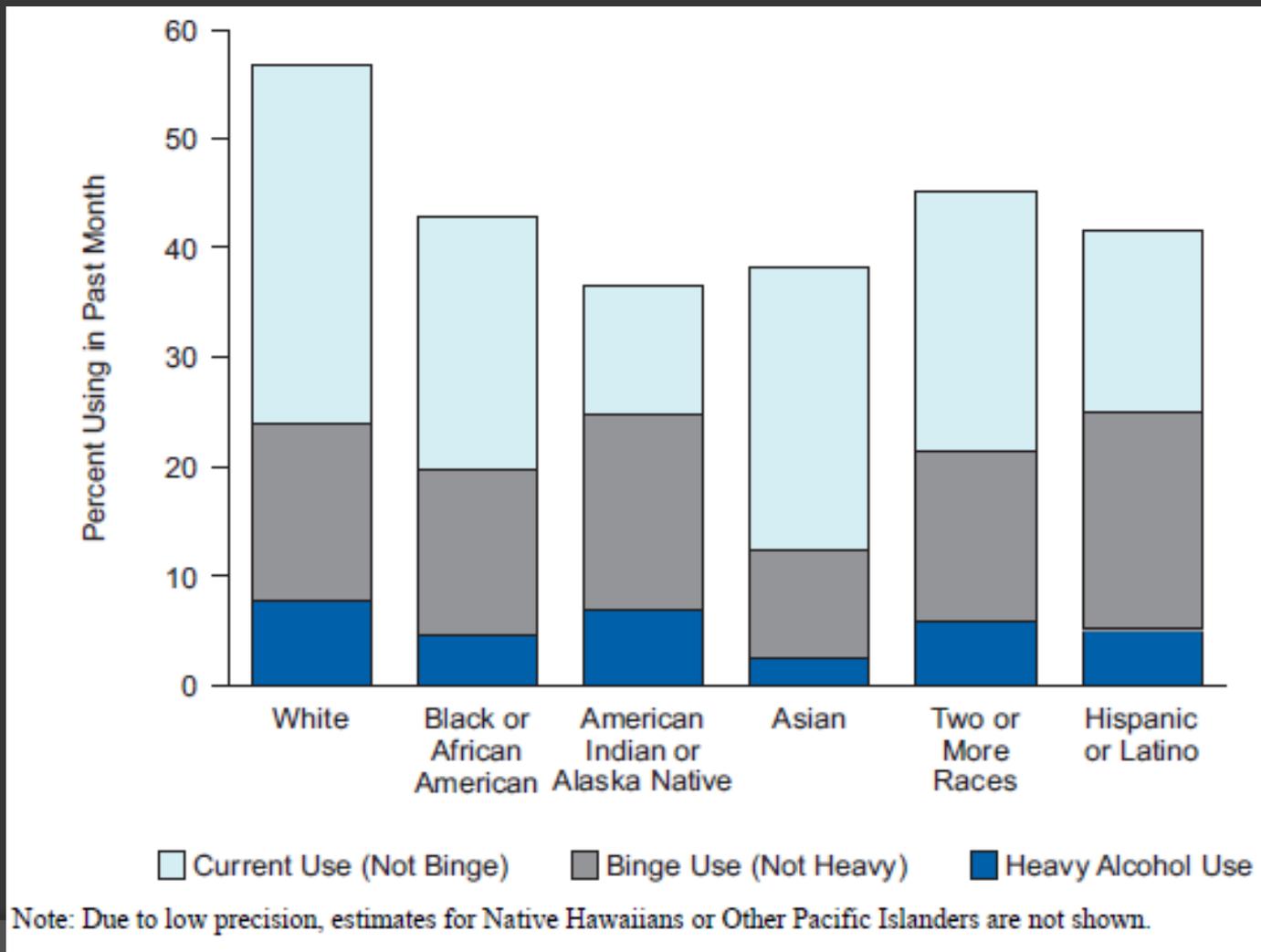
www.cdc.gov

American Diabetes Assn, 2011

Epidemiology of Addiction

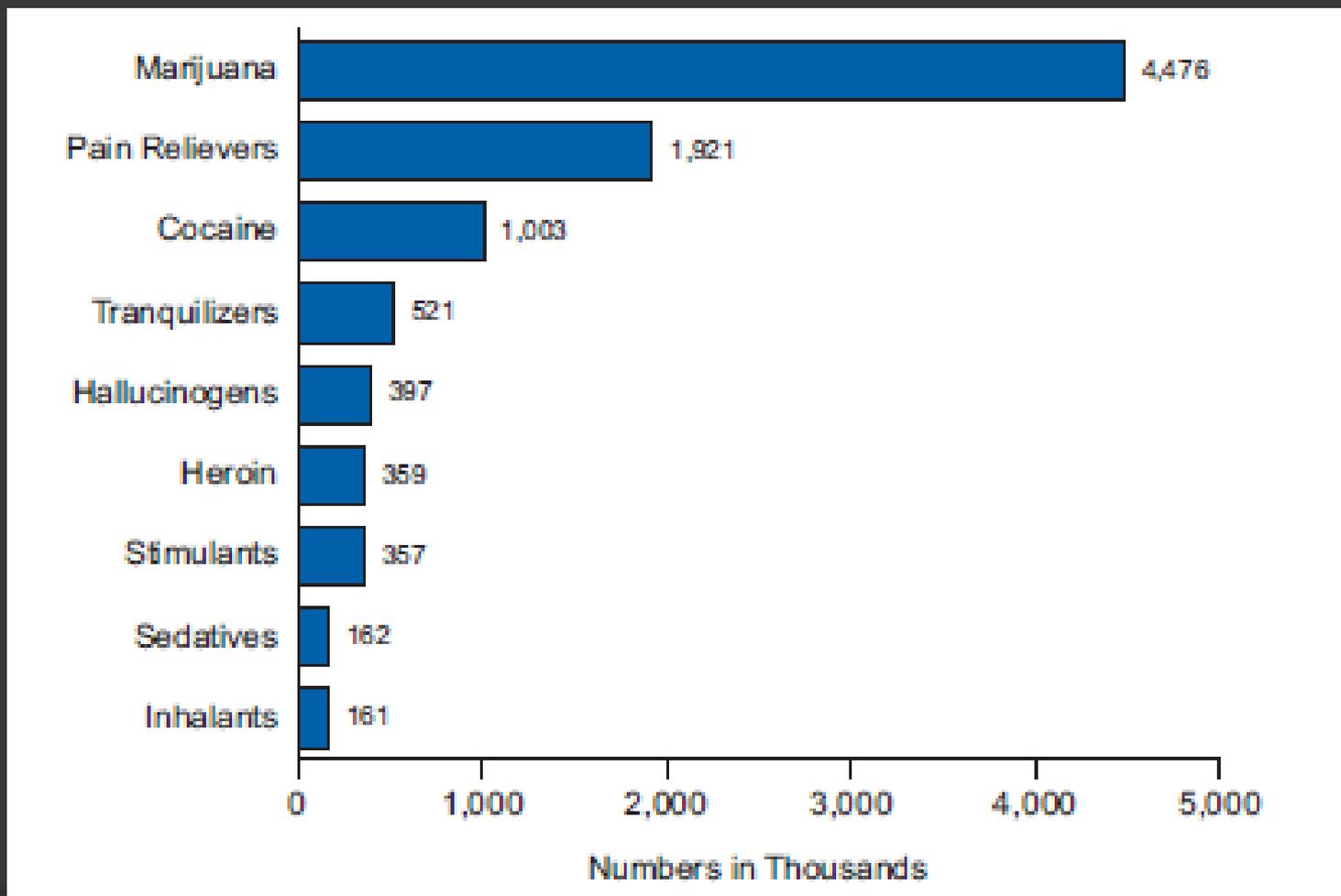
- ⦿ Men 2x more likely to have addiction than women
- ⦿ Adolescents: boys = girls
- ⦿ Use more likely in those who are:
 - Young adults
 - Single or cohabitating
 - Unemployed
 - Dropped out of high school
 - Have family history or other mental illness

