Opioid Neuroscience: Pain Control vs Euphoria Adults vs Adolescence

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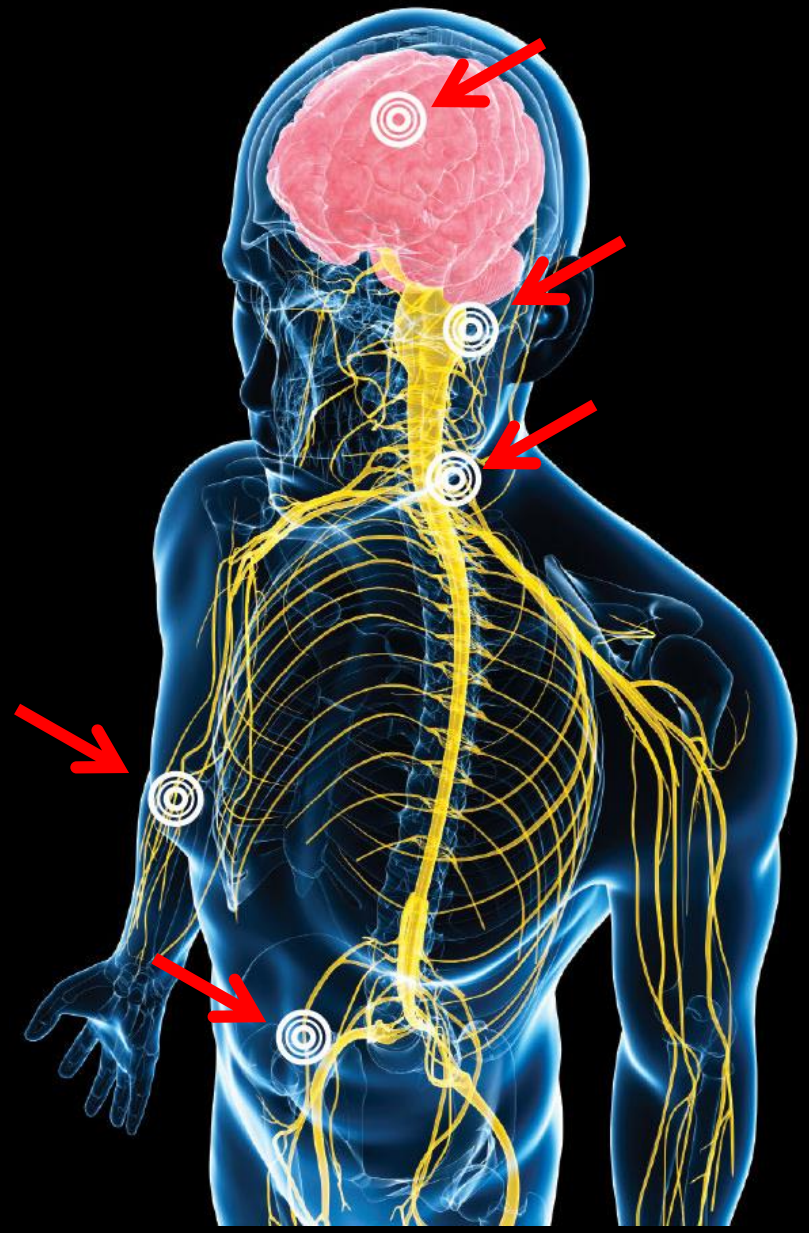
Professor, Department of Psychiatry
Director, Center for Compulsive Behavior and Addiction
Rush University Medical Center, Chicago IL

