

# ***The Brain and Addiction***

Neuroscience

Neuroanatomy

Psychopharmacology

Neurochemistry



***Opiate Addiction***  
***is a***  
***Brain Disease***

***NOW THERE IS NO DISPUTE***

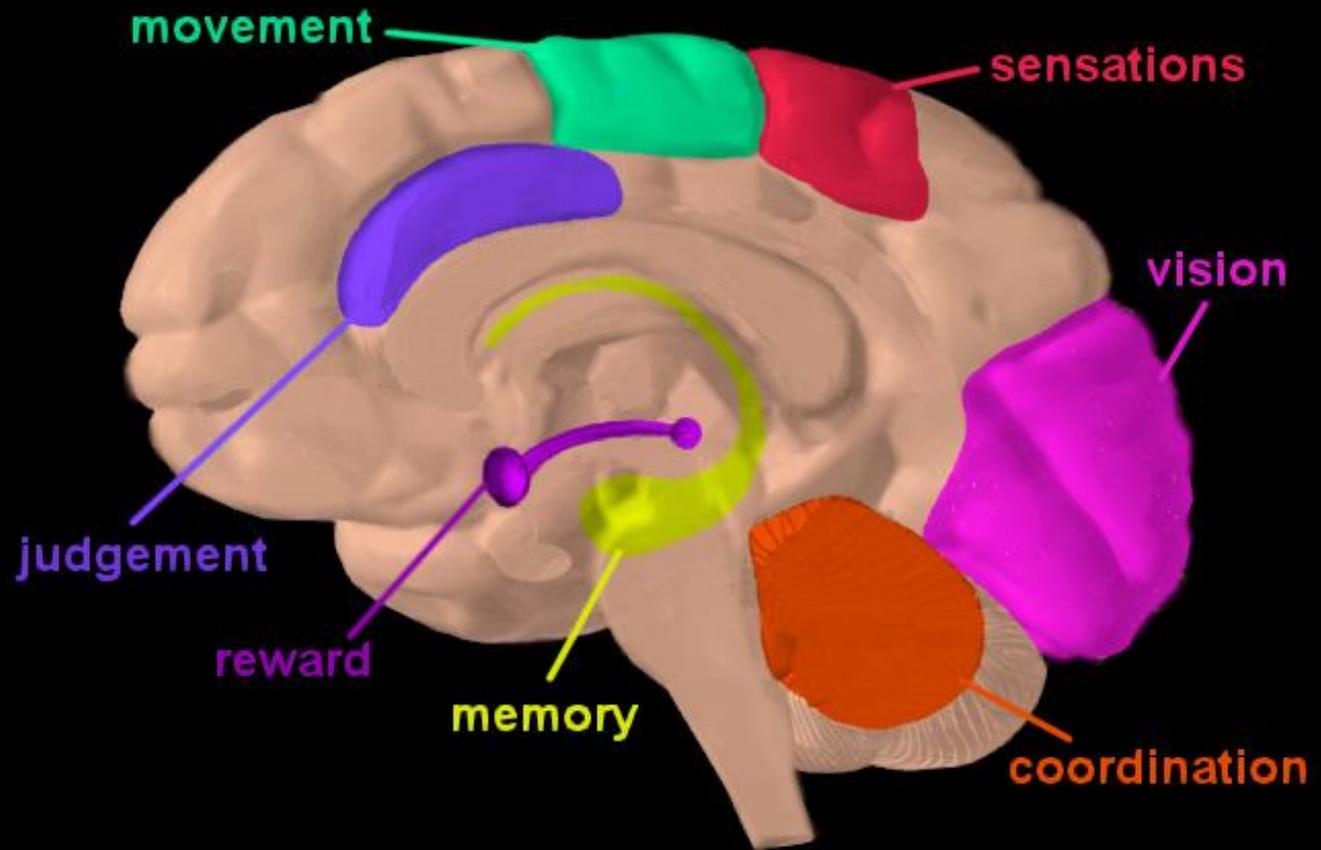
# ***Opiate Addiction is a Brain Disorder That is***

Characterized by Dysfunctional Internal Opioid System made up of the of the Opioid **Substances** and **Receptors** and their Interaction.