Current, Binge, & Heavy Alcohol Use, By Ethnicity

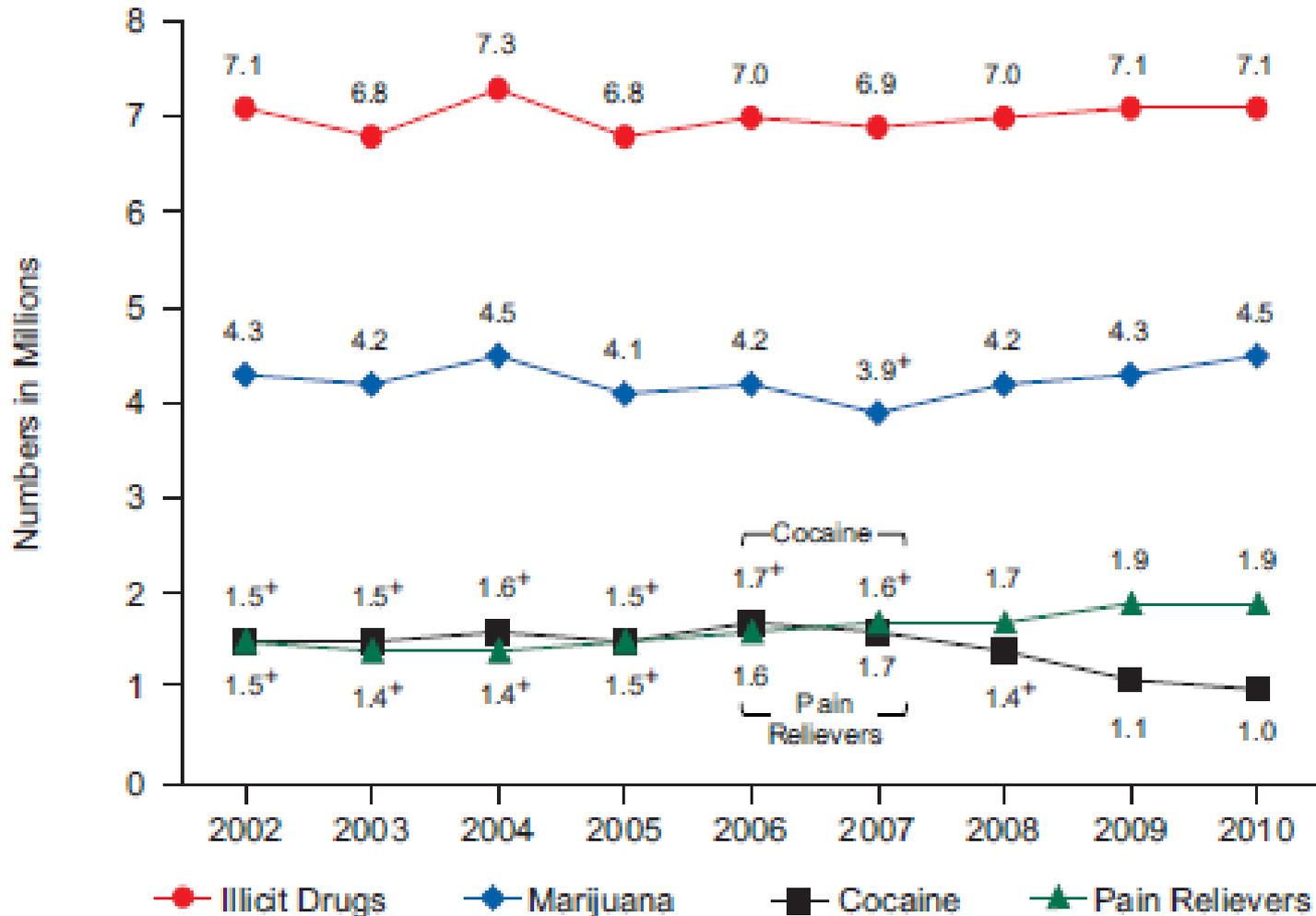


Dependence or Abuse:

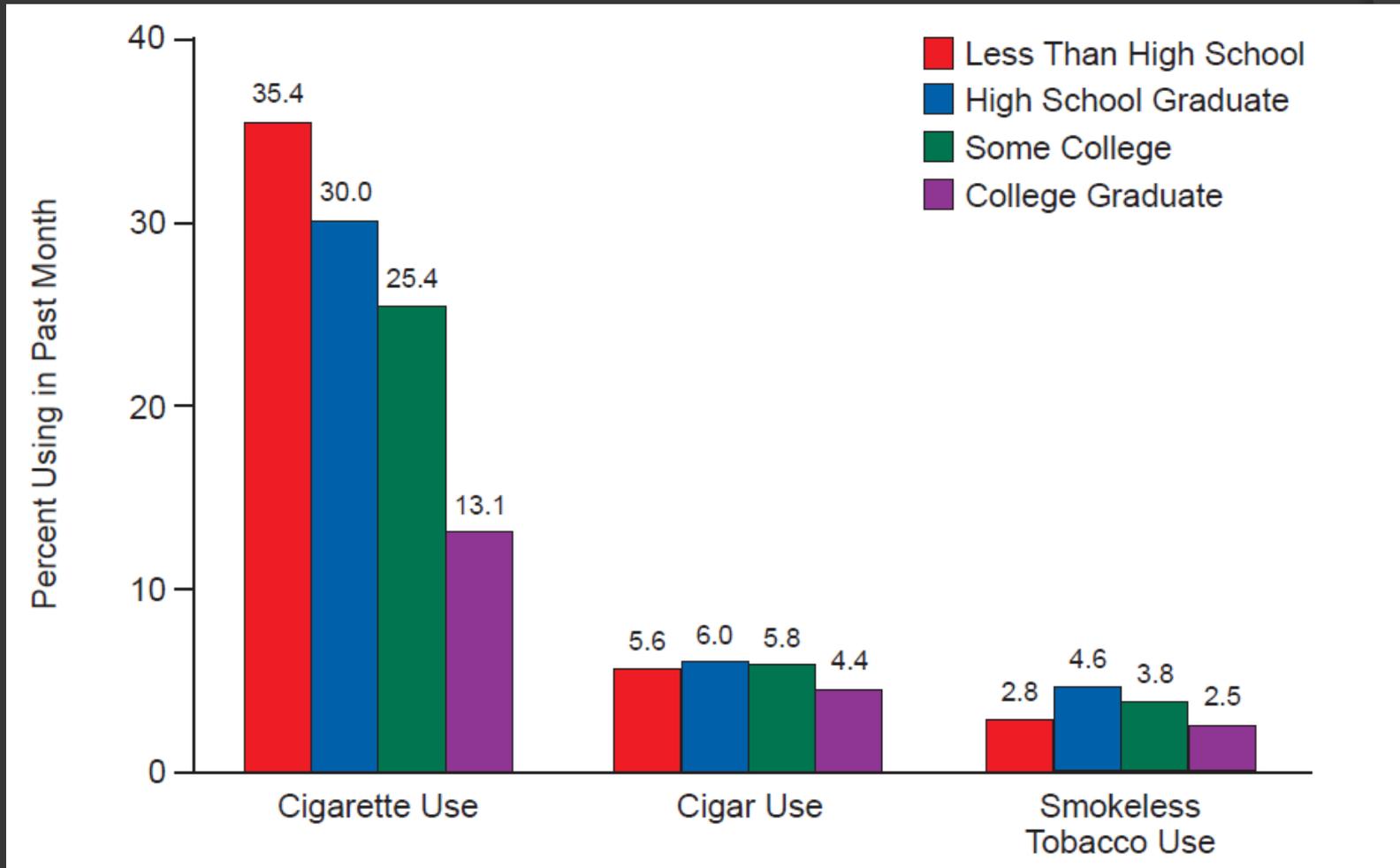
Specific Illicit Drugs, Past Year, Aged 12 & Above



