Understanding Brain and Behavior in Addiction

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Presentation Outline

- Describe concepts used to clinically define & characterize addiction
- Discuss the prevailing view of addiction
- Report evidence that addiction is a chronic medical illness
- Explain why addiction can happen
- Describe the brain changes that occur in addiction

"Addiction"

- Addiction is a non-specific term frequently used to refer to a variety of substance-related disorders & compulsive behaviors.

- Addiction = Substance Dependence (in DSM 4)

  = Substance Use Disorder (in DSM 5)

- **Addiction is not just <u>physiological</u> dependence**
  - Physical dependence indicates physiological change or adaptation in an organism in response to repeated administration of a drug.
  - A substance use disorder is present in an individual when there is a pattern of pathologic use.

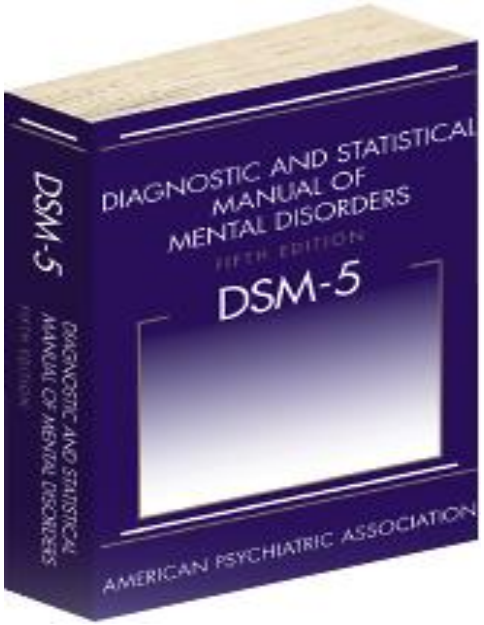
Definition of Addiction

"Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death."

American Society of Addiction Medicine, 2011

Substance-Related Disorders



- Substance Use Disorders
  - Patterns of use causing problems
  - Continued use despite problems
- Substance-Induced Disorders
  - Intoxication
  - withdrawal
  - Substance-Induced Mental Disorders

Substance Use Disorder Criteria

(6 of a total of 11)

- Taking the substance in larger amounts or for longer than intended
- Wanting to cut down or stop using the substance but not managing to
- Spending a lot of time getting, using, or recovering from use of the substance
- Cravings and urges to use the substance
- Not managing to do what you should at work, home or school, because of substance use
- Continuing to use, even when it causes problems in relationships

Substance Use Disorders Criteria (cont'd)

- Giving up important social, occupational or recreational activities because of substance use
- Using substances again and again, even when it puts you in danger
- Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance
- Needing more of the substance to get the effect you want (tolerance)
- Development of withdrawal symptoms, which can be relieved by taking more of the substance.

DSM5 SUD severity & qualifiers

- **Severity of substance use disorders is based on the number of criteria endorsed:**
  - **1 or 2 criteria = a mild disorder**
  - **3 to 5 criteria = a moderate disorder**
  - **6 or more criteria = a severe disorder**

Qualifiers:

in early remission
in sustained remission
on maintenance therapy
in a controlled environment

An Integrative Model of Addiction

Layers of cumulatively reinforcing variables

Upper layers reinforce conditions set up by lower levels

Considerable interaction between levels

Brizer & Castenada, Clinical Addiction Psychiatry, Chapter 2, Mark Schenker, pp 16-22

EXISTENTIAL

CULTURAL

SOCIAL

FAMILY

HABITS

PSYCHOLOGICAL

BIOLOGICAL

The view that **Addiction is primarily a Social Problem:**

- Causes many disturbing & expensive social problems
- Requires interdiction & law enforcement
- Most physicians do not screen for addiction on routine examinations
- Half of patients treated for addictions return to active use within a year

The view that **Addiction is a Chronic Medical Illness:**

- Diagnostic considerations
- Compared to:
  - Type 2 Diabetes Mellitus
  - Hypertension
  - Asthma
- Genetic Heritability
- Role of Personal Responsibility
- Treatment Response
- Pathophysiology

Genetic Heritability

- Comparing rates of monozygotic vs. dizygotic twins
- Twin studies estimates:
  - Hypertension 0.25-0.5
  - Diabetes mellitus 1 0.3-0.55
  - Diabetes mellitus 2 0.8
  - Adult onset asthma 0.36-0.7
  - Heroin addiction in males 0.34
  - Alcoholism in males 0.55
  - Marijuana addiction in females 0.52
  - Cigarette dependence (both sexes) 0.61
- Suggest genetic contribution of addiction is comparable to other chronic illnesses