The **Substances** are called Endorphins, Enkephalins or Dynorphins.

And they fit into things called **Receptors** or Opiate Receptors.

# ***This is a Brain!***

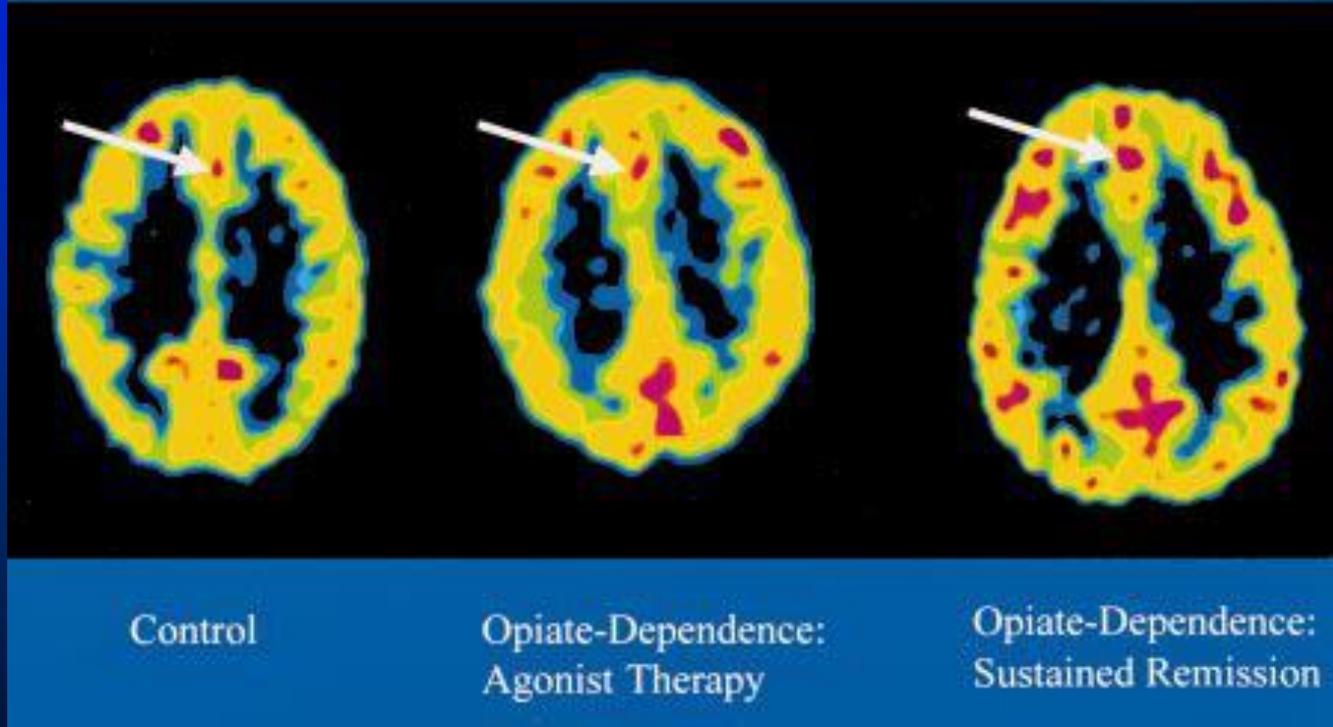


# ***This Use To Be Your Brain on Drugs***



# ***This is Your Brain Today***