Nonmedical Use of Psychotherapeutics



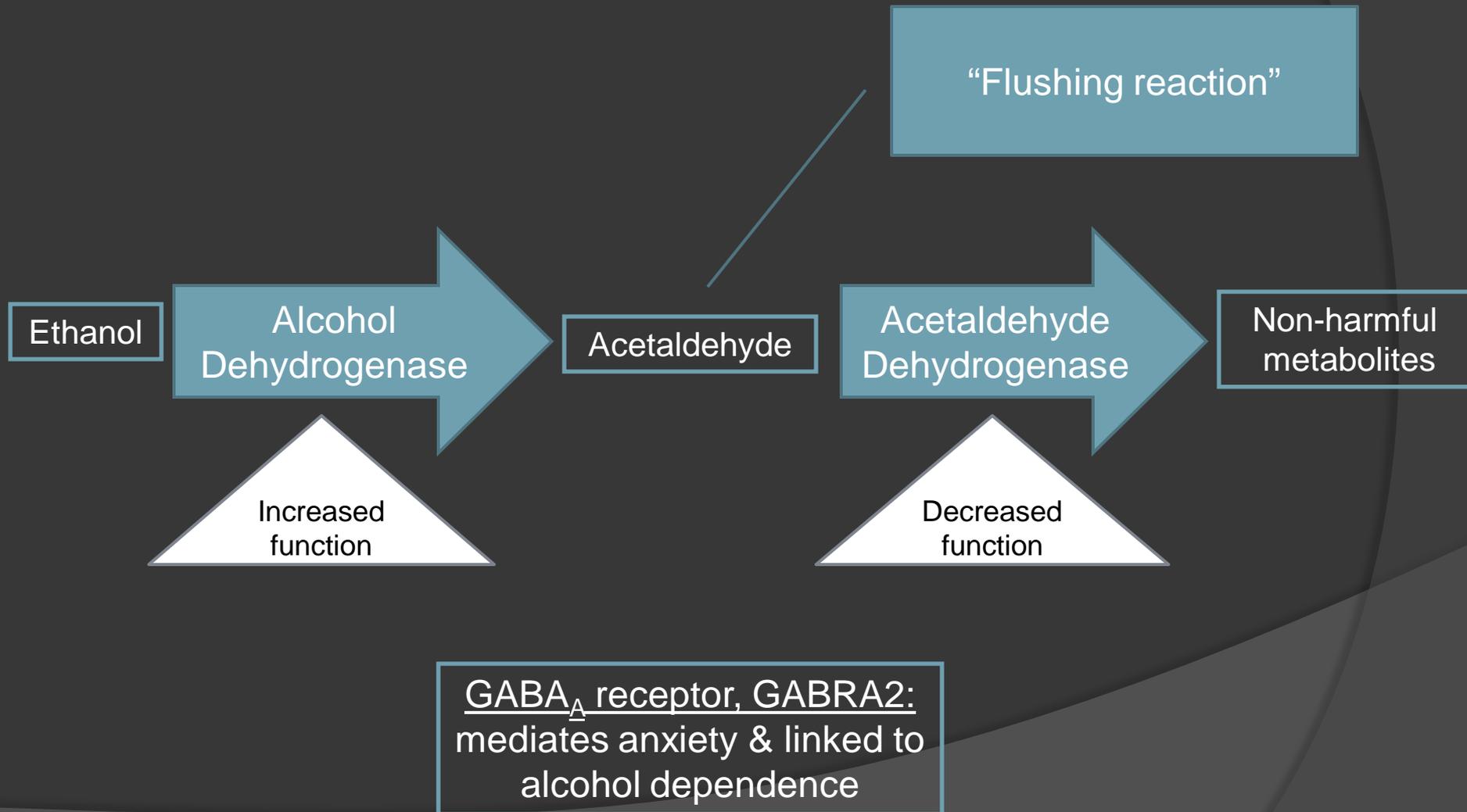
Past Month Tobacco Use



Genetics of Addiction



Genetics of Alcohol Dependence



μ Opioid Receptor Genes

- ◉ OPRM1 – linked to alcohol and opioid dependence

- Polymorphism causes:

- ↑ Binding of β endorphin to receptor site



- ↑ Pleasure received from the intake of alcohol
(??? Opioids)



- ↑ Alcohol Consumption

Nicotine Dependence Genetics

- Dopa Decarboxylase
 - Enzyme that helps in dopamine synthesis and serotonin biosynthesis
 - Variant in how this enzyme is produced that is linked to nicotine dependence
- Several other genes have been implicated in nicotine dependence genetics, but these studies need further replication

Gene-by-Environment

- 5-HTTLPR – polymorphism seen in the serotonin transporter gene

- “short” 5-HTTLPR + Stressful life events = Greater risk of depression

- “short” 5-HTTLPR + Stressful life events =  Frequent/heavy drinking & non-Rx drug use

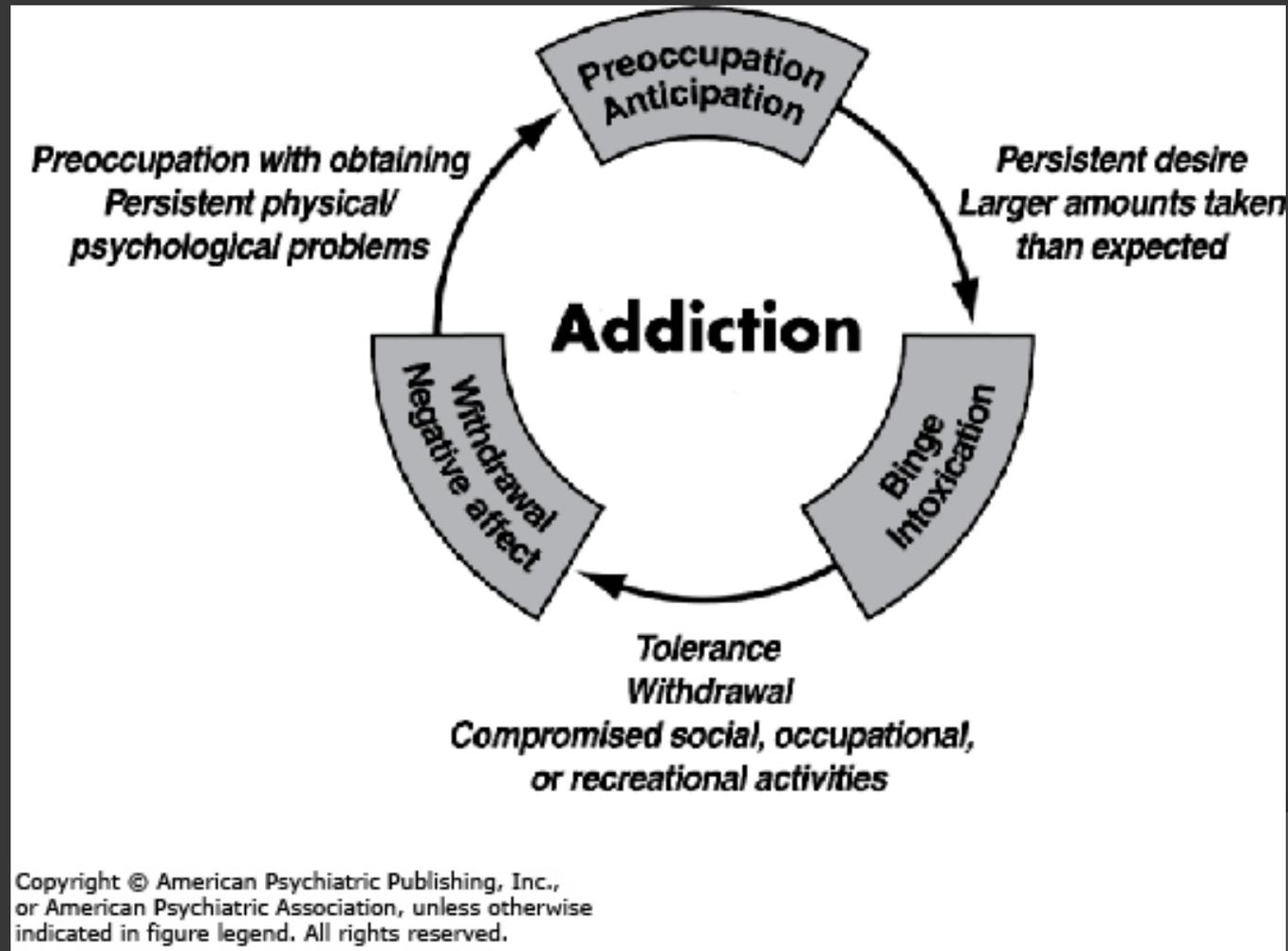
Genetics

⦿ Cocaine Dependence

- Group of genes of chrom 12 increasing risk of heavy cocaine use
- Genes on chrom 9 in African Americans increases risk of cocaine-induced paranoia

⦿ Opioid Dependence – certain genes on chrom 17 can increase or decrease risk of heavy opioid use

Stages of Addiction



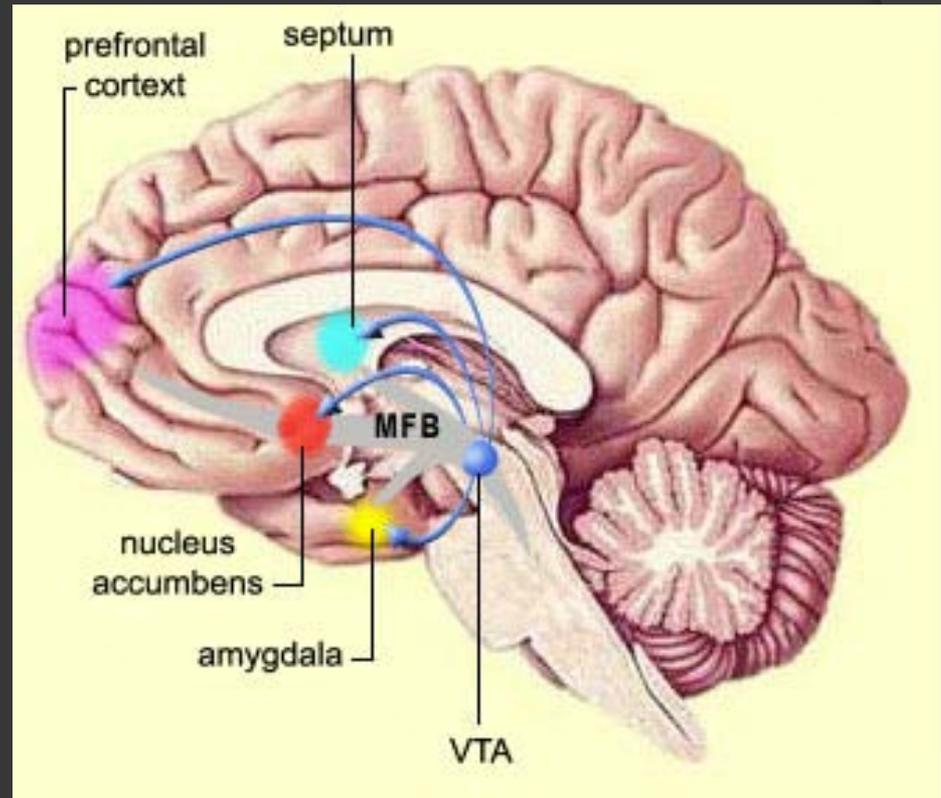
Binge/Intoxication: Reward Pathway and More