Role of Personal Responsibility

- Use of drug is voluntary
  - Individuals initiate behaviors that lead to substance use disorders
- Voluntary behaviors in other chronic medical illnesses
  - Hypertension and salt sensitivity
  - Familial, cultural, and personal choice factors

Role of Personal Responsibility

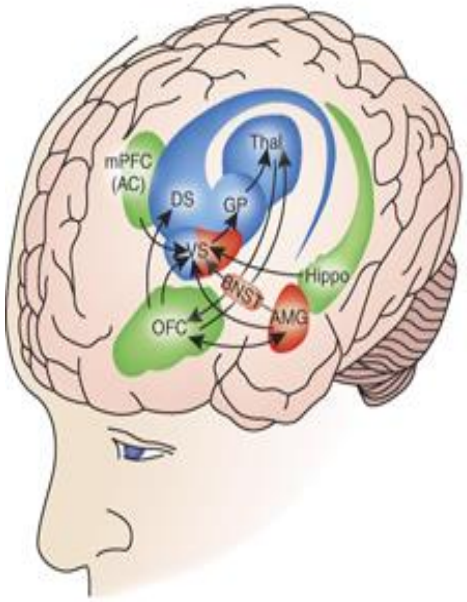
- Involuntary components embedded within seemingly volitional choices
  - Effects of a drug influenced by genetic factors
    - Aldehyde dehydrogenase genotype v. children of alcoholics

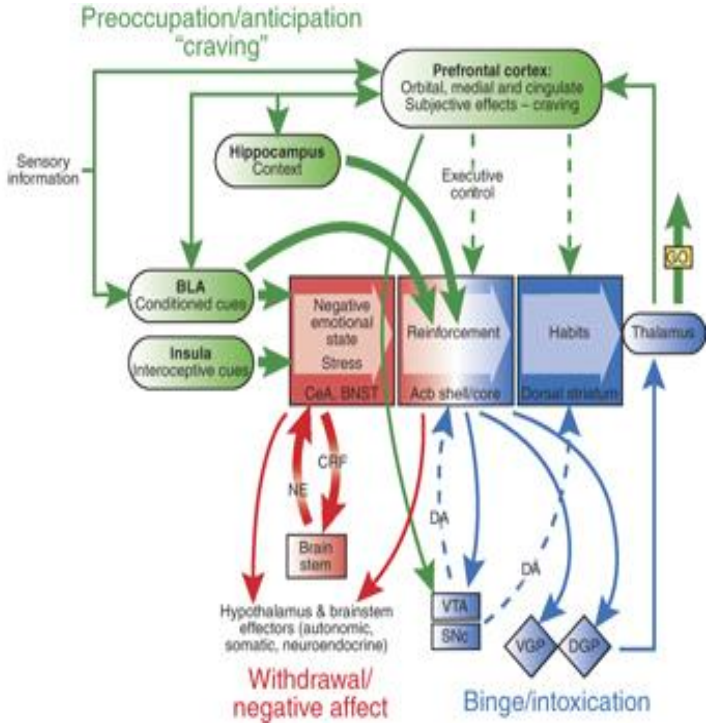
Treatment Response

- No reliable cure
- Favorable outcomes for patients who comply with the recommended regimen
  - Education, counseling, medications
- Noncompliance is not uncommon
  - 40-60% abstinent one year after discharge
  - Similar statistics for diabetes, hypertension, asthma

Pathophysiology

- Disordered physiological processes associated with a disease or injury





Drug addiction is a chronically relapsing disorder that is characterized by:

- (1) compulsion to seek and take the drug
- (2) loss of control in limiting intake
- (3) emergence of a negative emotional state
  - e.g. dysphoria, anxiety, irritability
  - reflects a motivational withdrawal syndrome
  - when access to the drug is prevented.

Aspects of impulse control disorders

- **Impulsivity:**
  - Defined behaviorally as a predisposition toward rapid, unplanned reactions to internal and external stimuli without regard for the negative consequences of these reactions to themselves or others.
  - Often measured in two domains:
    - the choice of a smaller, immediate reward over a larger, delayed reward
    - the inability to inhibit behavior by changing the course of action or to stop a response once it is initiated. Impulsivity is a core deficit in substance abuse disorders.