OPIOID FUNCTIONS IN THE BODY



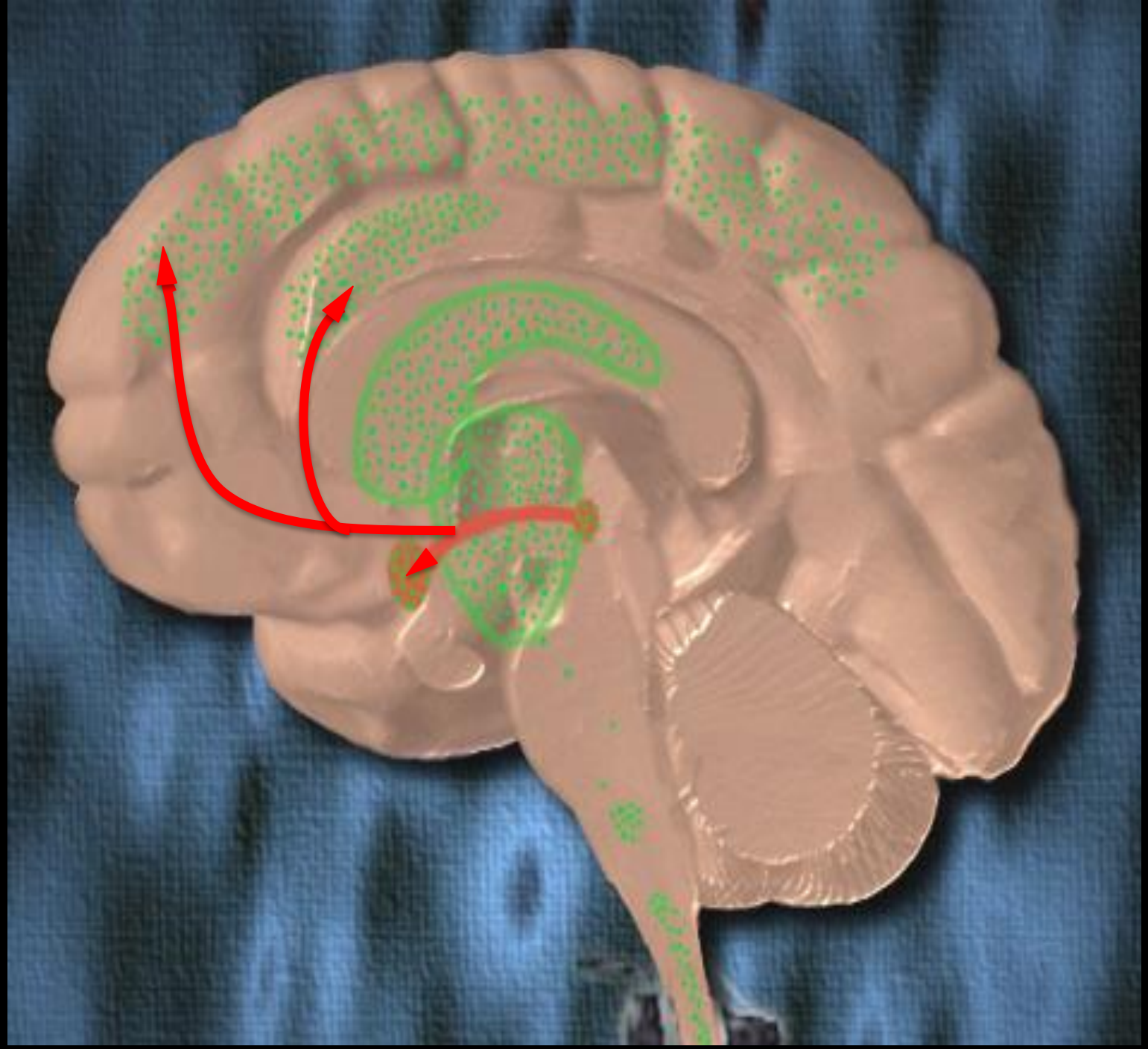
brain: pain perception, emotion, reward

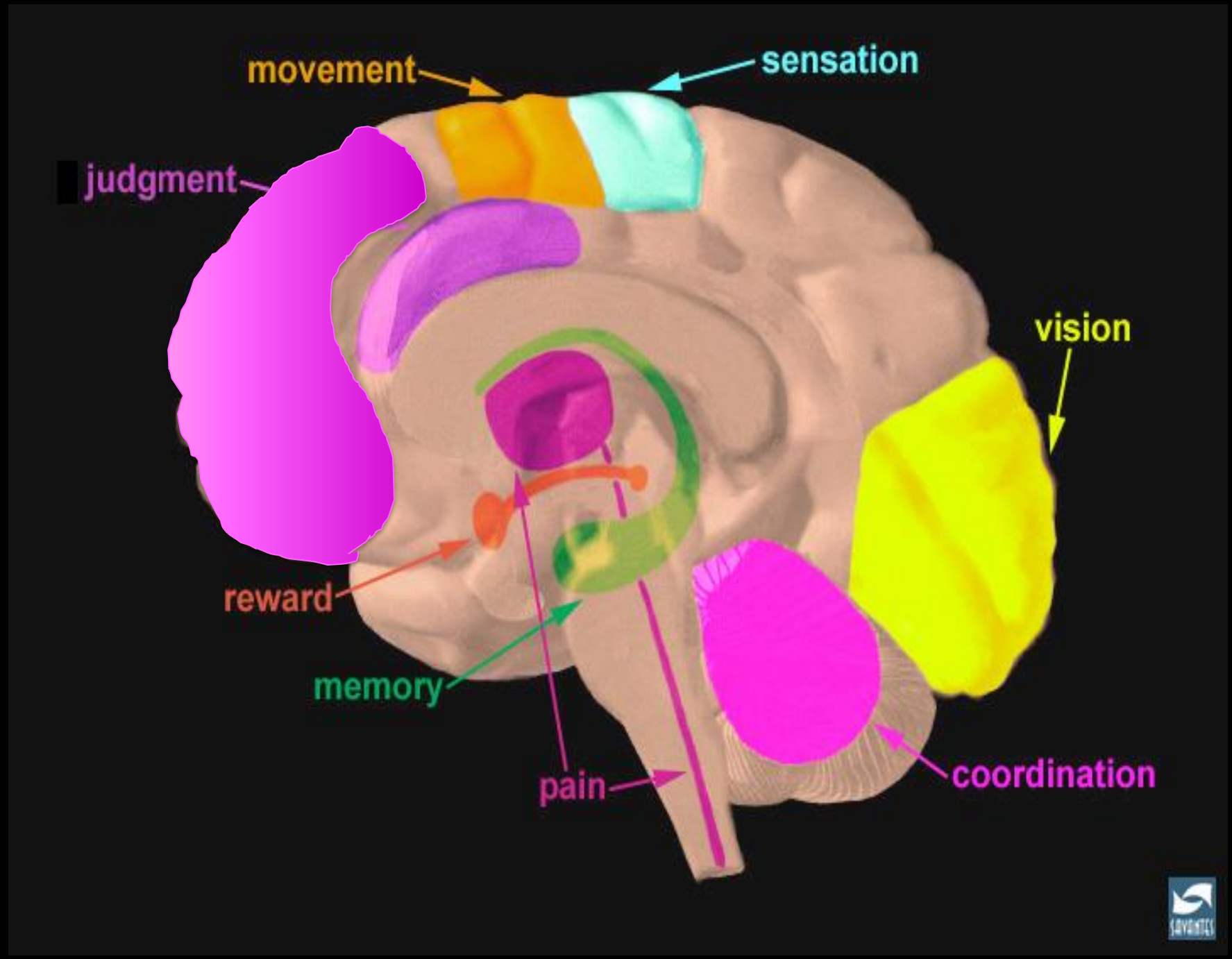
brainstem: respiratory suppression

spinal cord: dampening of pain signals

peripheral neurons: curbs pain sensation

intestine: inhibition of peristalsis




movement
sensation
judgment
vision
reward
memory
pain
coordination

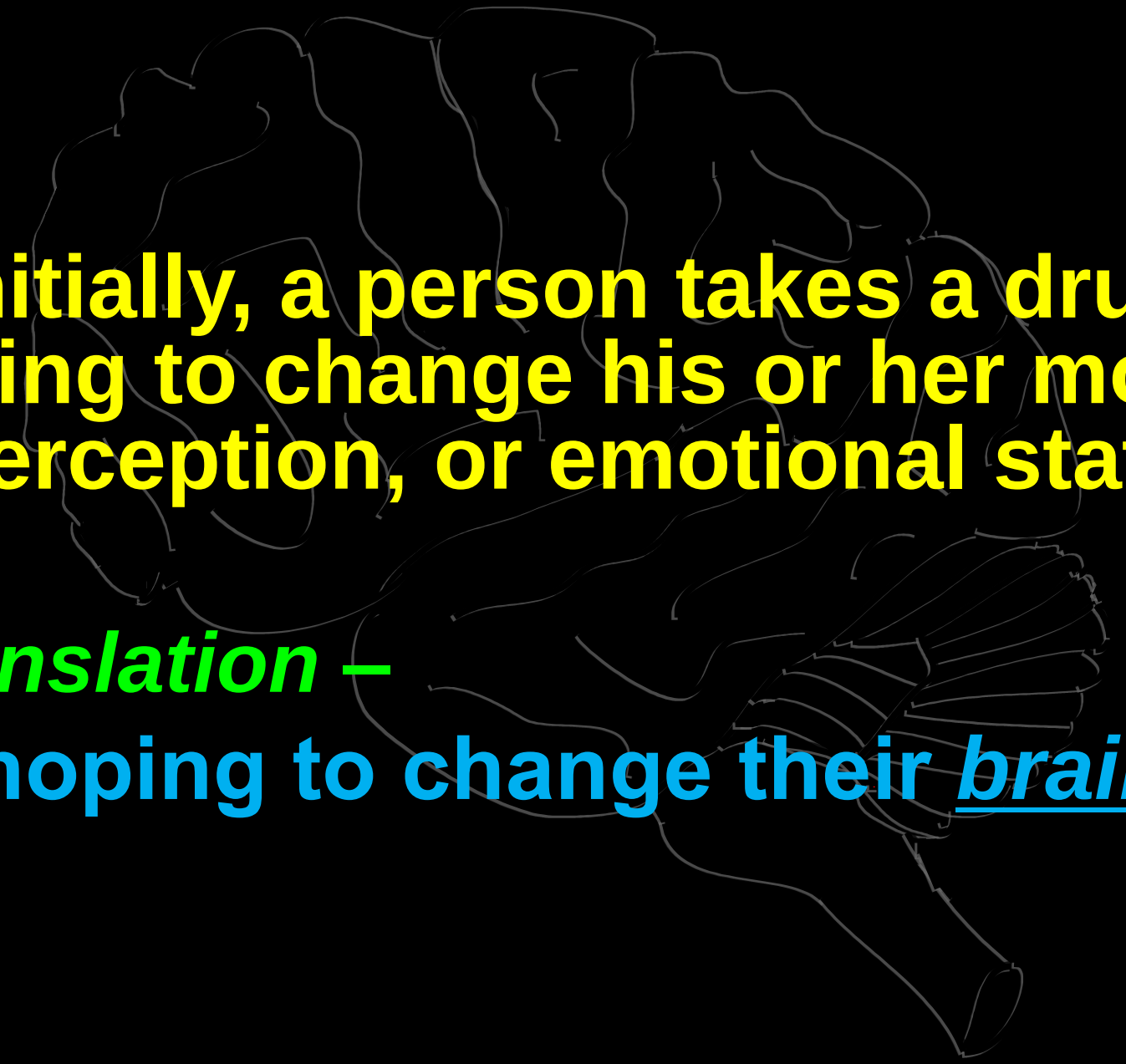
Why Do People Take Drugs in The First Place?

To feel good

To have new:
feelings
sensations
experiences
and
to share them

To feel better

To lessen:
anxiety
worries
fears
depression
hopelessness
pain



Initially, a person takes a drug hoping to change his or her mood, perception, or emotional state

Translation –

…hoping to change their *brains.*

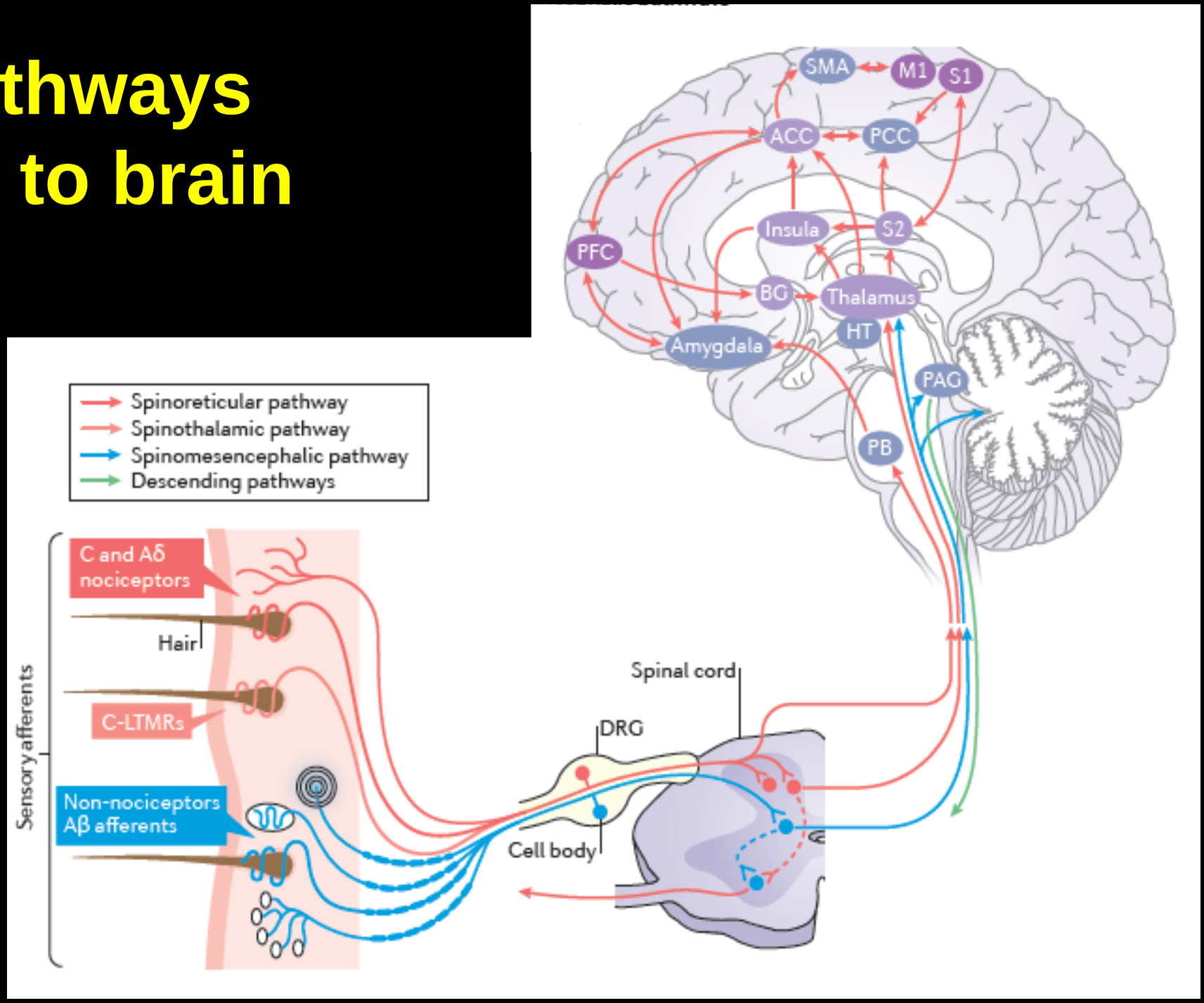
Differential Brain States

- Pain
- Chronic Drug Exposure
- Adolescence

Differential Brain States

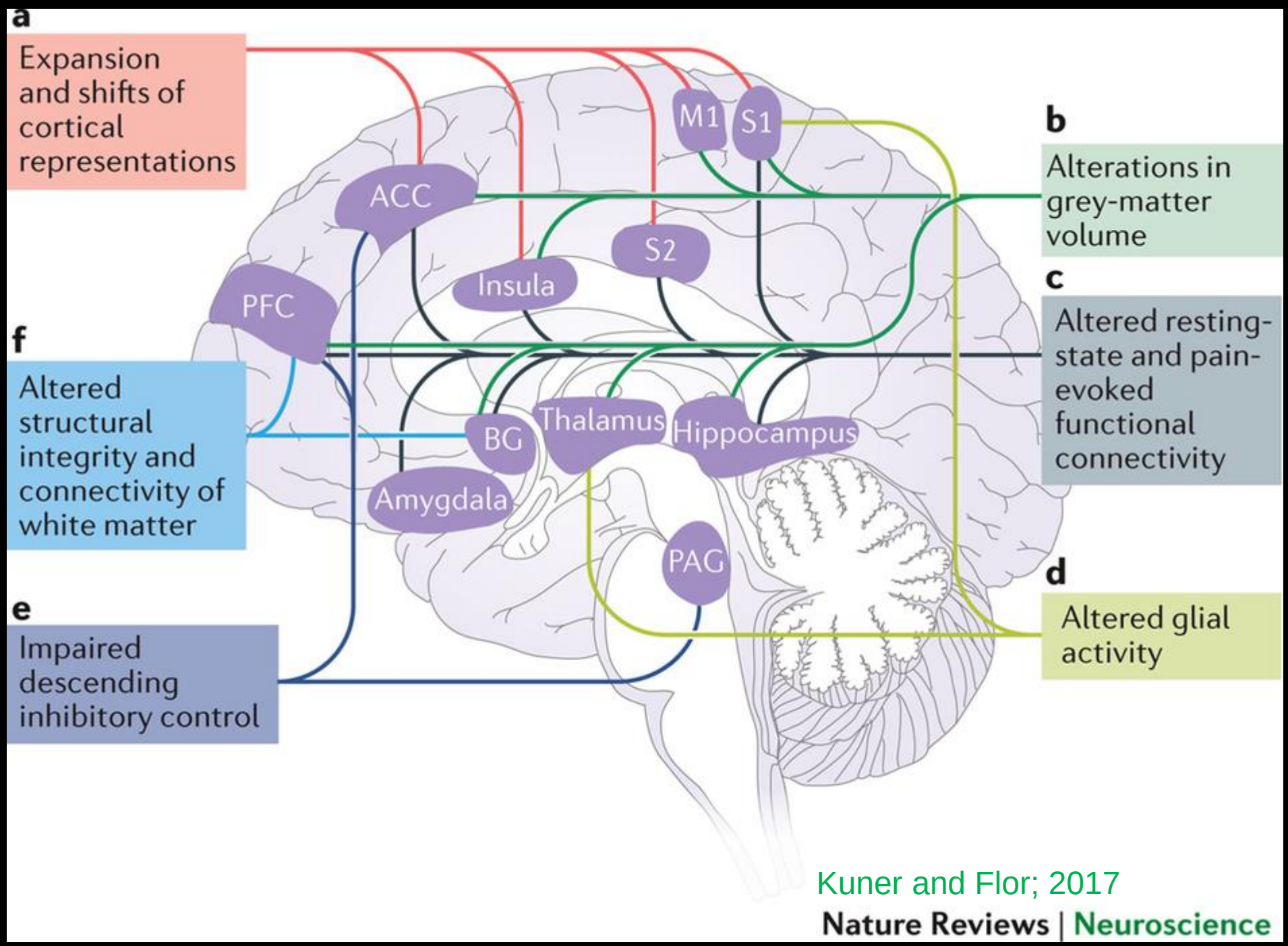
- Pain
  - Subjective emotions associated with pain
  - Transitions from acute to chronic pain
- Chronic Drug Exposure
- Adolescence