Clinical Picture:

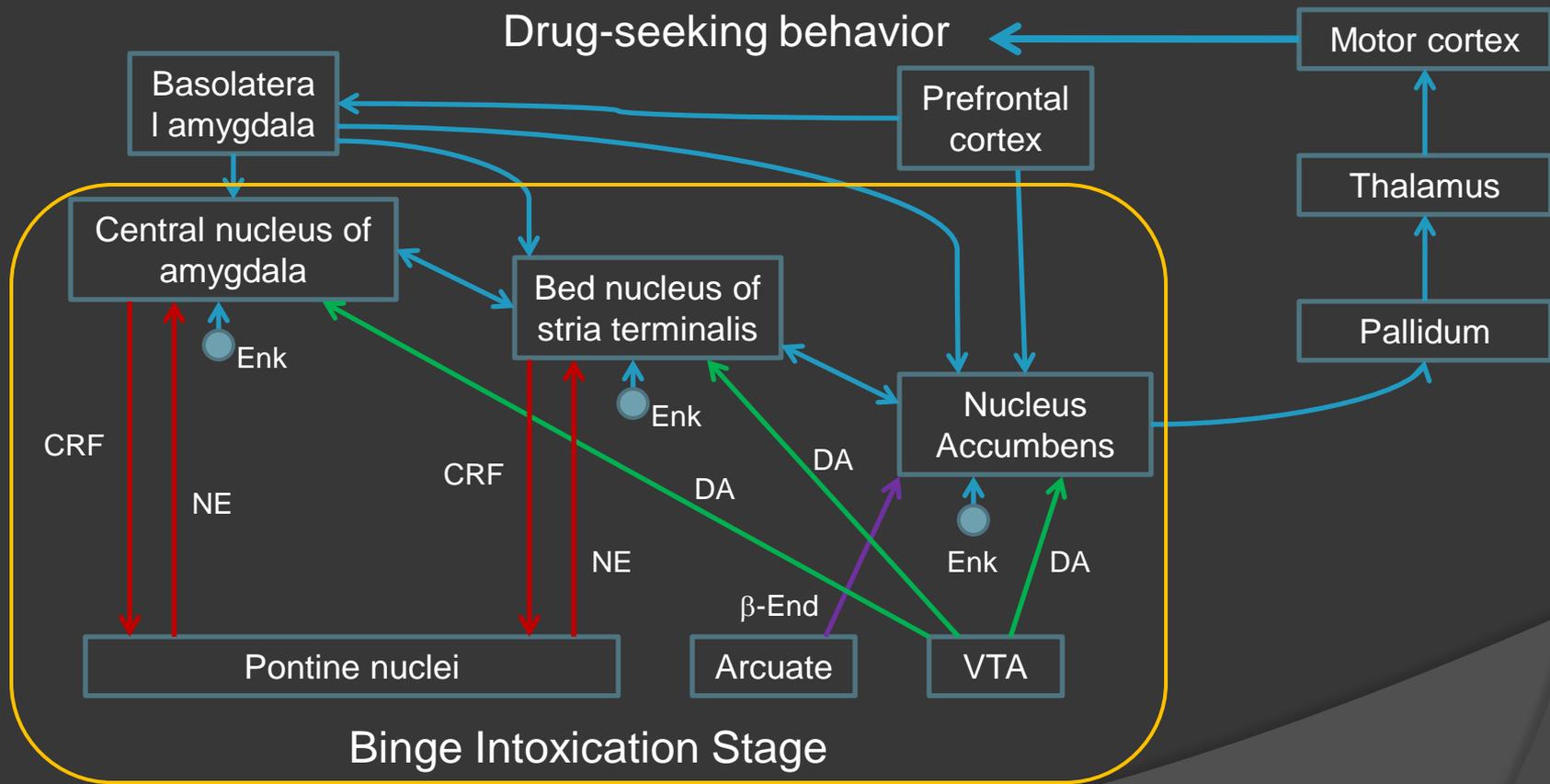
- ⦿ Acute Reward

Neurotransmitters:

- ⦿ Dopamine
- ⦿ Opioid Peptides
- ⦿ GABA
- ⦿ Serotonin
- ⦿ Endocannabinoids



Neurobiology of Addiction



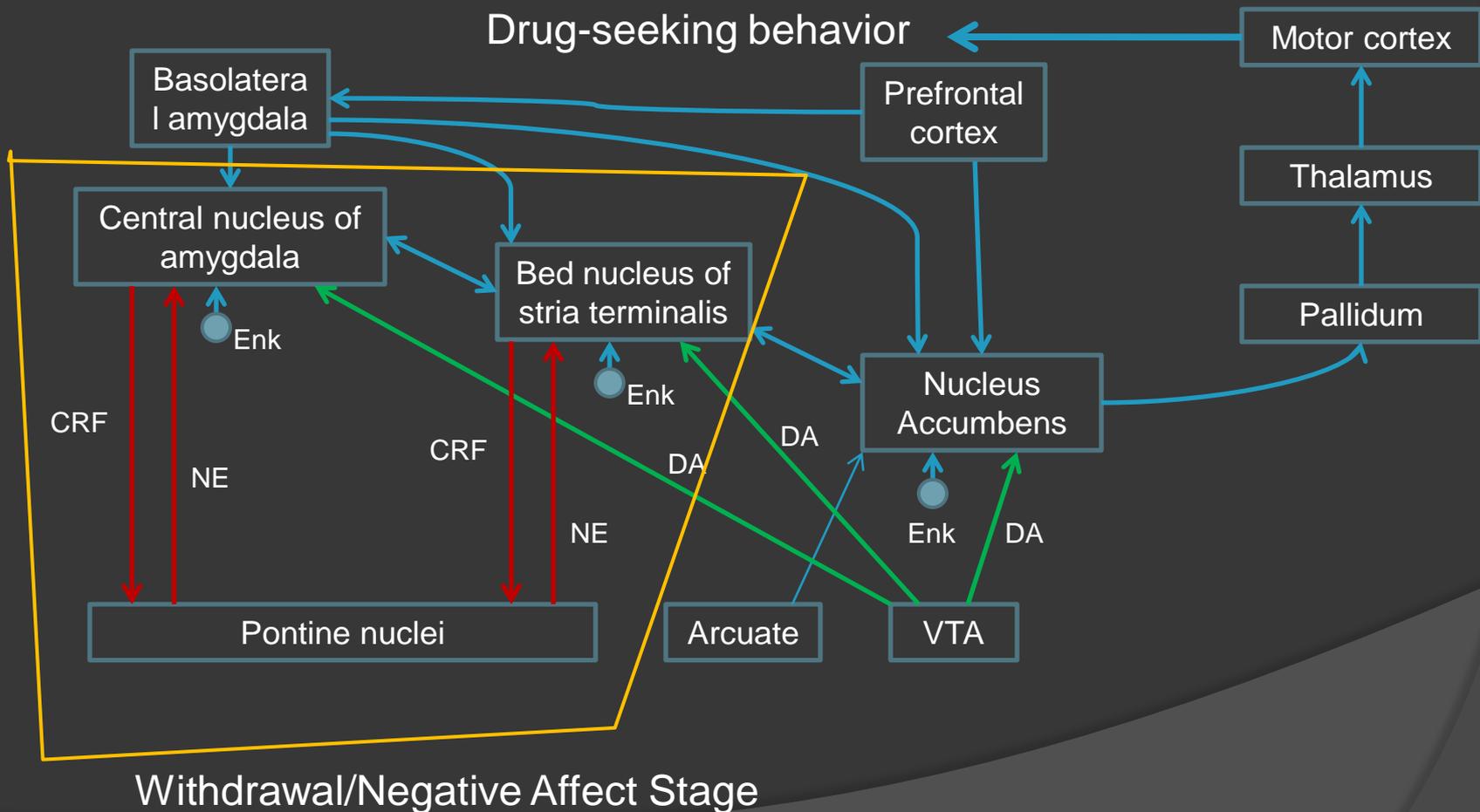
Withdrawal/Negative Affect

- ⦿ Disrupted reward systems – decreases in reward neurotransmitters
 - Acute withdrawal
 - Negative motivational state
- ⦿ Anti-reward systems – CRF & Norepinephrine
 - Emotional dysregulation – abnormal stress response
 - Craving

Negative Motivational State

Neurotransmitter	Functional Effect
↓ Dopamine	Dysphoria
↓ Serotonin	Dysphoria
↓ GABA	Anxiety, panic attacks
↓ Neuropeptide Y	Anti-stress
↑ Dynorphin	Dysphoria
↑ Norepinephrine	Stress
↑ Corticotropin-releasing factor	Stress