Aspects of impulse control disorders (cont'd)

- Impulse control disorders characterized by increasing sense of tension or arousal before committing an impulsive act
- Pleasure, gratification, or relief at the time of committing the act
- Largely associated with positive reinforcement mechanisms

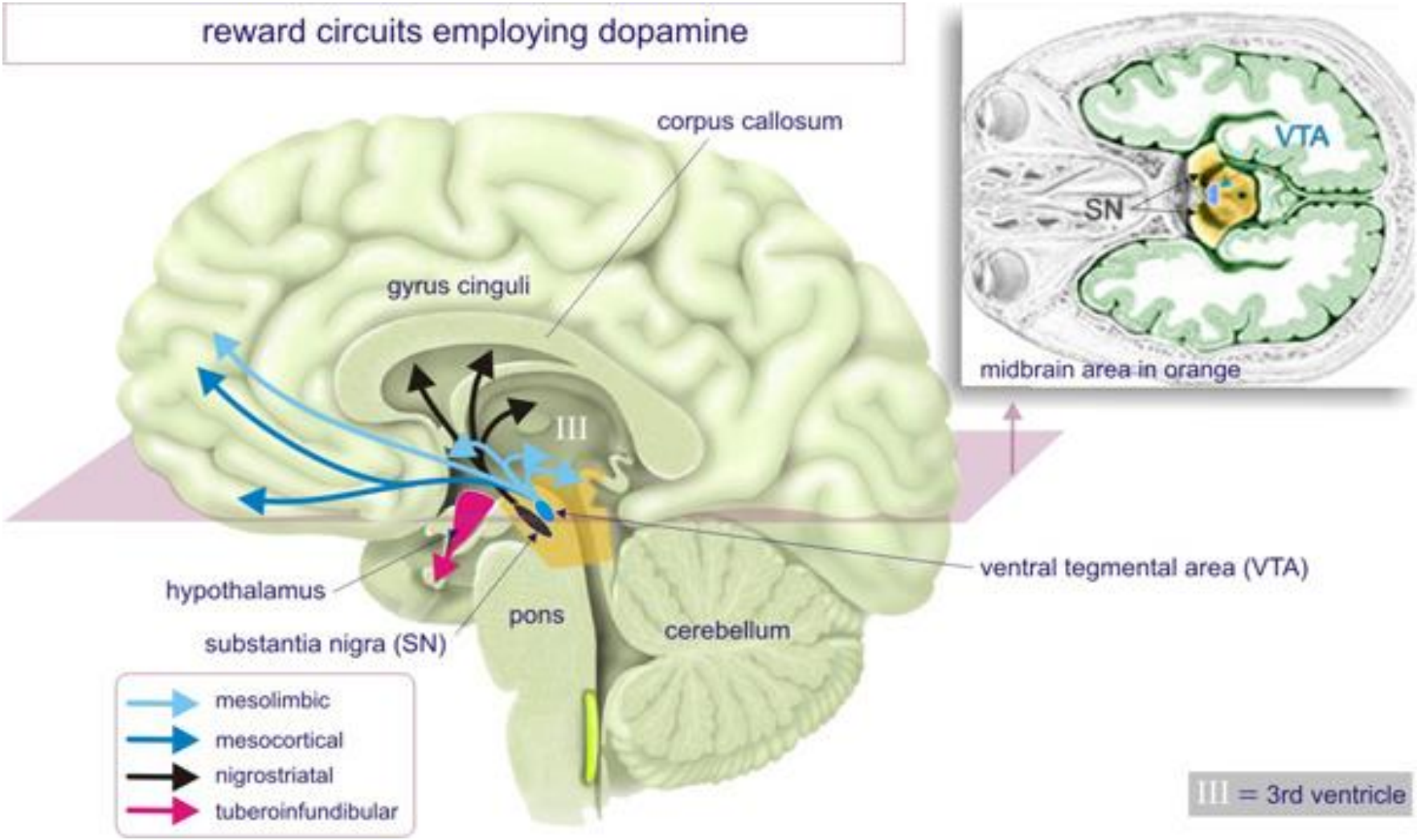
Aspects of compulsive disorders

- **Compulsivity:**
  - Defined as elements of behavior that result in preservation in responding in the face of adverse consequences, preservation in responding in the face of incorrect responses in choice situations, or persistent reinitiation of habitual acts.