## **ELEVATED GLUCOSE METABOLISM IN ANTERIOR CINGULATE GYRUS**



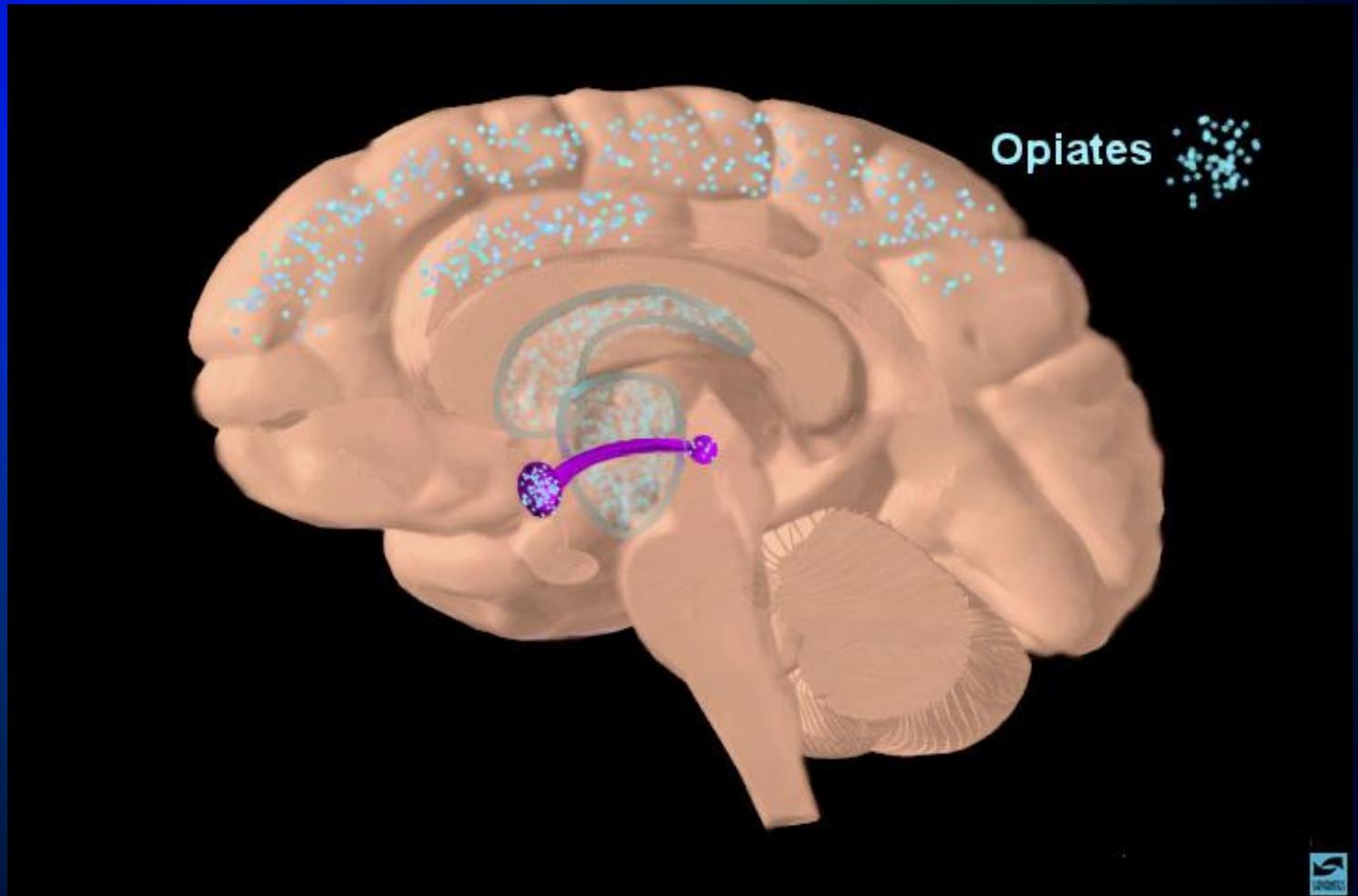
*Source: Galanter et al. Mt Sinai JOM 2000.*

# ***Humanity Receptors***

They are called **Opiate Receptors** because they were discovered when morphine was put on brain tissue.