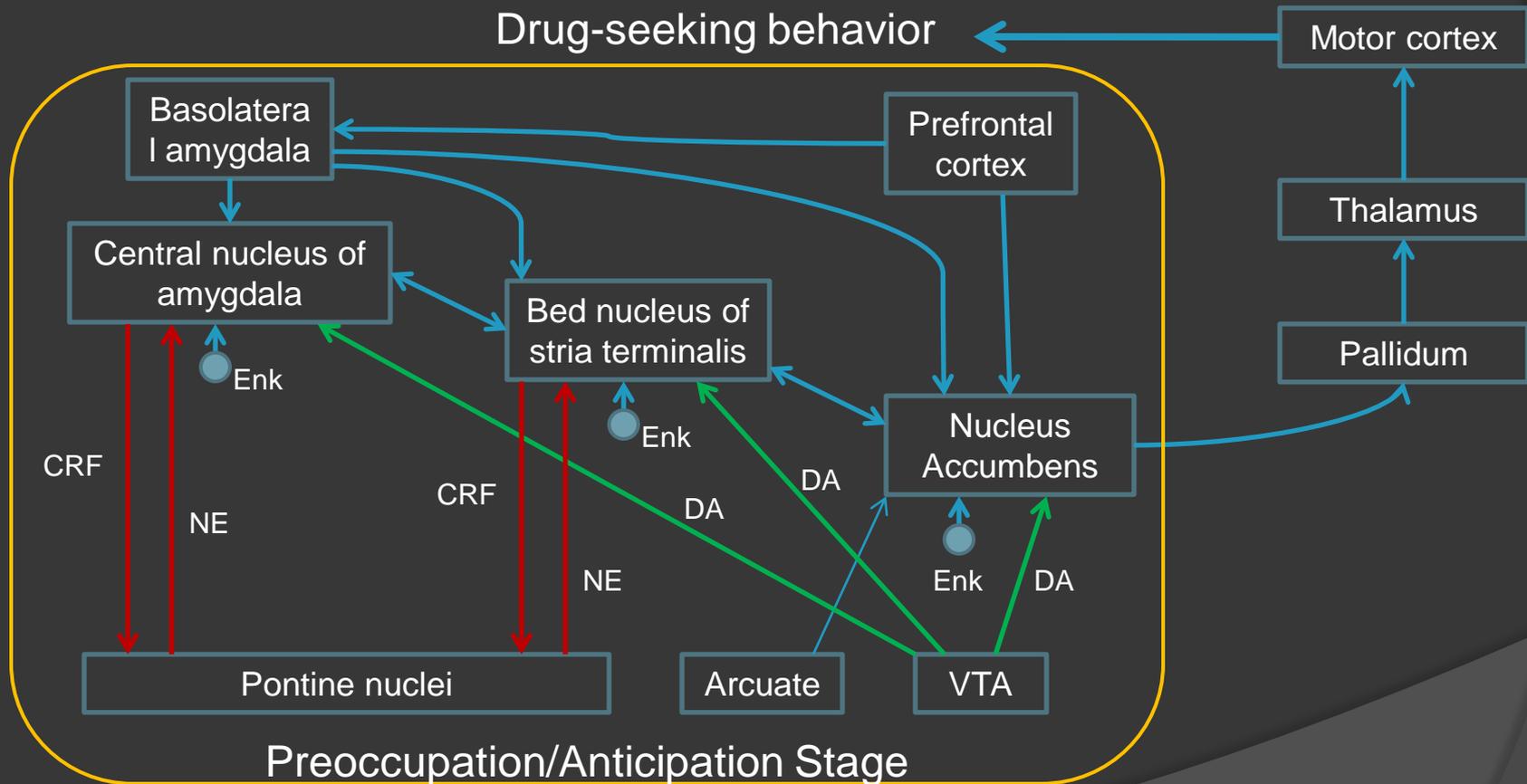
Neurobiology of Addiction



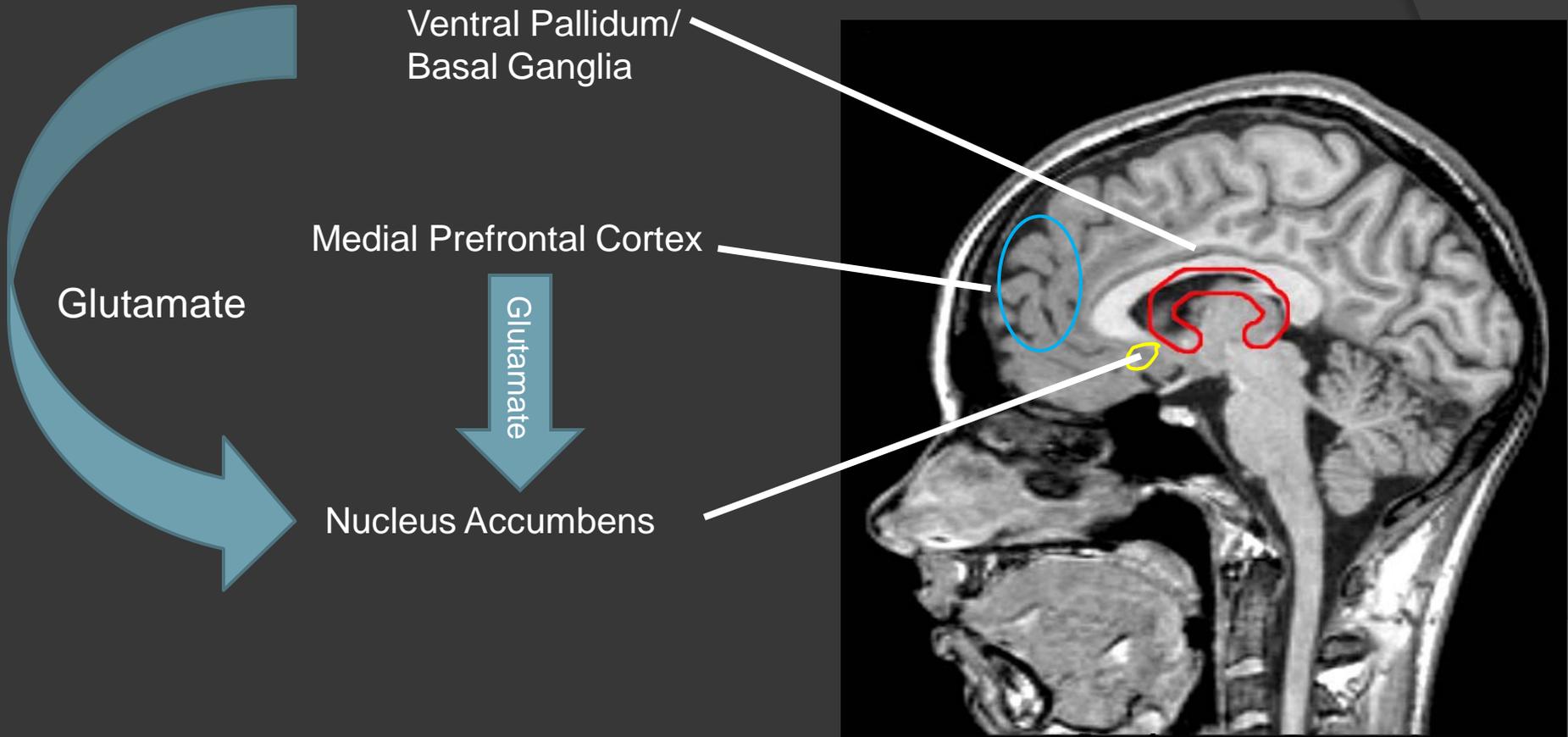
Preoccupation/Anticipation

- Key element in relapse
- Relapse may or may not be associated with craving
- Craving type 1/ Reward – environmental cues induce drug use
- Craving type 2/ Relief – Internal anxiety & dysphoria cause drug use