Aspects of compulsive disorders (cont'd)

- Compulsive disorders characterized by anxiety and stress before committing a compulsive repetitive behavior
- Relief from stress by performing the compulsive behavior
- Largely associated with negative reinforcement mechanisms and automaticity

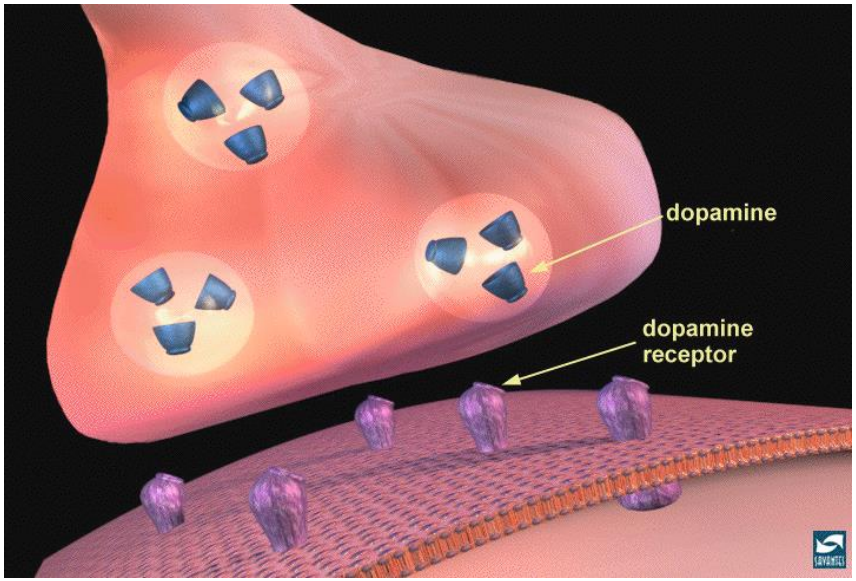
reward circuits employing dopamine

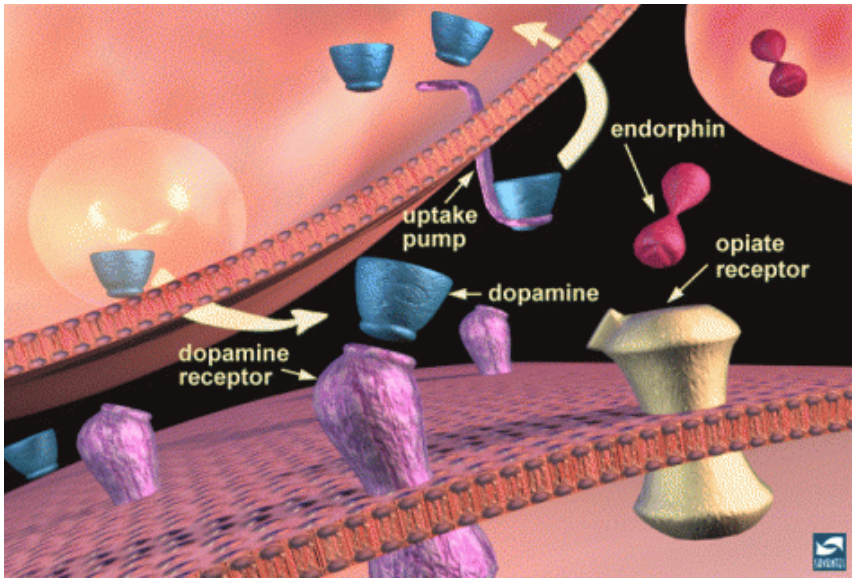


How does addiction start?

- Drugs of abuse can release 5 to 10 times the amount of dopamine as natural rewards
- In some cases, this occurs almost immediately (as when drugs are smoked or injected), and the effects can last much longer than those produced by natural rewards
- This creates a much stronger effect on the brain's (meaning to motivation to behavior to) reward circuitry than those produced naturally (e.g., food, sex)
- The effect of such a powerful reward strongly motivates people to take drugs again and again

Chronic over-firing results in compensatory reduction of receptor density in the target areas.





Effects of Chronic Drug Use

- Reduced dopamine receptor density in the brain cortex & reduced dopamine signaling
  - Addict no longer gets high from taking the drug
  - Normal satisfactions get a very weak signal to the decision areas
  - Loss of enjoyment and satisfaction

- Priorities are rearranged
  - Drug gives enough signal to remain salient
  - Must take the drug to feel normal or at least less abnormal
  - Normal reinforcers give less signal and are less important

Transition to addiction = Evolving neuroplasticity

- It begins with changes in the mesolimbic dopamine system.
- Dopamine system changes are followed by a cascade of neuroadaptations from the ventral striatum to the dorsal striatum & orbitofrontal cortex
- Eventually there is also dysregulation of the prefrontal cortex, cingulate gyrus, and extended amygdala.