Nociceptive pathways from periphery to brain



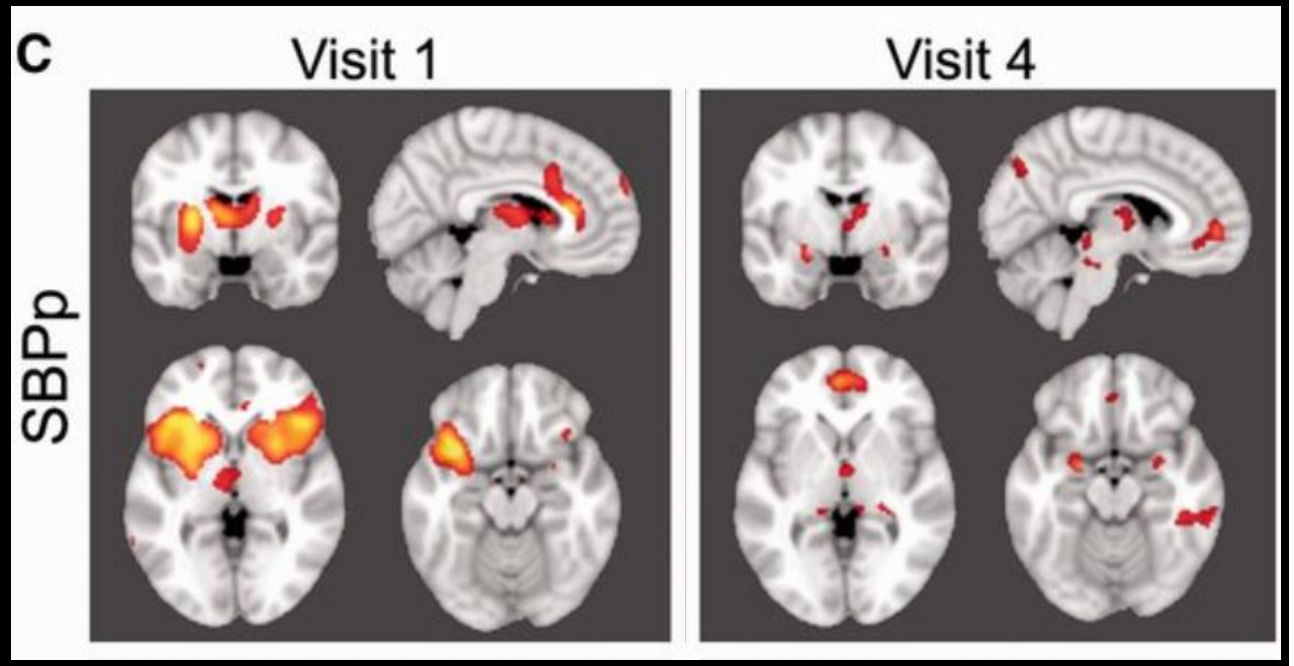
Kuner and Flor;
Nature Reviews Neuroscience, 2017

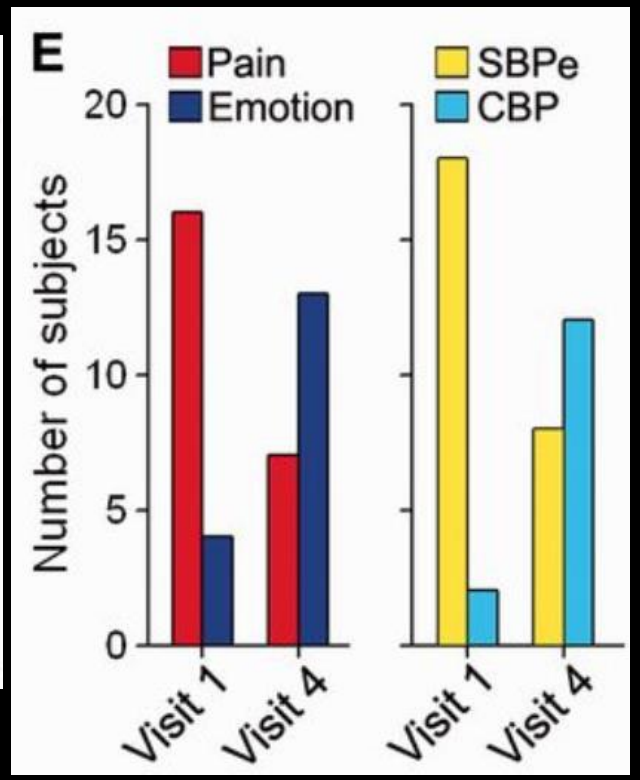
Changes in the brain during chronic pain



Transition from acute to chronic back pain

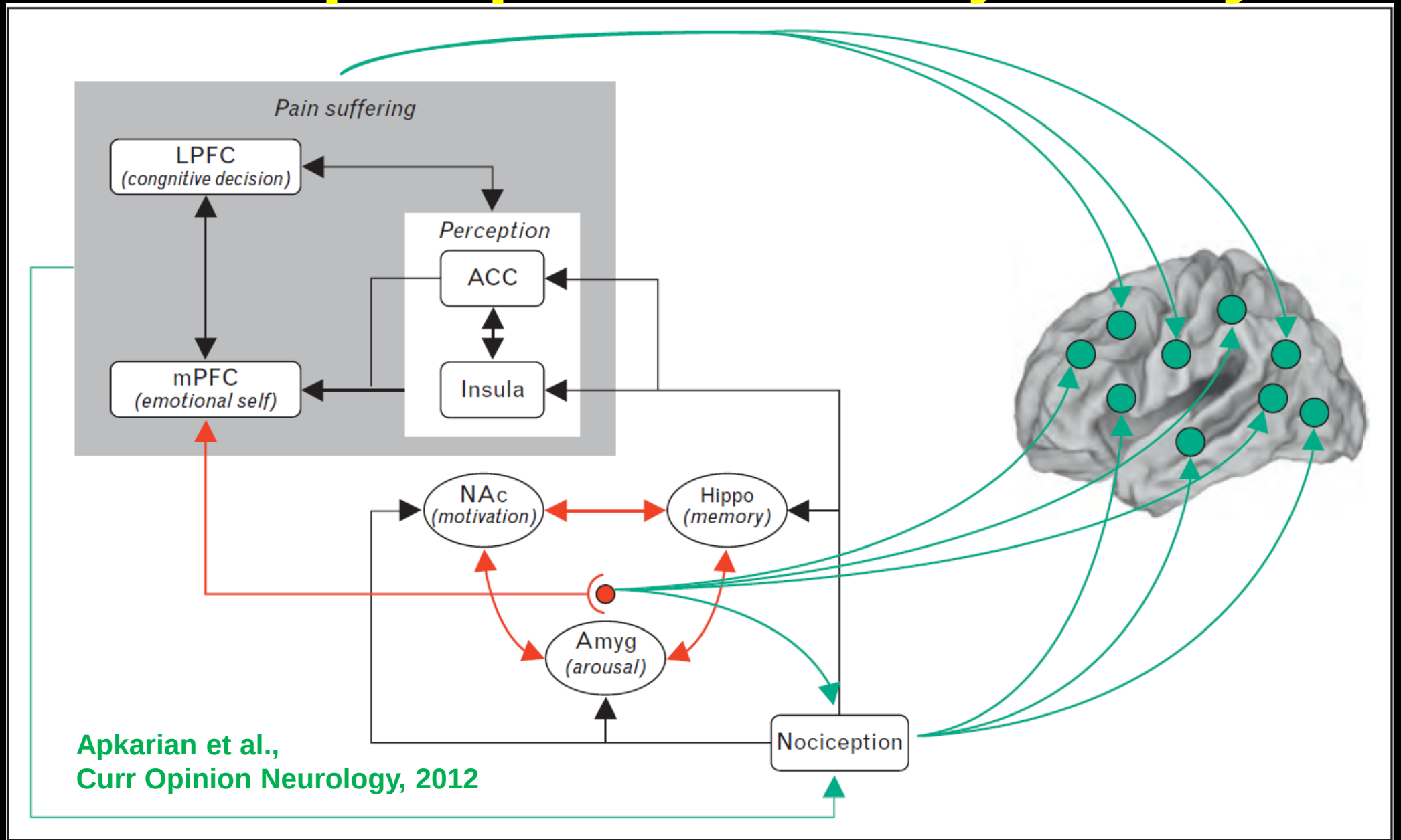
Brain representations shift from nociceptiove to emotional circuits