But a better name for them might be **Humanity Receptors**.

# ***Distribution of Opiate Receptors in Human Brain***



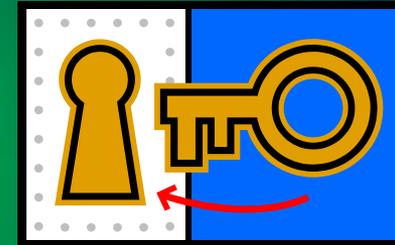
## ***So How Does All This Work?***

Receptors are a chemical on the membrane of a brain cell or neuron. When another chemical that the receptor is sensitive to is present the chemicals bond or stick together.

This is basically accomplished by chemical bonds and substances that are attracted to a specific receptor are said to have an **affinity** to it.

# ***An Easy Way to Think of Receptors and Endorphins***

- Is to think of the substance as a key and the receptor as a lock.
- When the substance binds to the receptor it opens the lock.
- This in turn sends another signal or causes the release of a substance.
- When a lot of signals are sent a function happens like the release of a hormone.



# FUNCTIONS OF ENDORPHINS

- Behavior and Mood
- Endocrine & Immune System
- Autonomic Effects
- Drive States (4 Fs)



Endorphins are found in all vertebrates that have been studied from the most primitive up to man.

# Endorphin Functions\*

Respiratory depression  
Smooth muscle motility  
Anti-convulsant activity  
Hemorrhagic shock  
Testosterone inhibition  
ACTH-cortisol release  
Antibody production  
Natural killer activity  
Prolactin release  
Body temperature  
Locomotor activity  
Blood pressure  
Endotoxic shock  
Spinal cord injury  
Monocyte and leukocyte chemotaxis

**Analgesia**  
**Euphoria**  
**Dysphoria**  
**Sedation**  
**Tolerance**  
**Opiate withdrawal**  
**Appetite**  
**Mental disorders**  
**Catatonia**  
**Psychosis**  
**Mydriasis**  
**Miosis**  
**Heart rate**  
**GH release**  
**ADH inhibition**

\* A partial list of endorphin functions.

# *The Endorphin System*

Endorphins	$\beta$ -endorphin
Enkephalins	Met)enkephalin (Leu)enkephalin (Met)enkephalin-8 (Met)enkephalin-Arg6-Phe7 Peptide E
Dynorphins	$\alpha$ -neo-endorphin $\beta$ -neo-endorphin Dynorphin A (1-8) Dynorphin A (1-17) Dynorphin B (1-13)

# Multiple Opiate Receptors

$\mu$	Morphine & Methadone	Physical dependence
$\kappa$	Ketocyclazocine	Cerebellum
$\sigma$	PCP?	May not be an opiate receptor
$\delta$	Enkephalin preferring	Vas deferens
$\epsilon$	$\beta$ -endorphin	Arcuate N.
Iota	Enkephalin preferring	Intestine

# ***Most People Have Normal Endorphins and Opiate Receptors***



- However with some people the lock (receptor) is damaged.
- No matter how much Endorphins may be near the receptor because it does not function right the lock can not be opened.

# ***A Number of Things Can Cause This***

## **Genetics/Birth Defect**

A person can be born with defective receptors. This can make an individual more susceptible to addiction

## **Further Damage**

And using opiates - not for pain - but when the brain is flooded over and over again – the receptors stop working normally.

# ***The Body Seeks to Maintain Equilibrium***

- In the normal course Opiate Receptors and Endorphins are kept in balance with one another.
- When the brain is flooded with exogenous opiates (heroin) that mimic endorphins the system gets confused.
- It thinks it is making too many endorphins and shuts that down,
- But it still has all this excess (heroin) and thinks that it also needs to make more receptors.