Neurocircuitry Dynamics in the Transition to Addiction

- **Mesolimbic Dopamine System:** Incentive Salience Pathways, Salience Attribution
- **Ventral Striatum:** Incentive Salience Pathways, Salience Attribution
- **Ventral Striatum/Dorsal Striatum/Thalamus:** Voluntary to Habitual Drug-Seeking
- **Dorsolateral Frontal Cortex, Inferior Frontal Cortex & Hippocampus:** Cognitive Control, Delayed Gratification & Memory
- **Extended Amygdala:** Negative Reinforcement Pathways

Correlating clinical features:

- Initial impulsive action turns compulsive, (eventually) becomes chronic & relapsing.
- This transition involves reprogramming of neuronal circuits that process:

  (1) reward and motivation

  (2) memory, conditioning and habituation

  (3) executive function and inhibitory control

  (4) interoception and self-awareness

  (5) stress reactivity

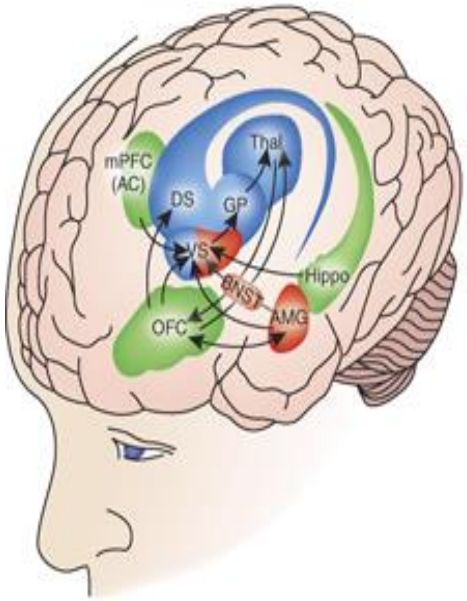
- This transition is heavily influenced by genetic, developmental & environmental factors and their dynamic interactions, which will determine the course and severity of the addiction.

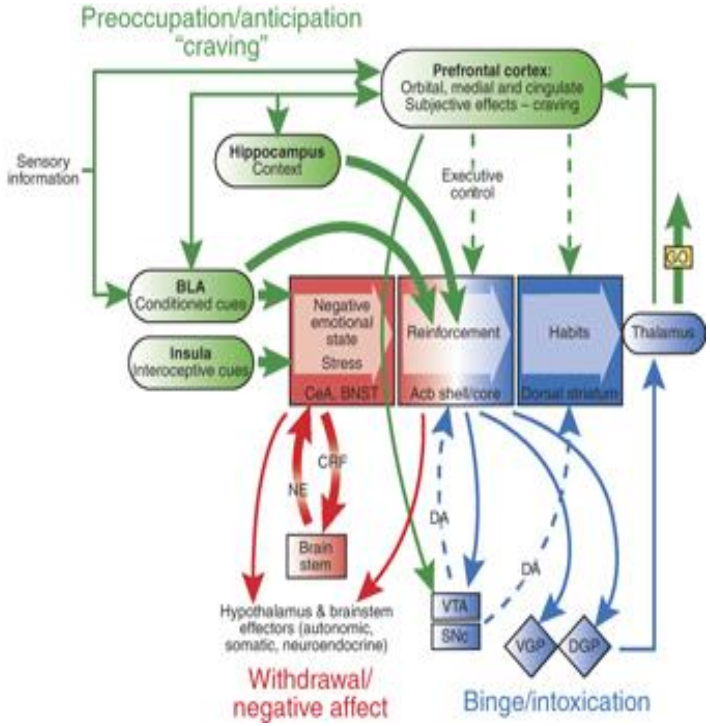
ALLOSTASIS

In endocrinology, a chronic state of disordered homeostasis (dyshomestasis) that allows survival of the organism at the expense of its well-being and life expectancy.

The view that addiction is the pathology that results from an allostatic mechanism using the circuits established for natural rewards provides a realistic approach to identifying the neurobiological factors that produce vulnerability to addiction and relapse.