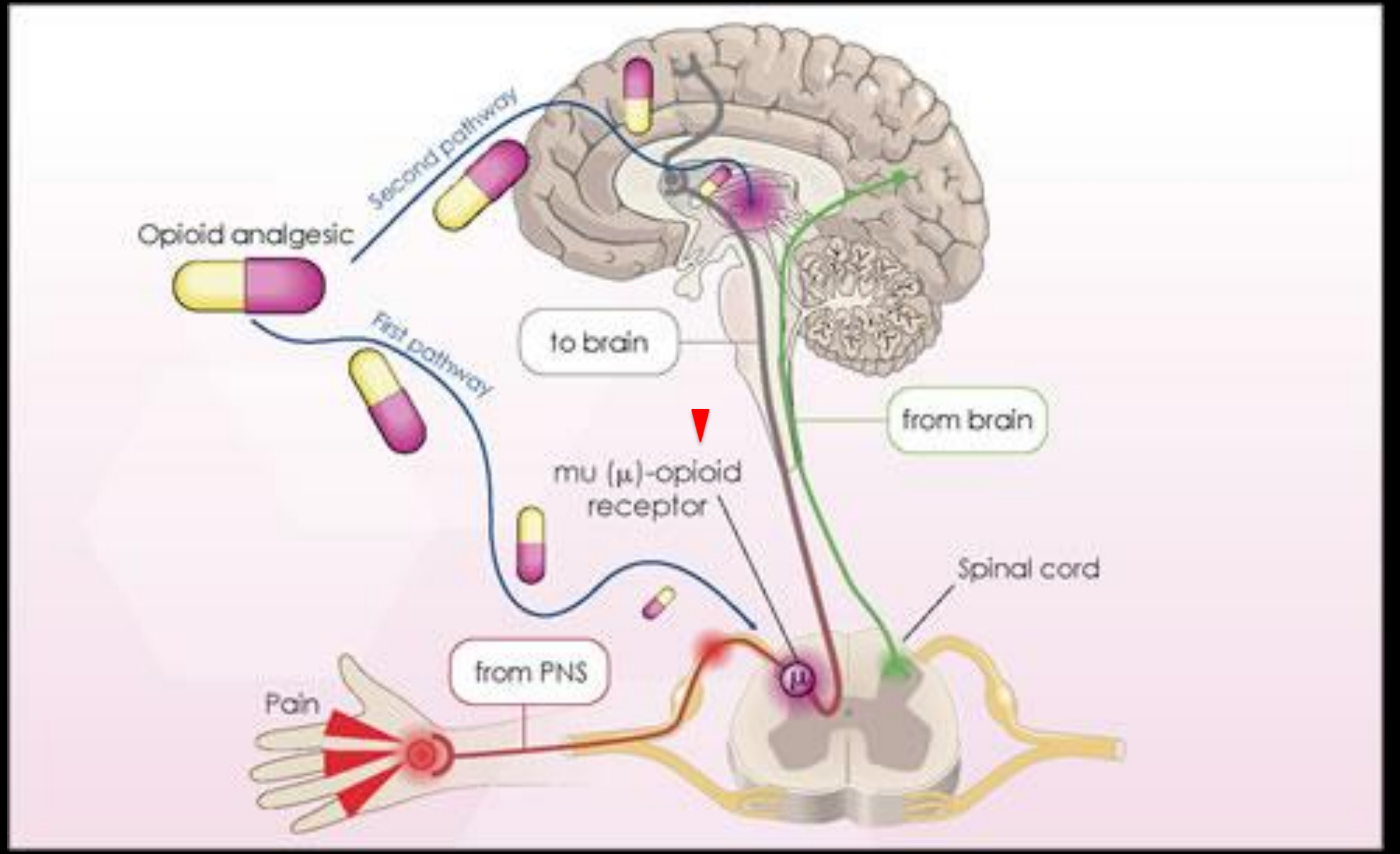


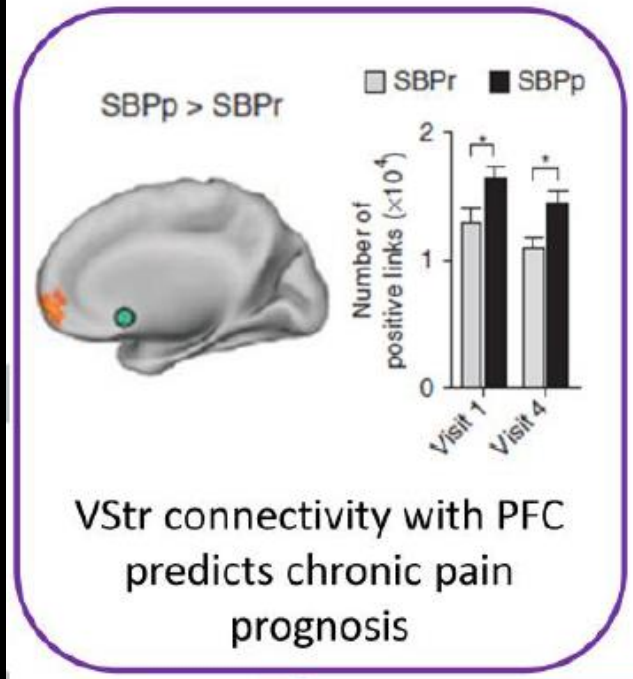
Hashmi *et al. Brain.* 136:2751, 2013

Overlap of pain and subjectivity

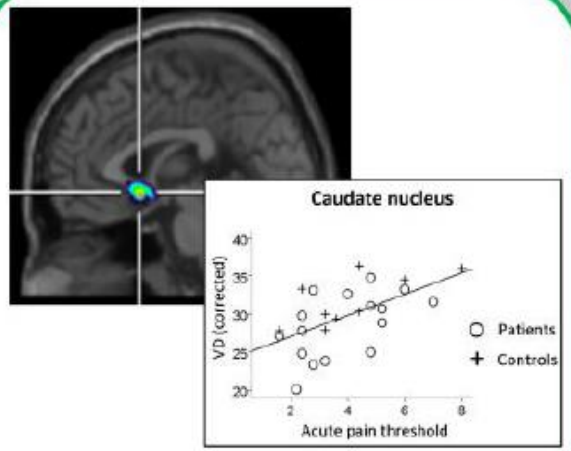


Apkarian et al.,
Curr Opinion Neurology, 2012


Second pathway
Opioid analgesic
First pathway
to brain
from brain
mu (μ)-opioid
receptor
Spinal cord
from PNS
Pain



VStr connectivity with PFC predicts chronic pain prognosis



VStr opioid availability correlates with pain threshold

A. Internal and external context

B. Aversive learning

PFC / ACC

Ains, Amy

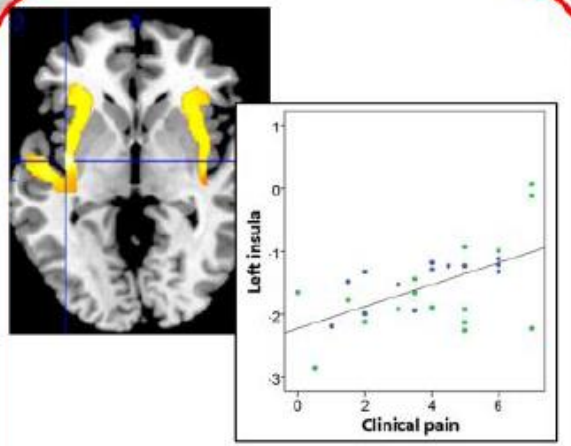
vStr

C. Reward learning

PAG

D. Shared output pathway

RVM

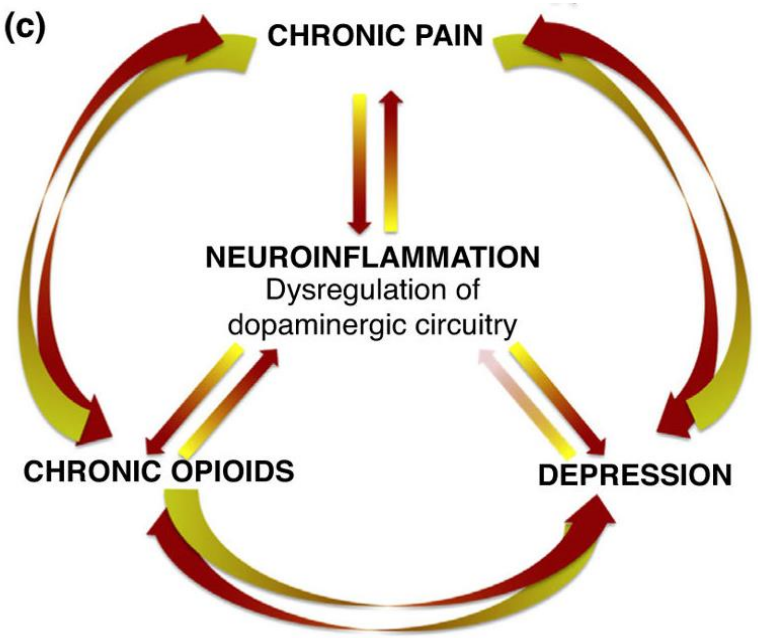


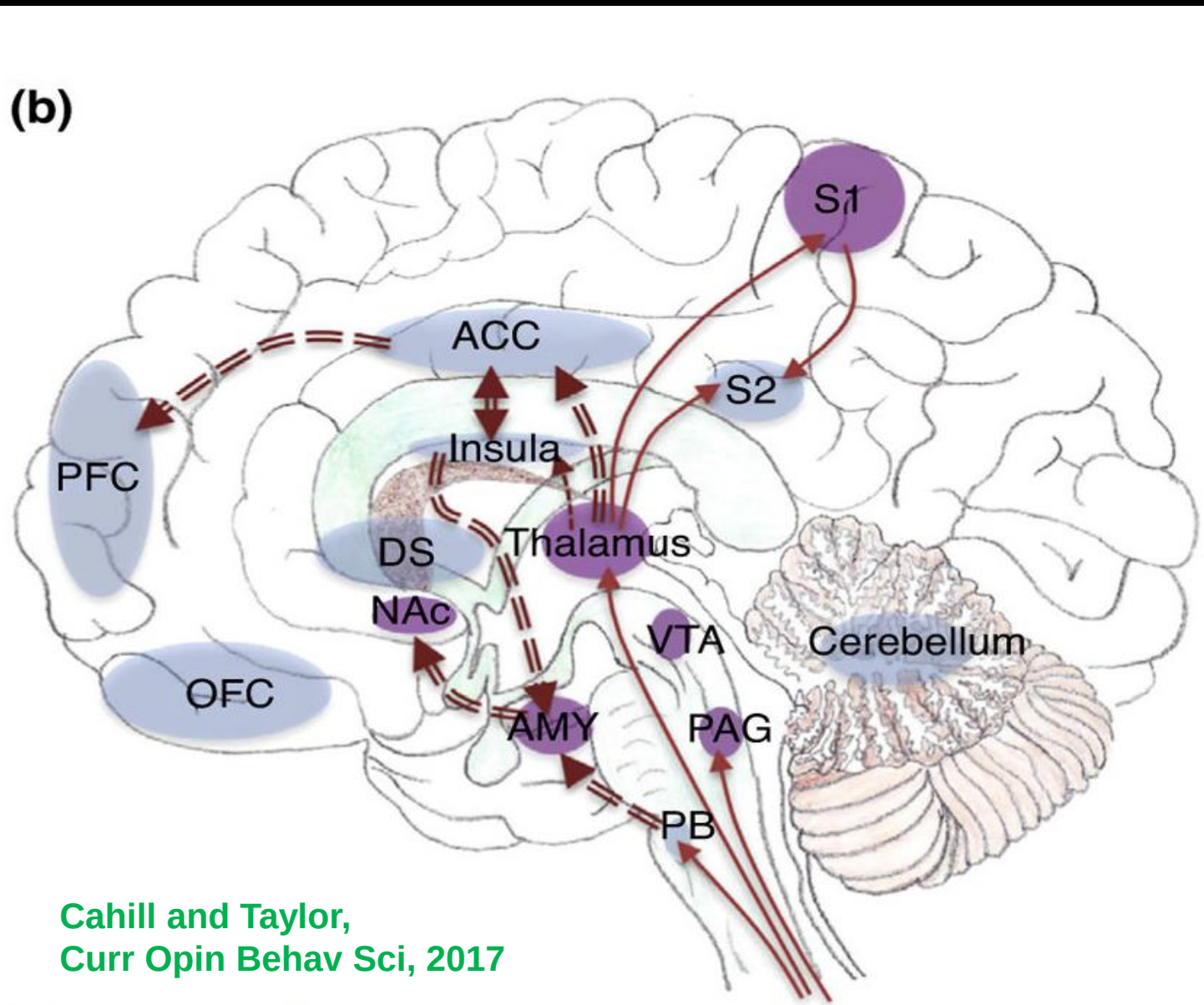
Anticipatory activity in AIns and PIns correlates with chronic pain ratings

Neuroinflammation co-occurs with chronic pain and opioid dependence

(a) Opioid Misuse
Risk factors in Chronic Pain Populations

- Depression
- Catastrophizing
- Long term and high dose opioid use
- Impulsivity
- Distress Intolerance
- Post traumatic stress disorder





Cahill and Taylor,
Curr Opin Behav Sci, 2017

Opioid Use for Chronic Pain

Chronic pain is a major **public health problem.** It affects…

…more than **one-third** of people in the United States…

…and about **20 to 30%** of the world's population.[1]

The prevalence of persistent pain is expected to rise as the incidence of diseases increases in the aging U.S. population. These diseases include:

diabetes

cardiovascular disorders

obesity

arthritis

cancer

Opioids are powerful analgesics which are commonly used and effective for many types of pain. However, opioids can produce **significant side effects**, including:

- mental clouding
- respiratory depression (which can sometimes lead to death)
- physical dependence
- nausea
- constipation

The prescribing of opioids by clinicians has **increased 300%** in the last 20 years, contributing to the problem of prescription opioid abuse.