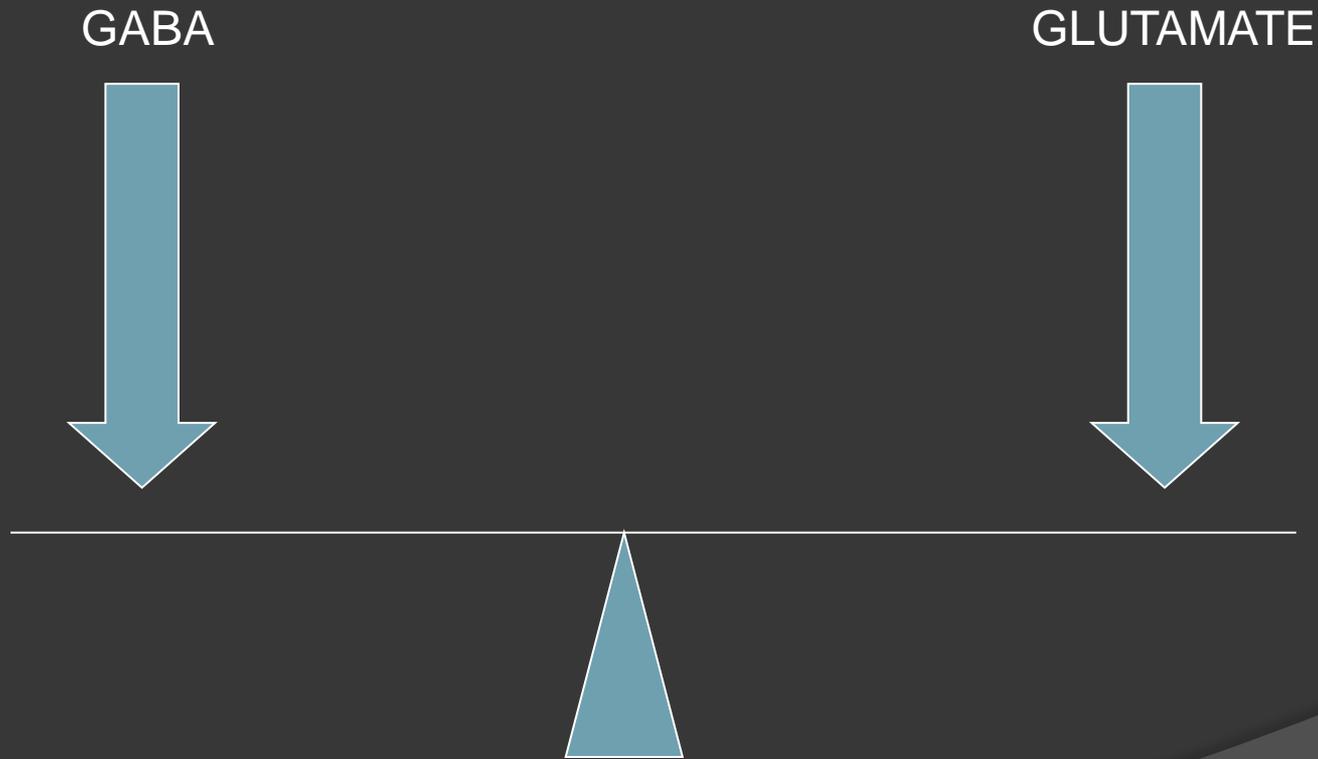
Neurobiology of Addiction



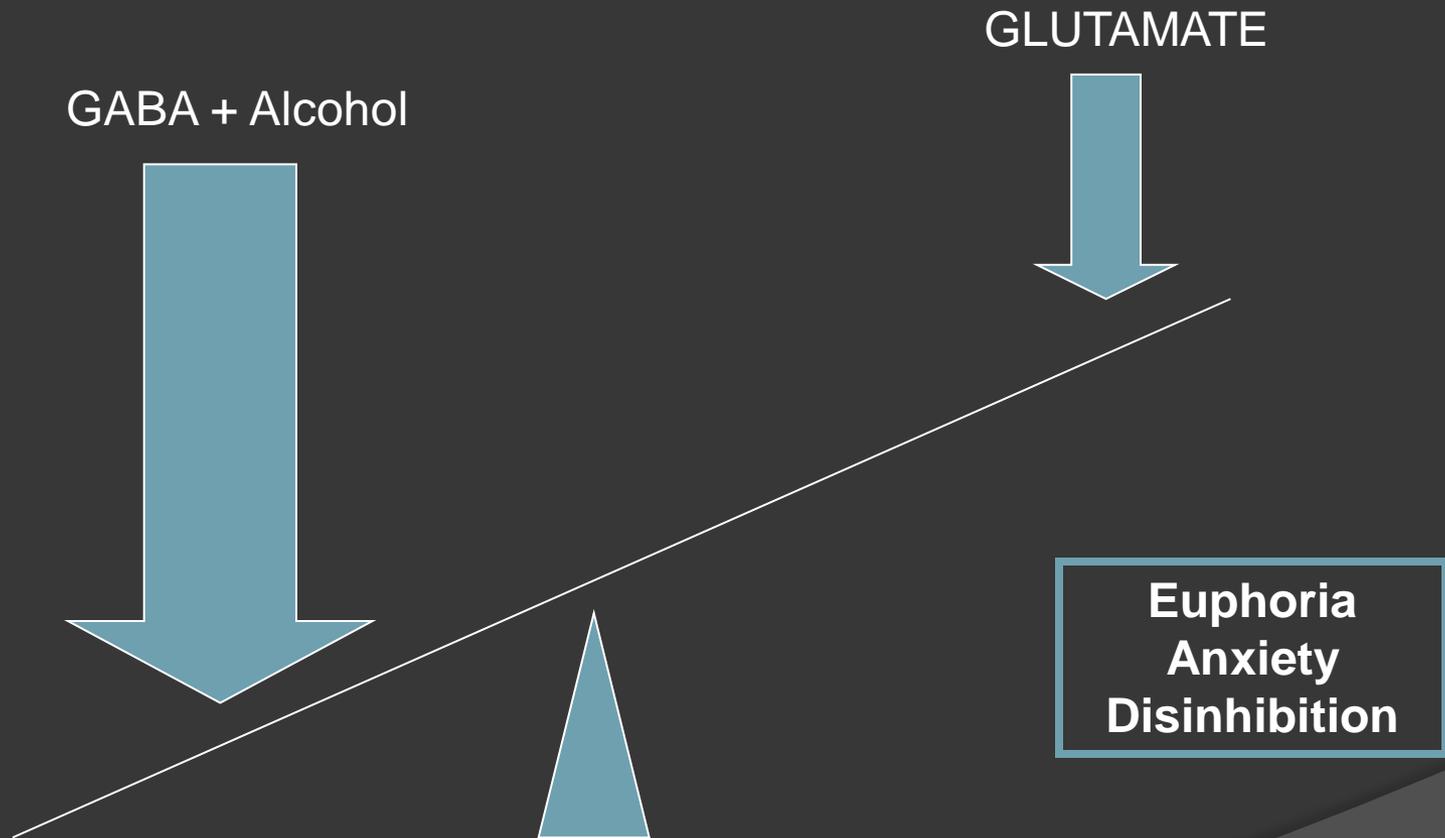
Craving Type 1: Reward Craving



Reward Craving: Alcohol



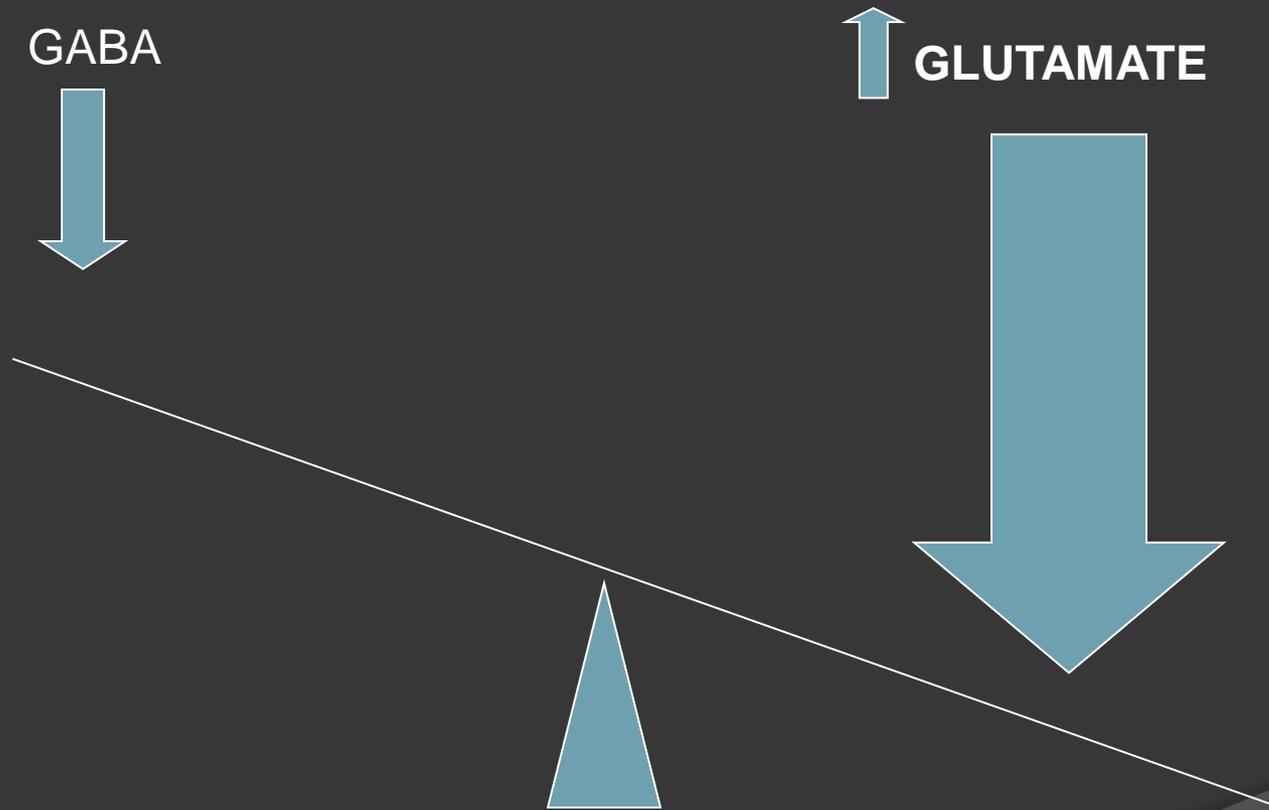
Reward Craving: Acute Alcohol Use



Reward Craving: Chronic Alcohol Use