# ***What Happens Next....***

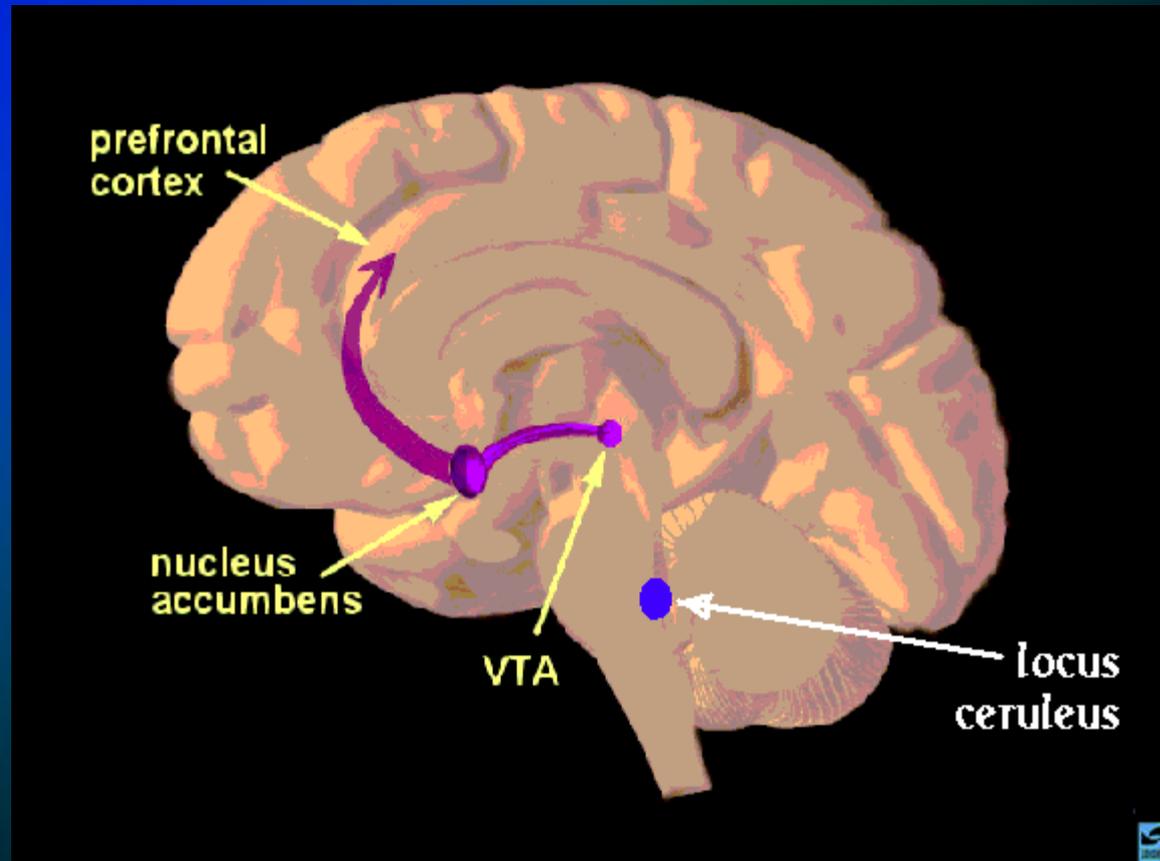
- As more Opiate Receptors are made you need more heroin to get the same effect so you use more.
- And more receptors are made to accommodate the extra what the brain thinks is endorphins.

**This is how Tolerance occurs - You need more substance to get the same effect.**

# ***Can Methadone Fix to Many Opiate Receptors?***

- Methadone does normalize the damage caused by drug use.
- And there is some evidence that for persons who have not used drugs very long that methadone will stop the damage they are doing and over time can normalize the system.
- But this is a small minority – 30%.

# Reward/Motivation Pathway



# ***Questions for Future Research***

- The majority of individuals do not find opiates at all pleasant.
- Why is it that a small segment experiences opiates as pleasant. Some will even say there was something missing before they used opiates.
- This tends to run in families so there is most likely a genetic component to it.