Today, the number of people who die from prescription opioids **exceeds** the number of those who die from heroin and cocaine combined.[2]

The 2014 National Institutes of Health Pathways to Prevention Workshop on the Role of Opioids in the Treatment of Chronic Pain will seek to clarify the following:

- Long-term effectiveness of opioids for treating chronic pain
- Potential risks of opioid treatment in various patient populations
- Effects of different opioid management strategies on outcomes related to addiction, abuse, misuse, pain, and quality of life
- Effectiveness of risk mitigation strategies for opioid treatment
- Future research needs and priorities to improve the treatment of pain with opioids.

[1] Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 2000–2010 on CDC WONDER Online Database. http://wonder.cdc.gov/wonder/help/ucd.html. Accessed Feb.11, 2013.

[2] Centers for Disease Control and Prevention. Vital Signs: Overdoses of Prescription Opioid Pain Relievers and Other Drugs Among Women—United States, 1999–2010. *MMWR*. 62(26);537–542. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6226a3.htm. Accessed July 9, 2014.

NIH National Institutes of Health
Office of Disease Prevention

Why Do People Take Drugs in The First Place?

To feel good

To have new:
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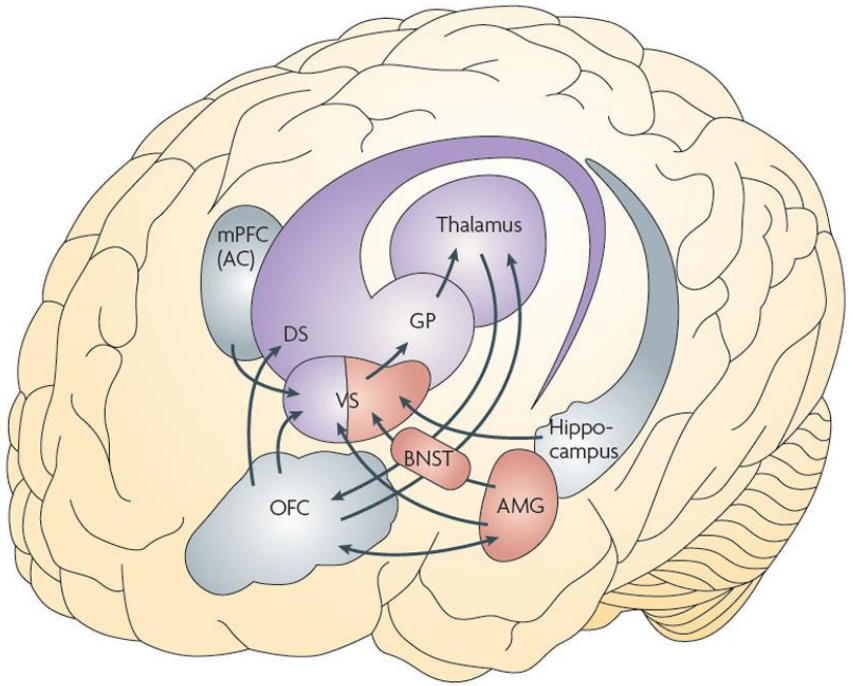
Koob et al.,
Nat Rev Drug Discov.
8:500–515,2009.



Prefrontal cortex (orbital, medial and cingulate nuclei): subjective effects

Sensory information

Hippocampus: context

BLA: conditioned cues

• Negative emotional state
• Stress
CeA and BNST

• Reinforcement
Acb shell and core

• Habits
Dorsal striatum

Thalamus

NA CRF

DA

DA

Brain stem

VTA

SNc

Hypothalamus and brainstem effectors (autonomic, somatic and neuroendocrine)

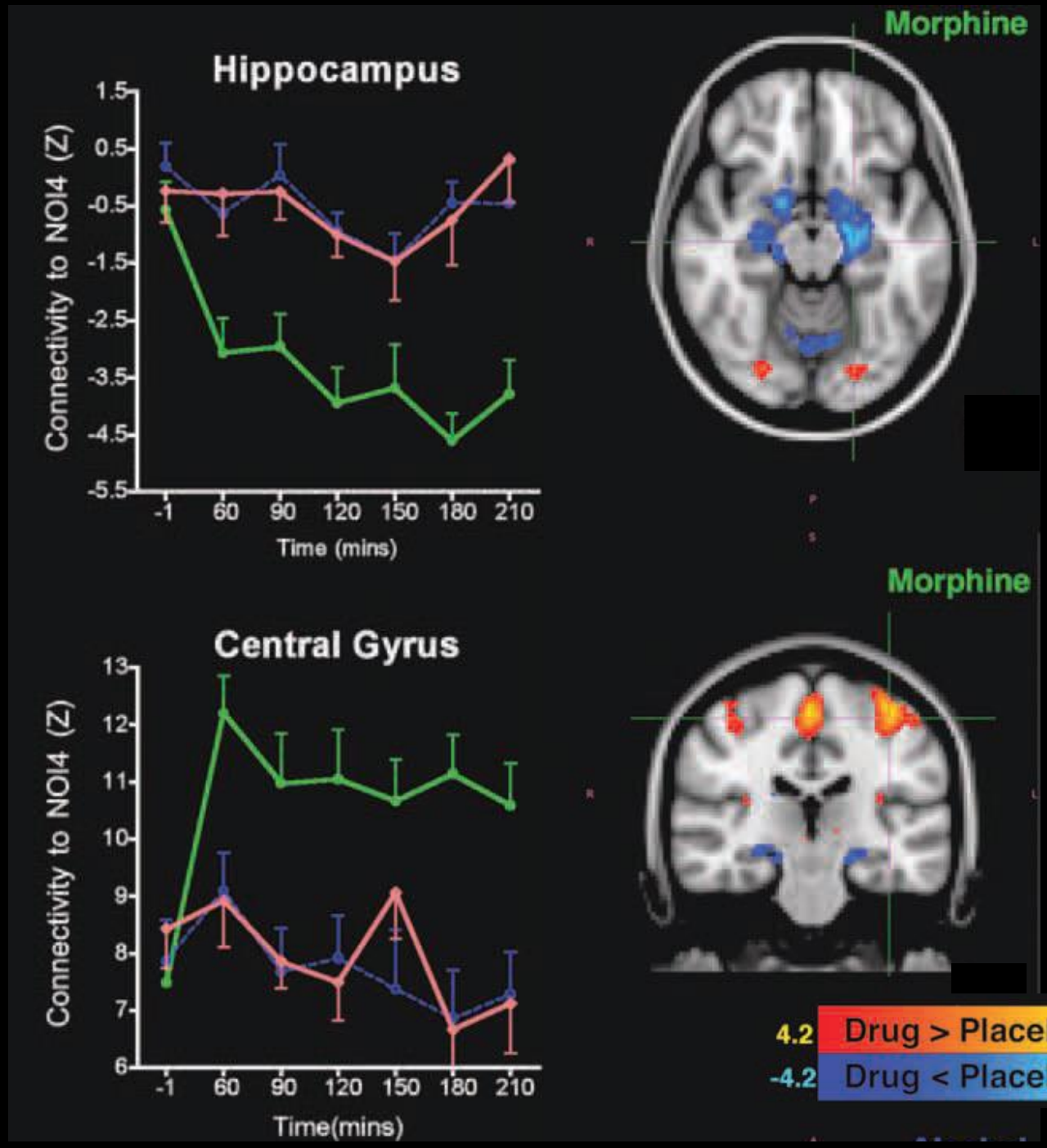
VGP

DGP

Differential Brain States

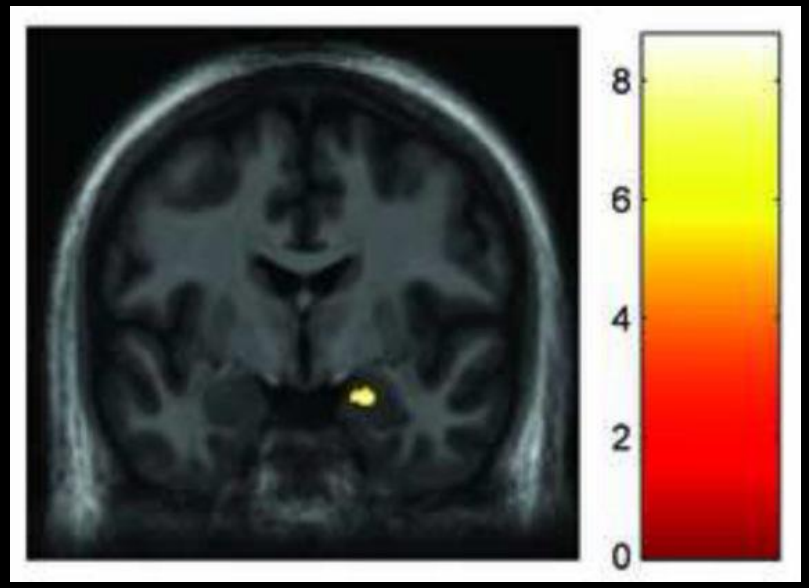
- Pain
- Chronic Drug Exposure
  - consequence of remapping during abuse
- Adolescence

Acute morphine changes connectivity

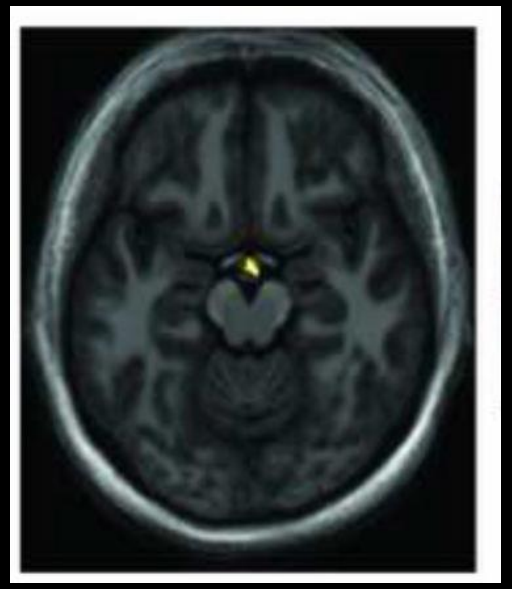


Khalili-Mahani et al.,
Human Brain Mapping, 2012.