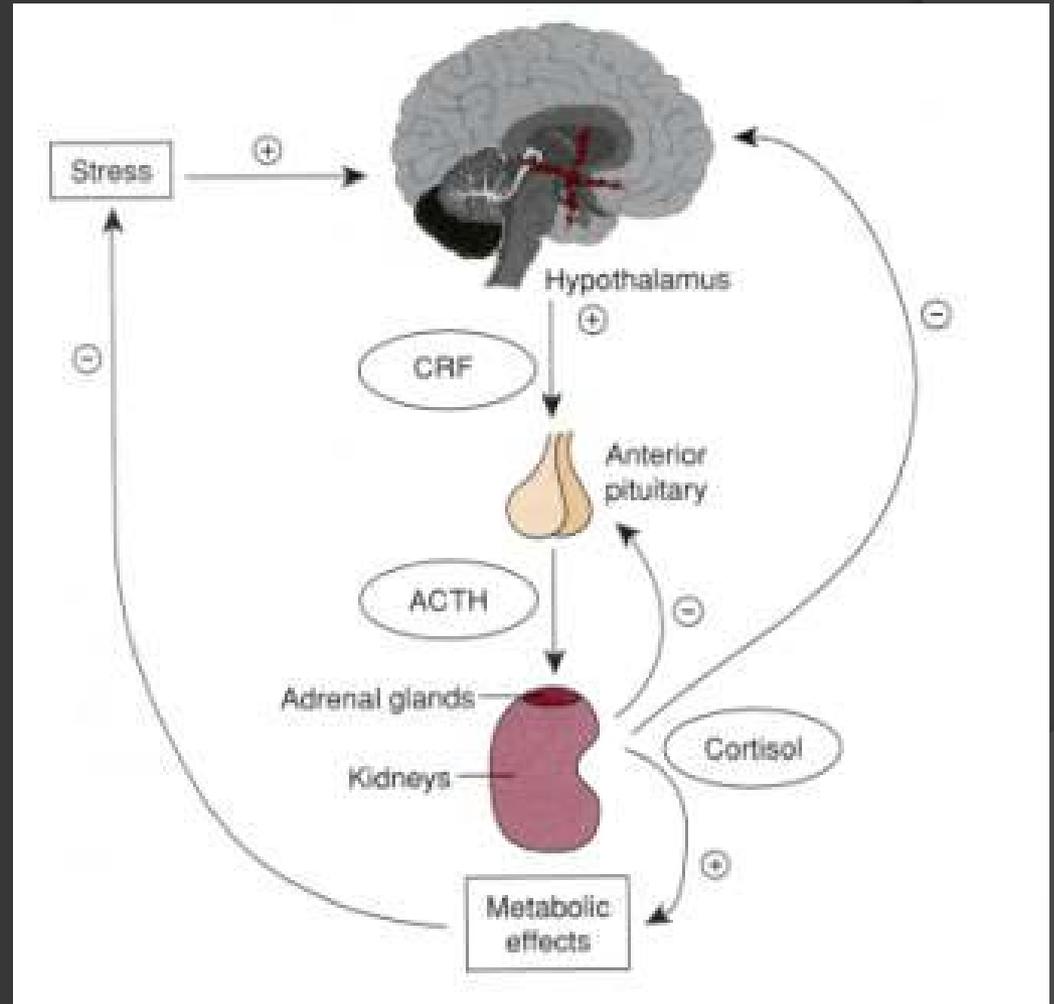


Reward Craving: Removal of Alcohol



Craving Type 2: Relief Craving

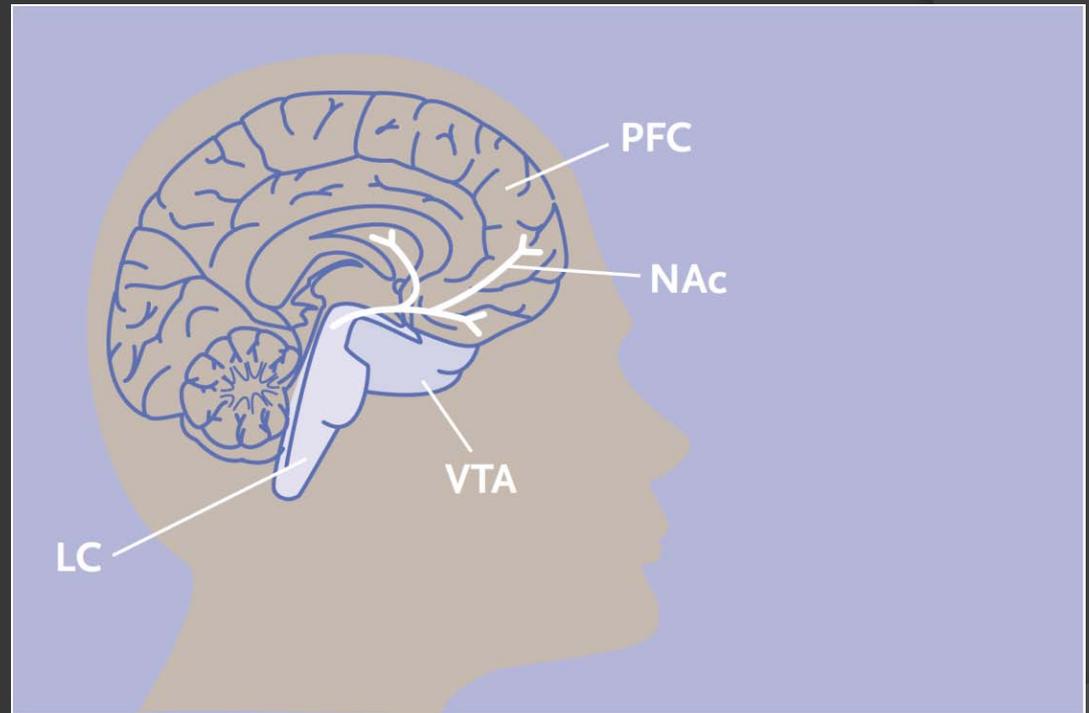
- HPA Axis - CRF
- Norepinephrine



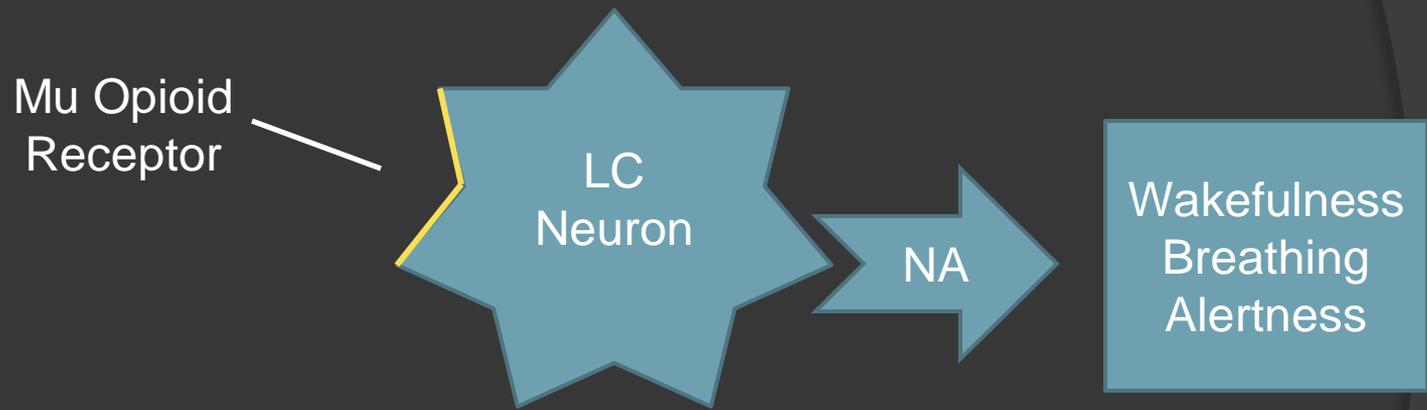
Relief Craving: Role of Norepinephrine

● Norepinephrine (NA):