Neuropsychopharmacology (2001) **24,** 97–129. doi:10.1016/S0893-133X(00)00195-0





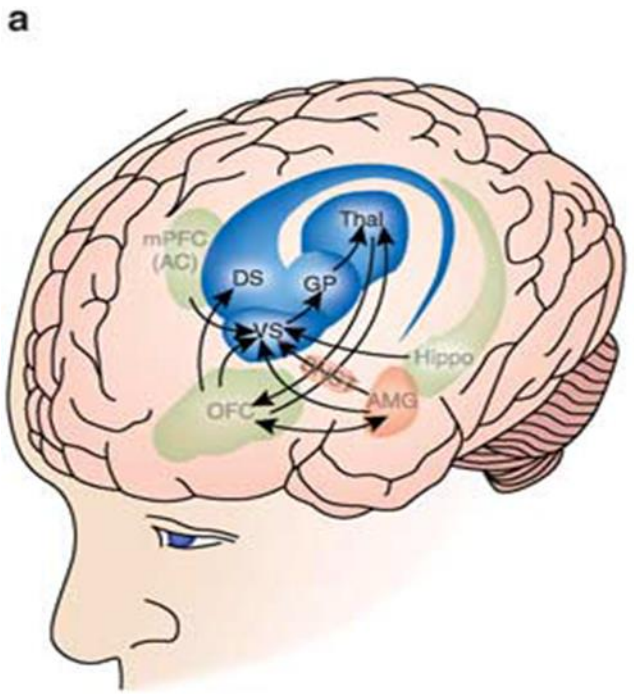
The Stages of Drug Addiction

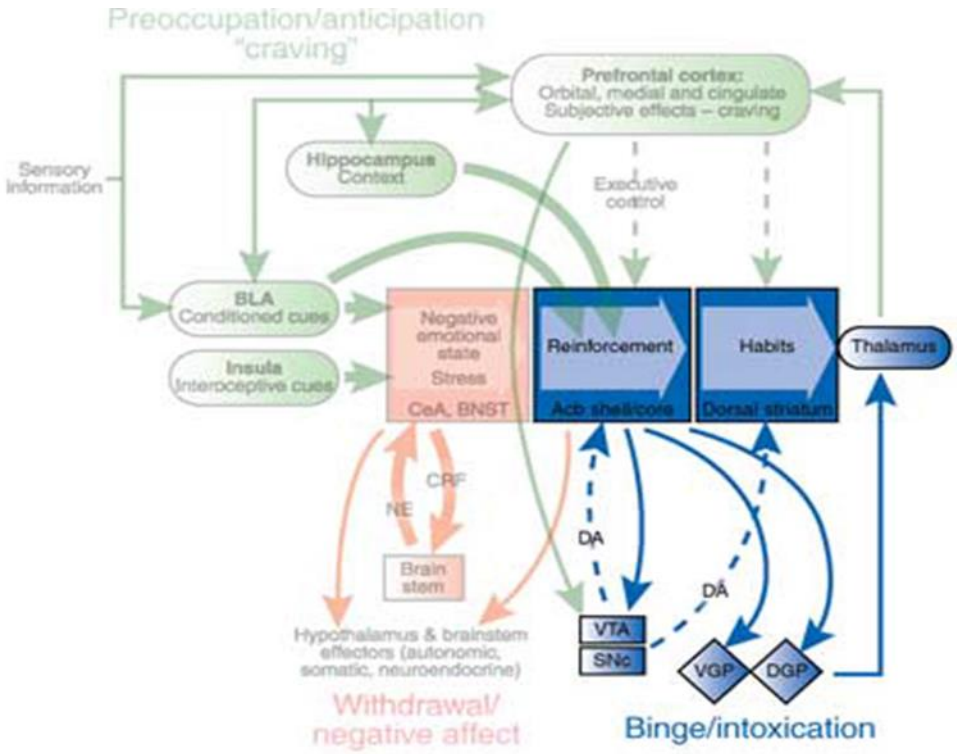
- A disorder that involves elements of both impulsivity & compulsivity that yield a composite addiction cycle composed of three stages:
- (1) ‘binge/intoxication’
- (2) ‘withdrawal/negative affect’
- (3) ‘preoccupation/anticipation’ (craving)

Discrete circuits mediate the three stages of the addiction cycle:

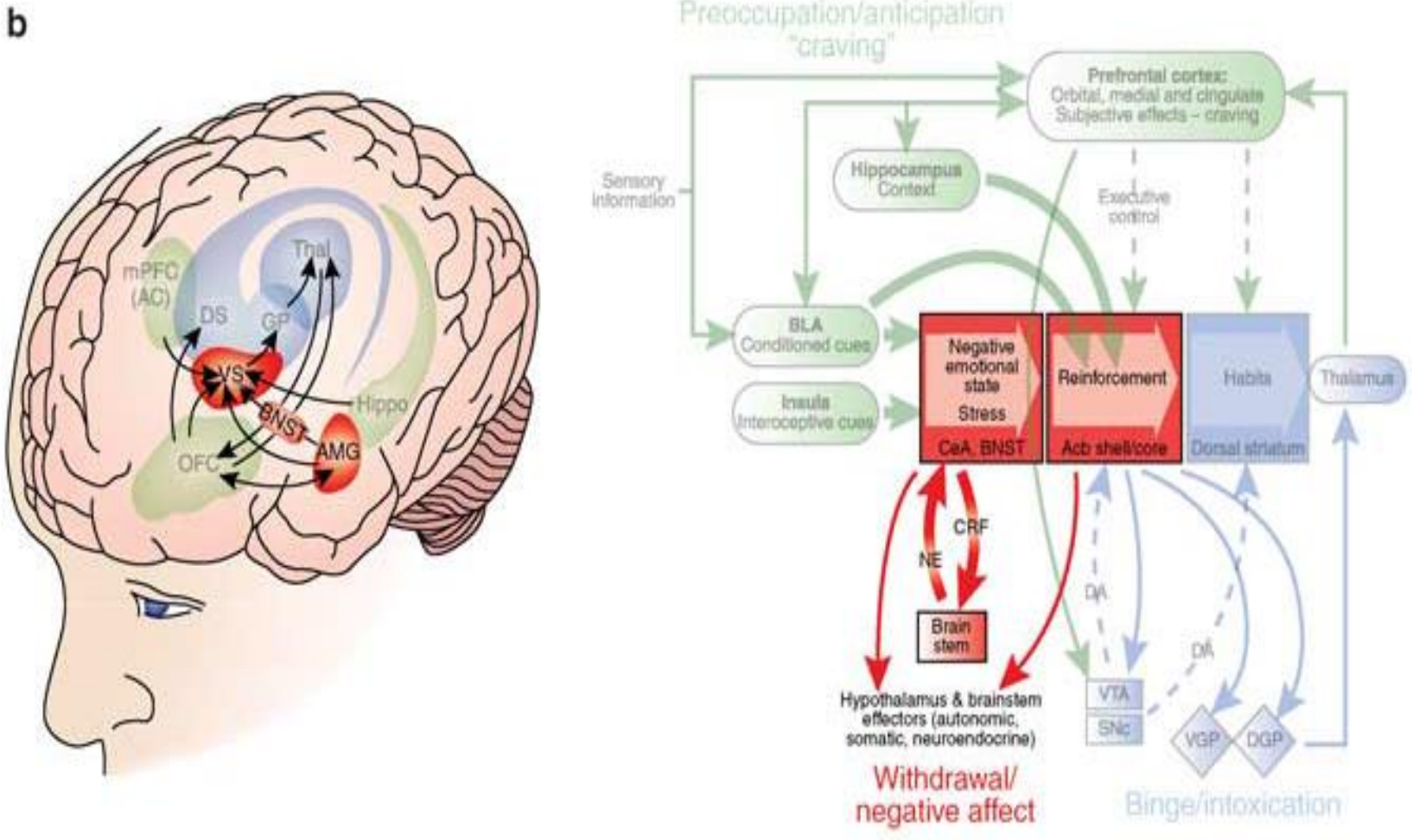
- **Binge/intoxication stage** -ventral tegmental area & ventral striatum
- **Withdrawal/negative affect stage**-extended amygdala
- **Craving/preoccupation/anticipation stage**-a widely distributed network involving the orbitofrontal cortex–dorsal striatum, prefrontal cortex, basolateral amygdala, hippocampus & insula