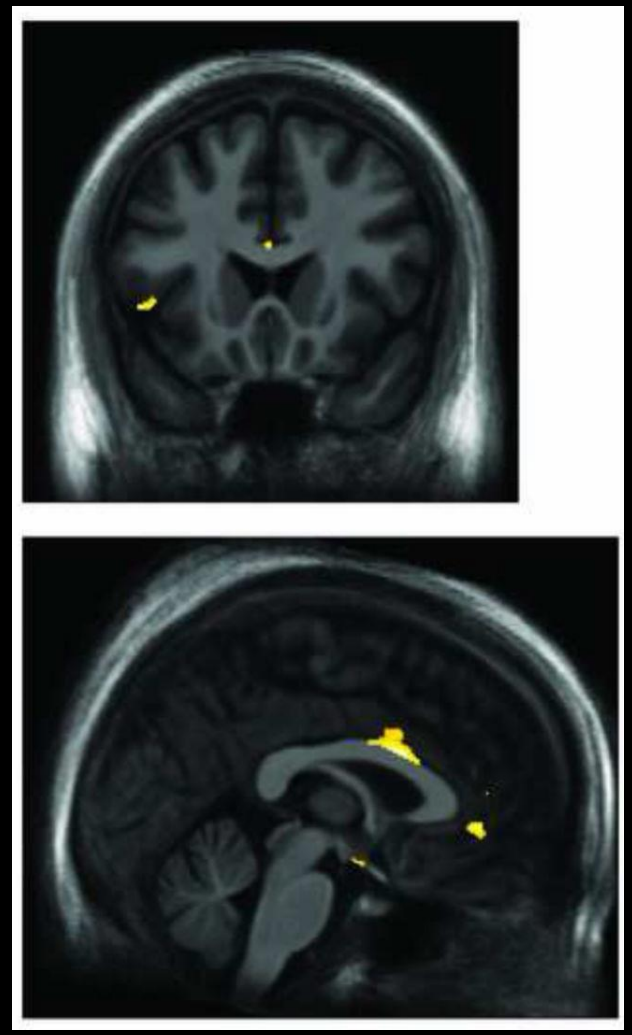
Gray matter volume changes following one month of daily morphine exposure



Amygdala



Hypothalamus



Cortex

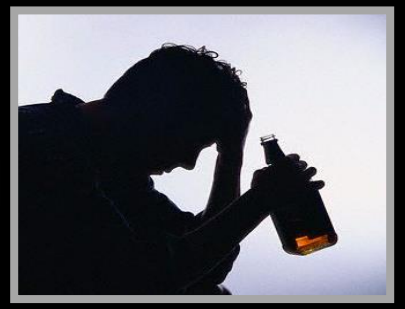
Younger et al.,
Pain, 2011

Dopamine Receptors are Lower in Addiction

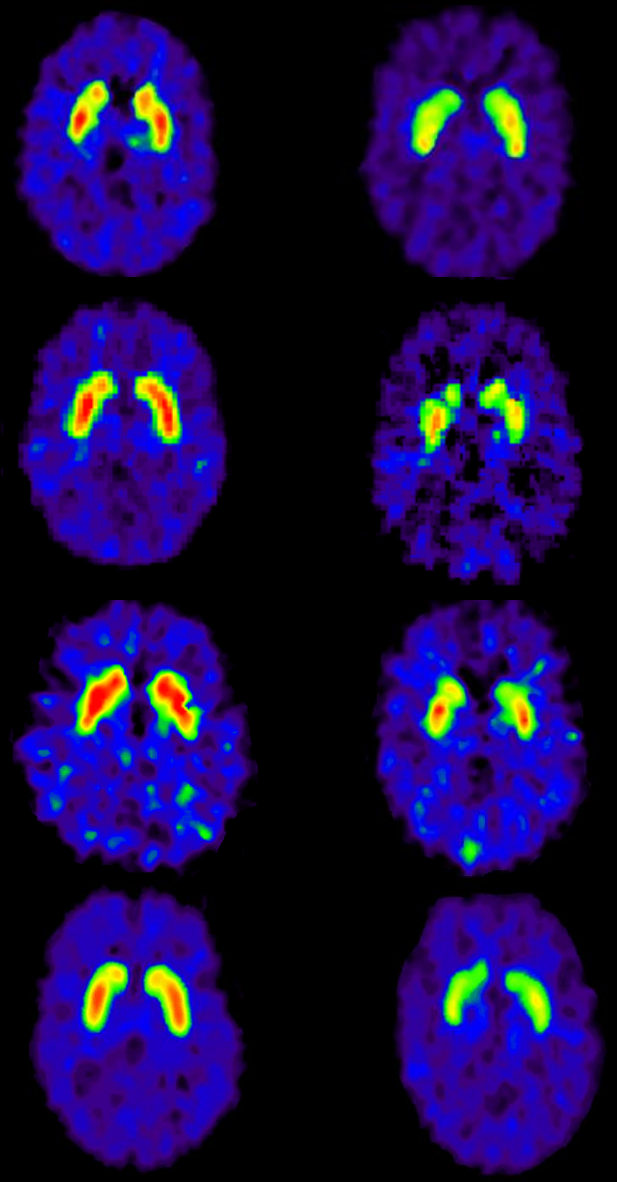
Cocaine

Meth

Alcohol



Heroin



Control

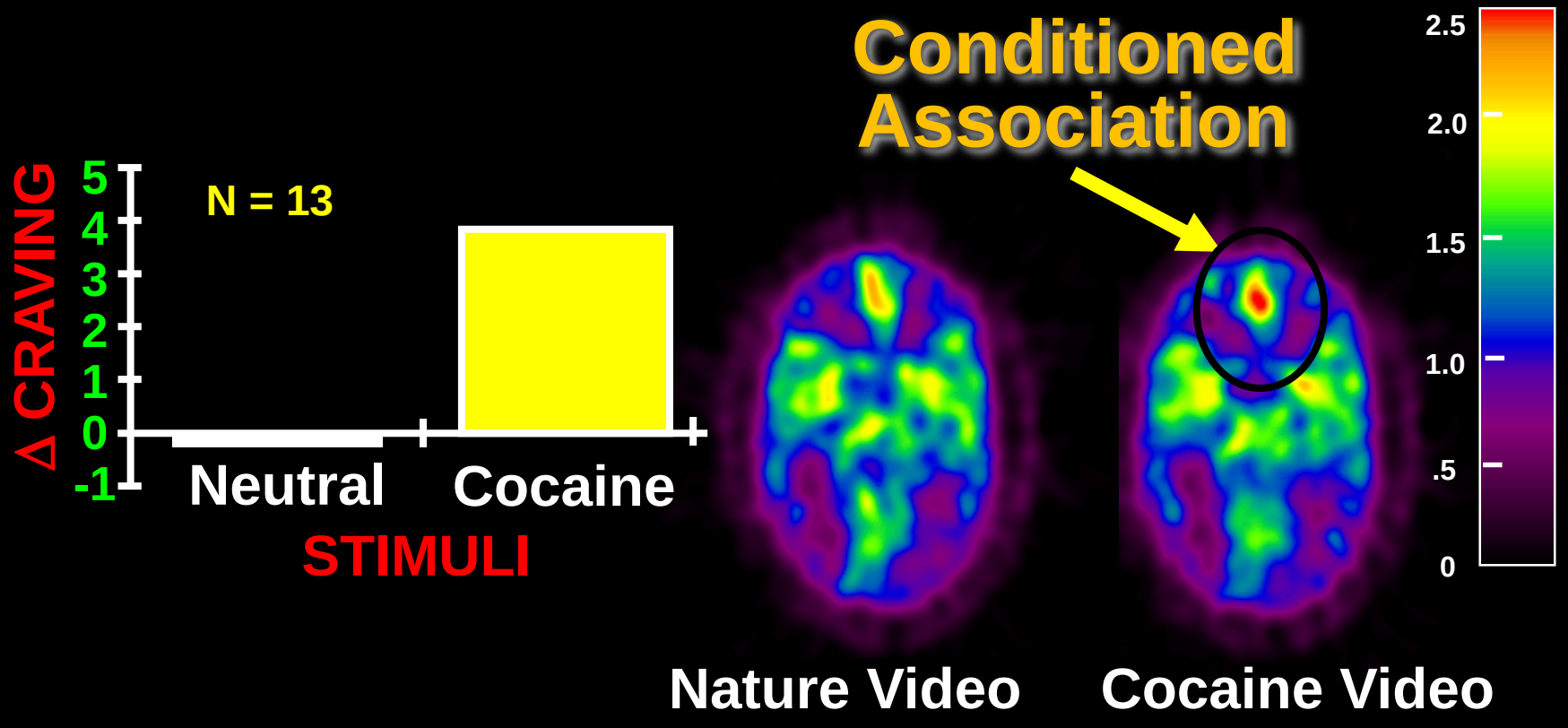
Addicted

DA D2 Receptor Availability

Memories Comprise a Critical Part of Addiction

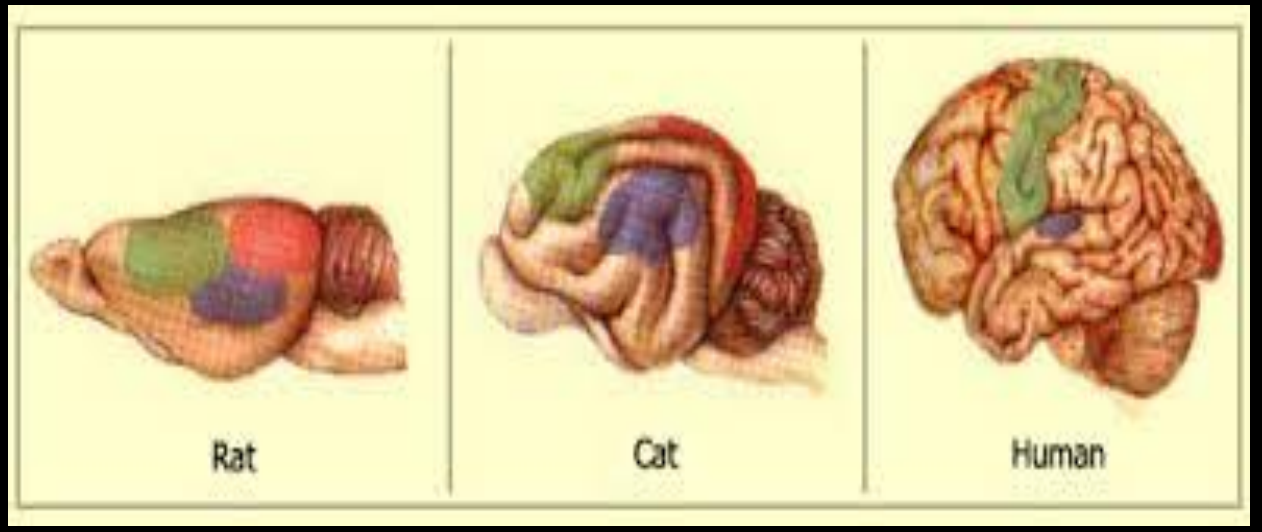
It's about people, places, and things.