- Produced in LC
- Stimulates wakefulness



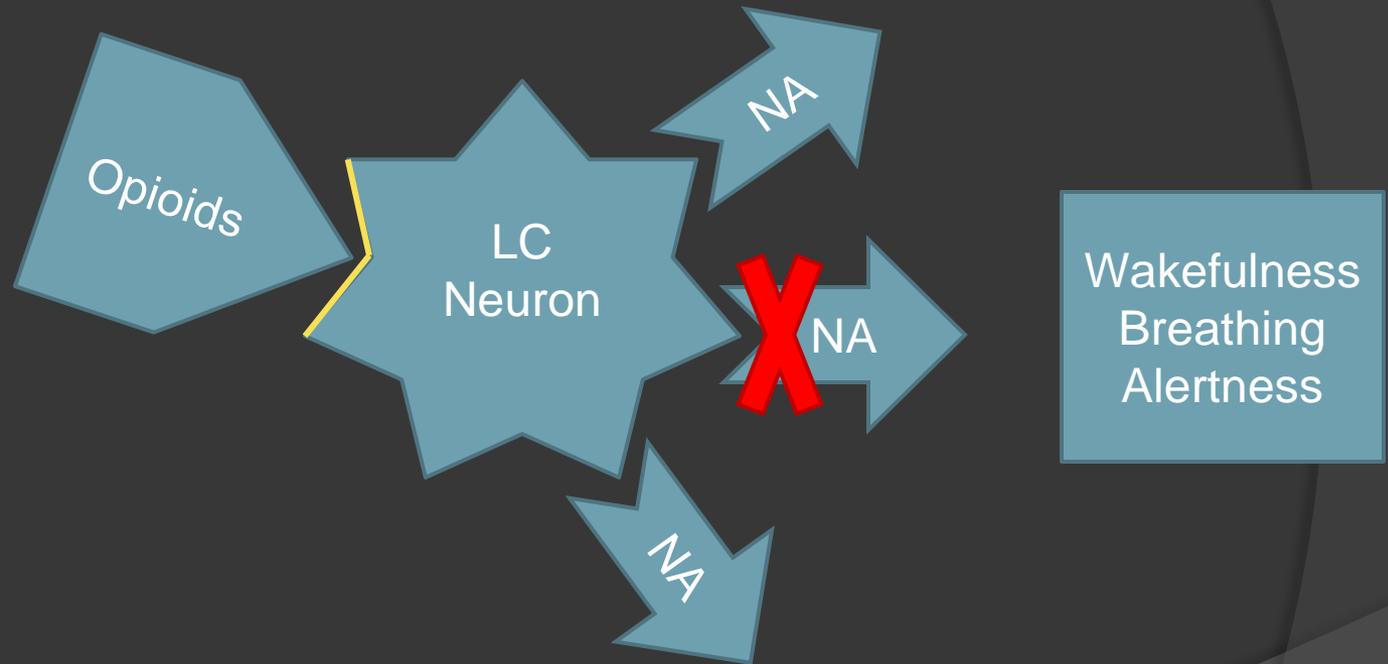
Relief Craving: Opioids



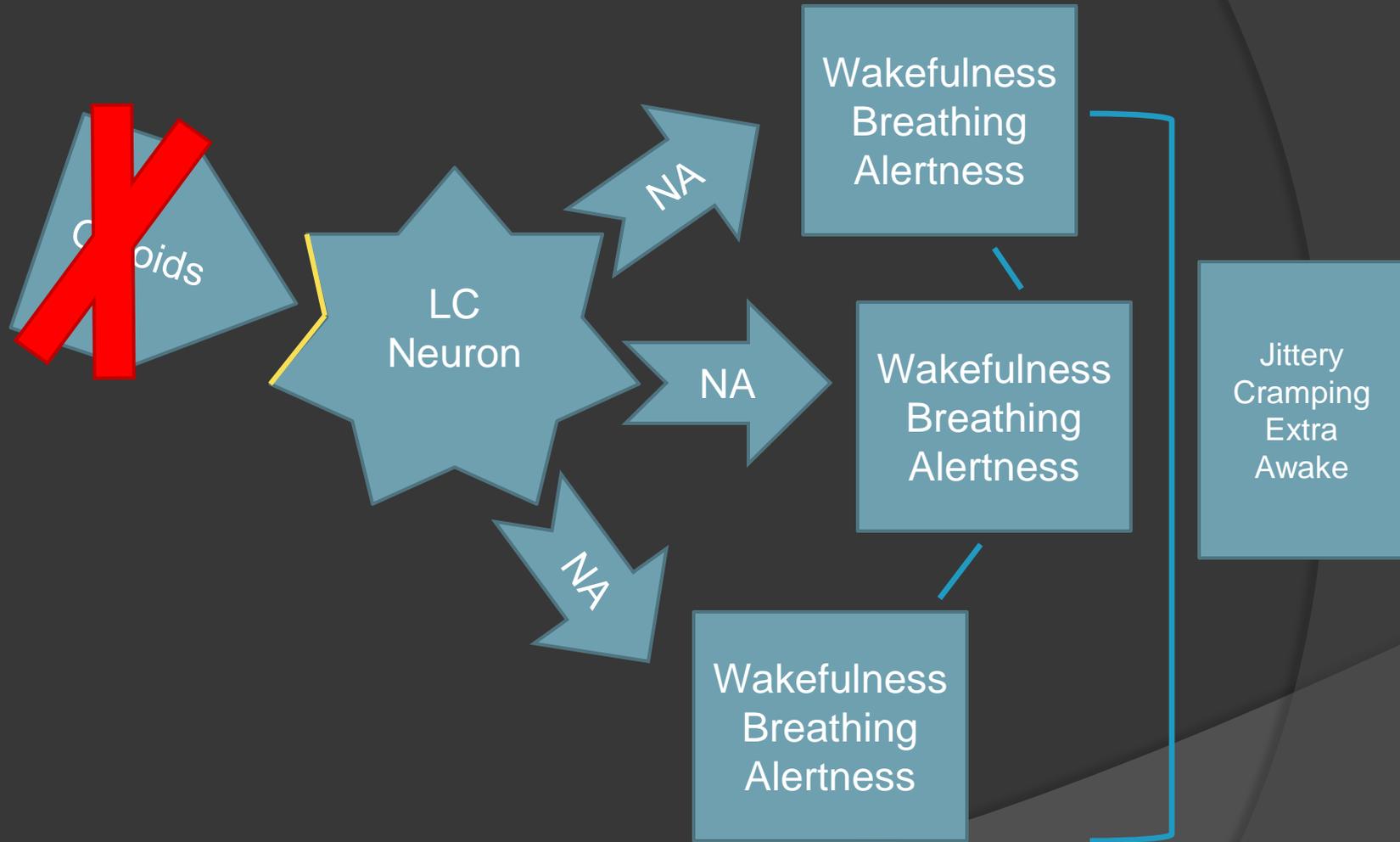
Relief Craving: Acute Opioid Use



Relief Craving: Chronic Opioid Use



Relief Craving: Removal of Opioids



Summary of Neurobiology

- Addiction occurs in 3 stages:
 - Binge/Intoxication – classic reward pathway
 - Withdrawal/Negative Affect – decreased reward neurotransmitters
 - Preoccupation/Anticipation – new set-point in anti-reward pathway & craving:
 -  Glutamate
 -  Norepinephrine
 - Stress response & CRF

Addictions Psychopharmacology

- ⦿ Alcohol
- ⦿ Nicotine
- ⦿ Opiates
- ⦿ Stimulants

Medications for Alcohol Dependence

- ◉ Disulfiram – classic flushing reaction from build-up of acetaldehyde; caution in certain populations
- ◉ Naltrexone – opioid antagonist; works best in those with strong family history
- ◉ Acamprosate – effects glutamate neurotransmission; ? efficacy
- ◉ Carbamazepine & Divalproex – acute withdrawal, irritability, & reduced heavy drinking days
- ◉ Baclofen – GABA_B receptor agonist; increases days abstinent but also has some abuse potential

Medications for Nicotine Dependence

- Nicotine Replacement Therapy – patches mainstay, supplement with gum/lozenges/inhalers; can combine with bupropion, nortriptyline, clonidine
- Bupropion – augments NA & DA; reduces craving; 30% quit rate
- Varenicline – partial nicotine agonist/antagonist; 44% quit rate; don't combine with replacement therapy
- Nortriptyline – 2nd line but maybe as efficacious as bupropion
- Clonidine – alpha agonist; reduces withdrawal symptoms; 2nd line

Medications for Opioid Dependence

- ◉ Methadone – gold-standard; long-acting mu opioid agonist; must be in methadone clinic
- ◉ Buprenorphine – partial mu opioid agonist & kappa opioid antagonist; combined with naltrexone (Suboxone); office-based treatment
- ◉ Naltrexone – opioid antagonist; reduces euphoria from opioids, precipitating withdrawal if taken with opioids
- ◉ Clonidine – reduces withdrawal symptoms only

Medications for Stimulant Dependence

⦿ Cocaine Dependence

- Desipramine – mixed results; best for those with depression, antisocial
- Disulfiram – aversion reaction to cocaine via dopamine beta hydroxylase; caution if still using cocaine
- Anticonvulsants – Tiagabine, Topiramate
 - Block cocaine-induced kindling; small positive trials

⦿ Amphetamine Dependence

- Naltrexone – some positive studies
- Bupropion – possibly, for those with lower levels of use
- Risperidone (?) – reduced use in open-label trials
- Modafinil – controversial but promising results in early trials

Questions ?

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