BINGE/INTOXICATION

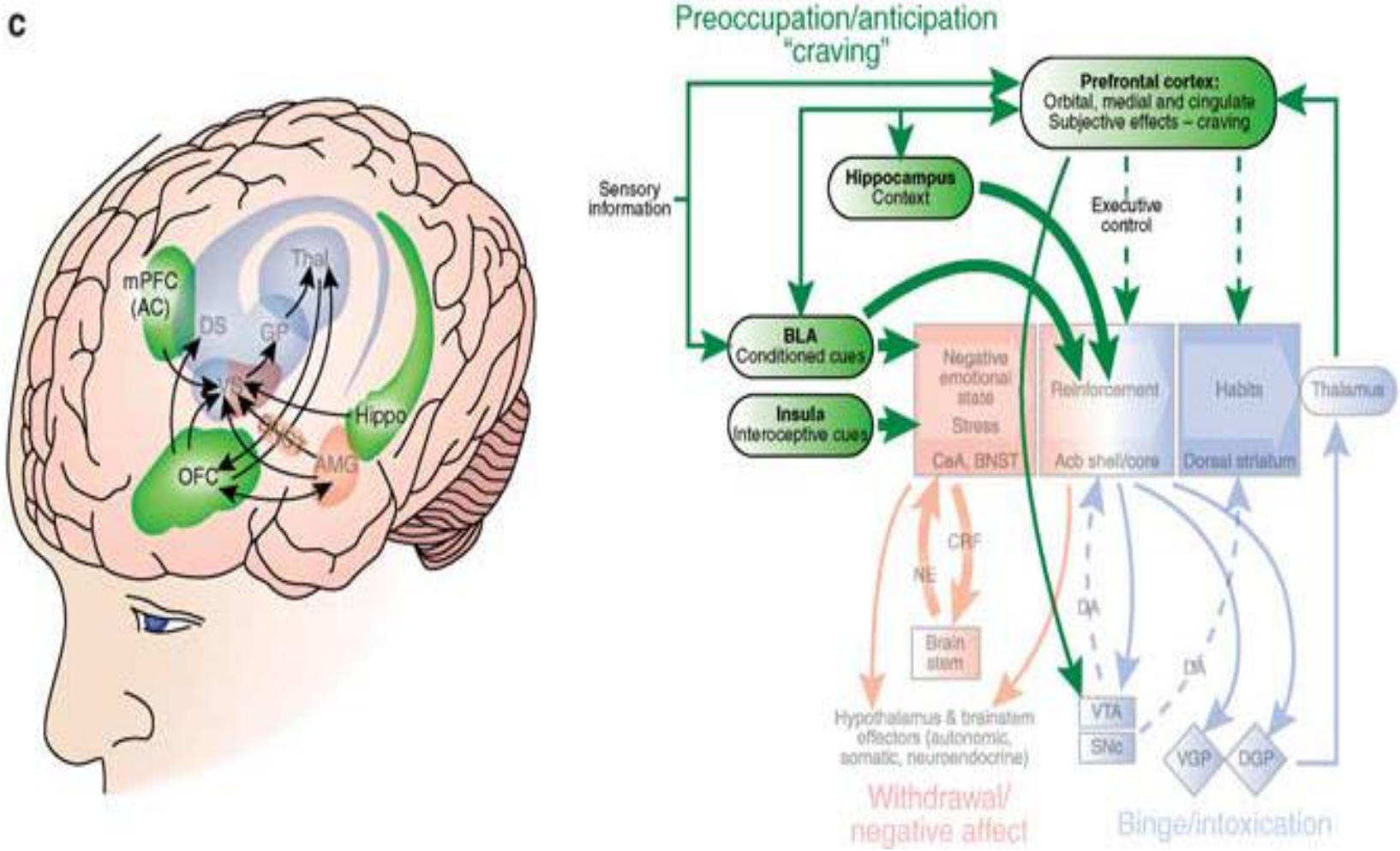




WITHDRAWAL/NEGATIVE AFFECT



PREOCCUPATION/ANTICIPATION (craving)



Delineation of the neurocircuitry of the addiction syndrome:

- Grounds our thinking when planning & carrying out addiction treatment
- Forms a heuristic basis for the search for the molecular, genetic & neuropharmacological neuroadaptations key to vulnerability for developing and maintaining addiction.

Mind/Brain Changes in Addiction

- **Chronic, relapsing disorder** with compulsive use, loss of control, & a negative affective state
- Transition to addiction rests on **evolving neuroplasticity**
- Neural re-programing of circuits underlying:
  - (1)reward & motivation
  - (2) memory, conditioning & habituation
  - (3) executive function & inhibitory control
  - (4) interoception & self-awareness,
  - (5) stress reactivity
- Negative reinforcement shapes behavior
- 3 stages: (1)binge/intoxication, (2) withdrawal/negative affect, (3) preoccupation/anticipation (craving); each with discrete circuitry