Addiction;
it's about people, places and <u>things</u> …



Childress et al., Am. J. Psychiatry, 1999

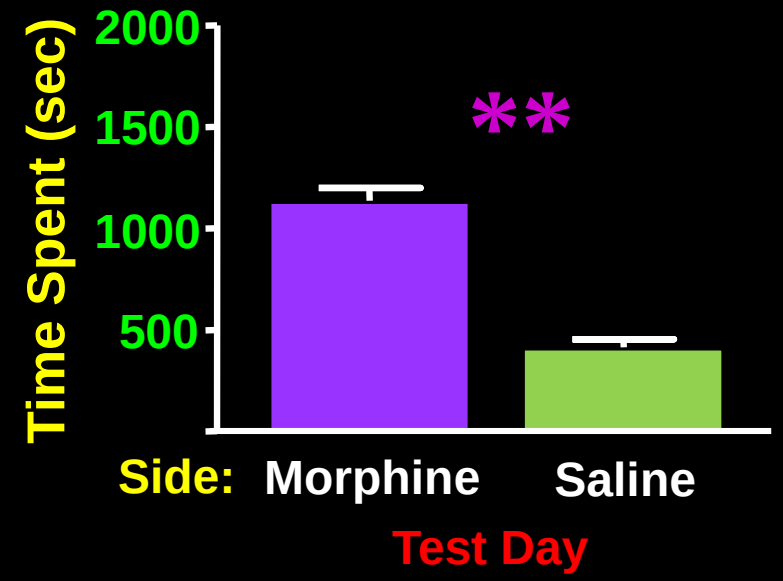
Comparative Functional Neuroanatomy



Addiction; it's about people, places and things

Associative learning:

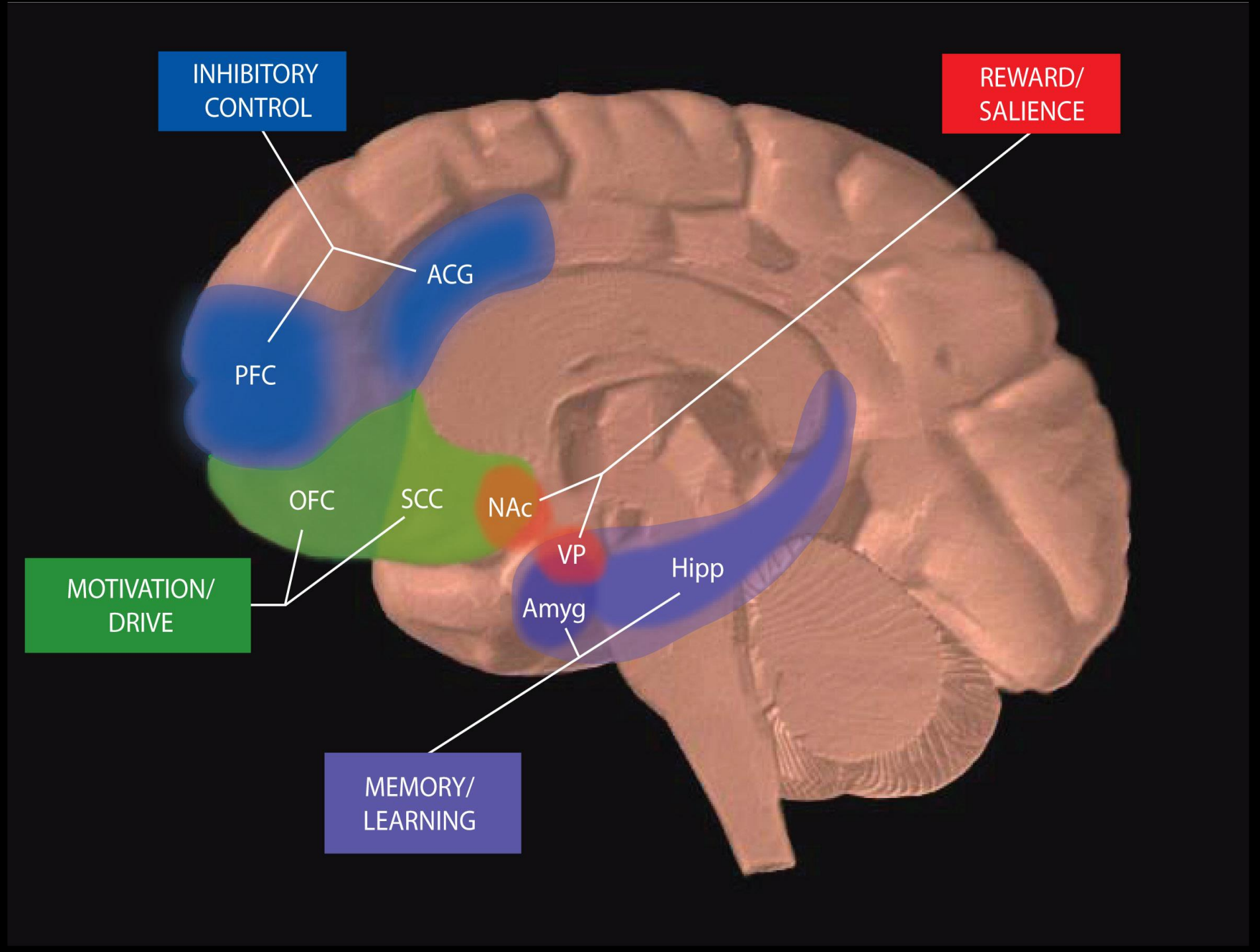
Conditioned Place Preference

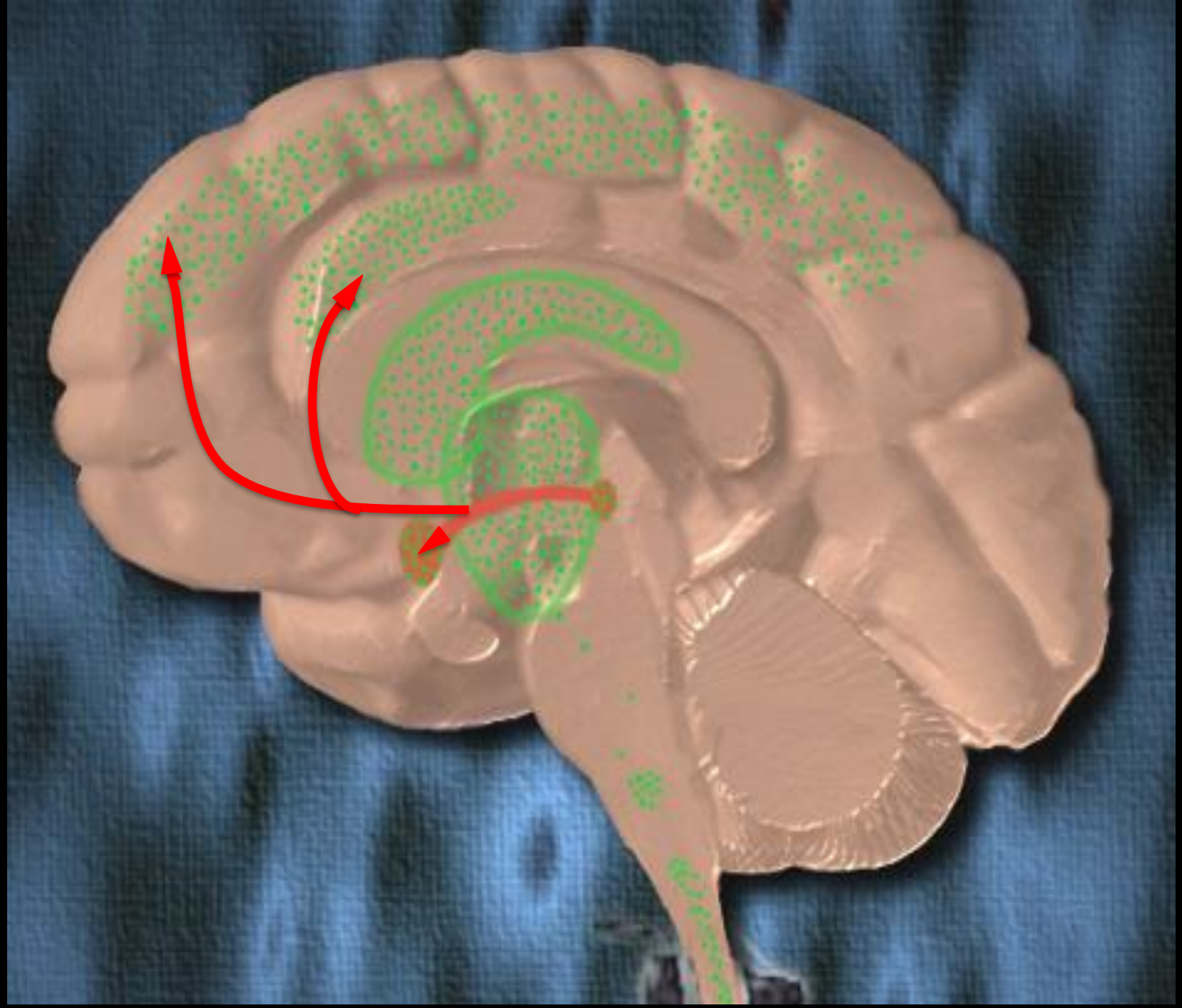


Pretest:
No Treatment

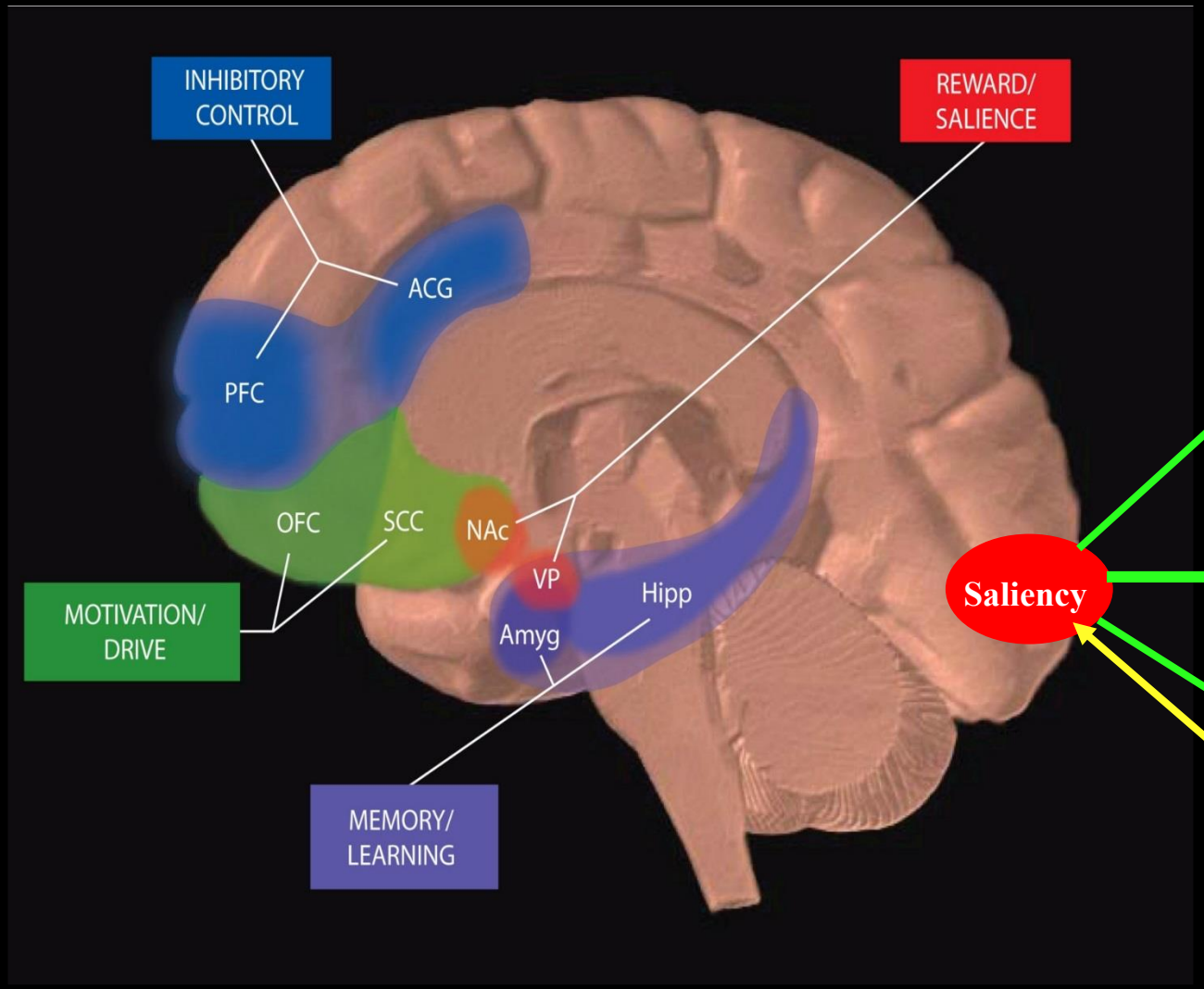
Conditioning:
Morphine vs Saline

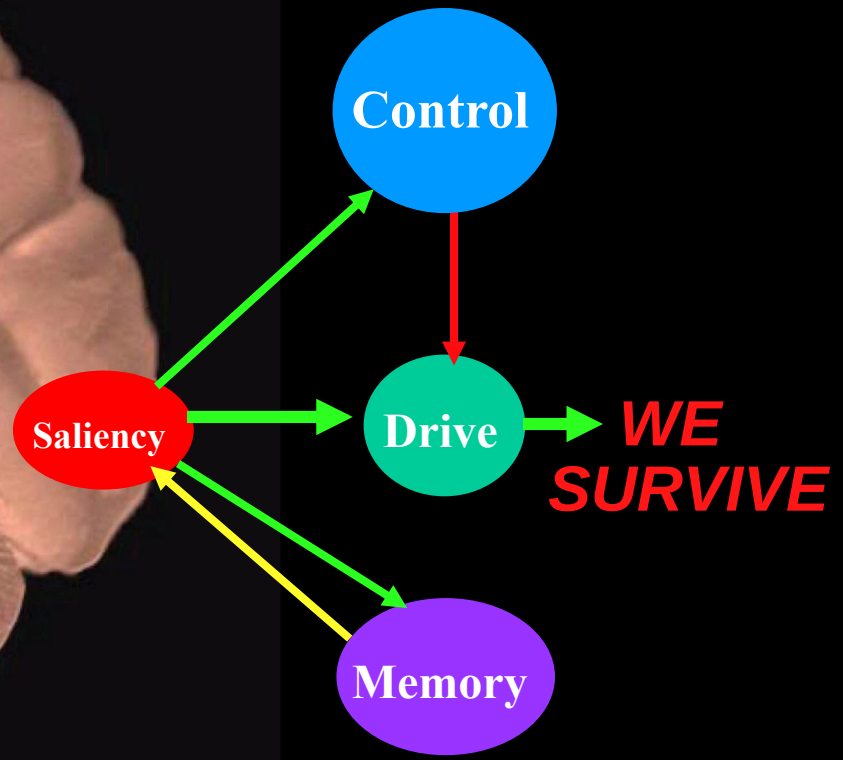
Test Day:
No Treatment


INHIBITORY CONTROL
REWARD/ SALIENCE
ACG
PFC
OFC
SCC
NAc
VP
Hipp
Amyg
MOTIVATION/ DRIVE
MEMORY/ LEARNING



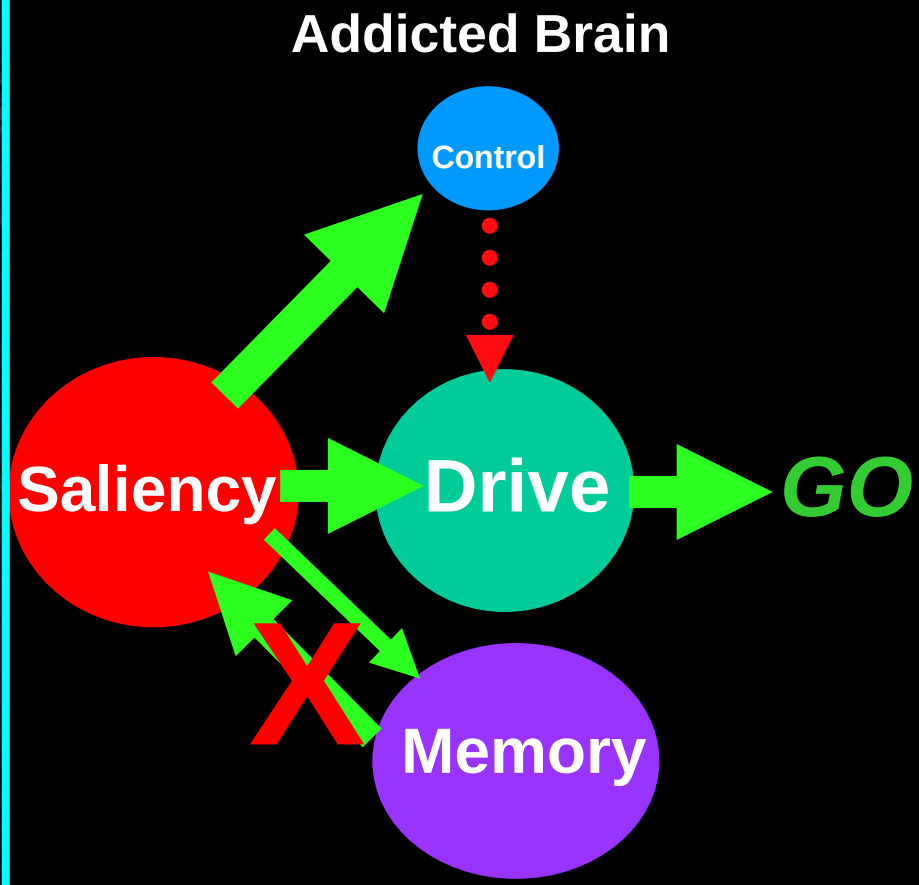
Why We Do What We Do…





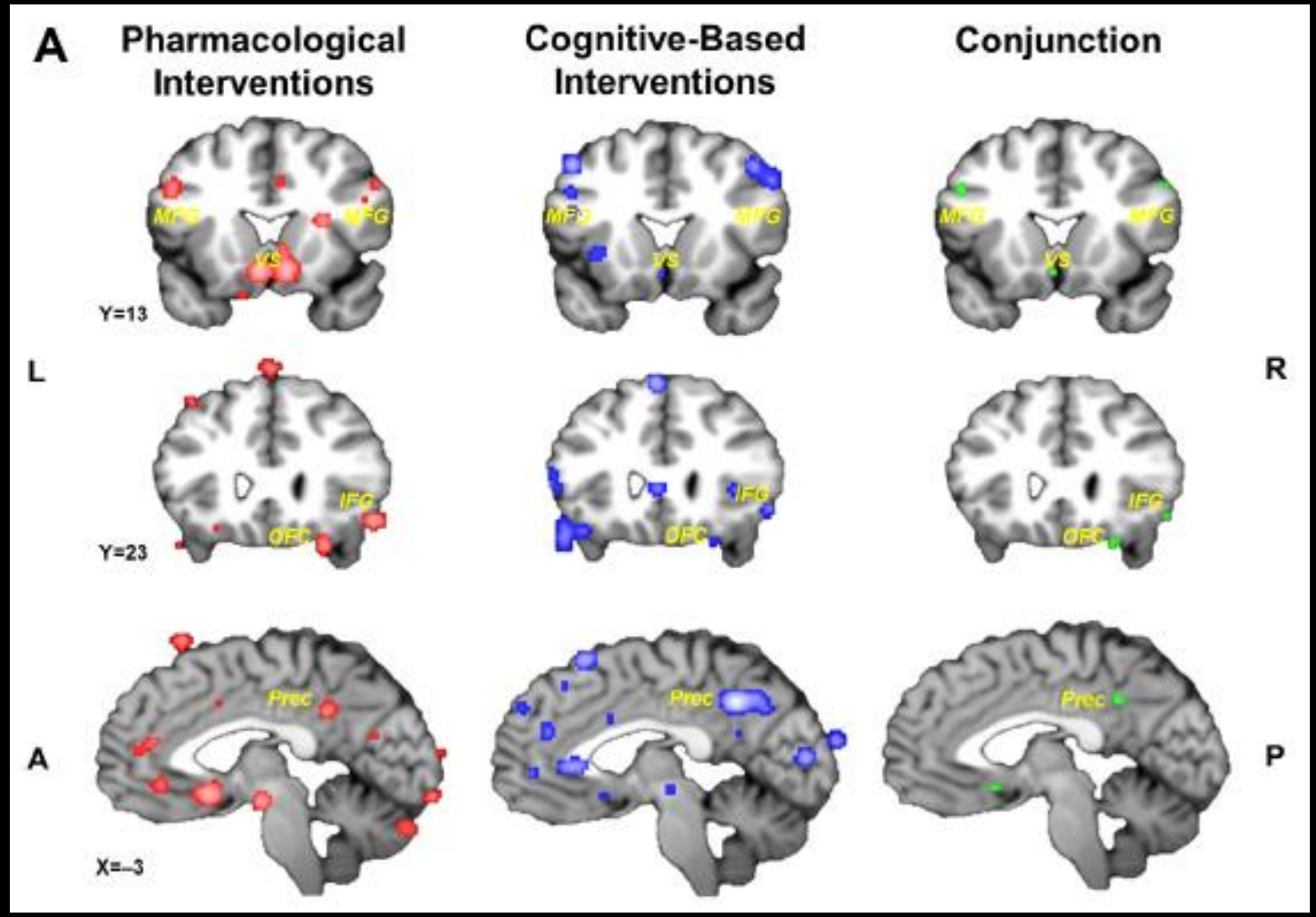
Adapted from Volkow et al., Neuropharmacology, 2004

Addiction Changes Brain Circuits that Govern Decisions



Adapted from Volkow et al., Neuropharmacology, 2004

Multi-faceted Treatment



Konova et al., Neurosci & Biobeh Rev 37:2806, 2013.

Differential Brain States

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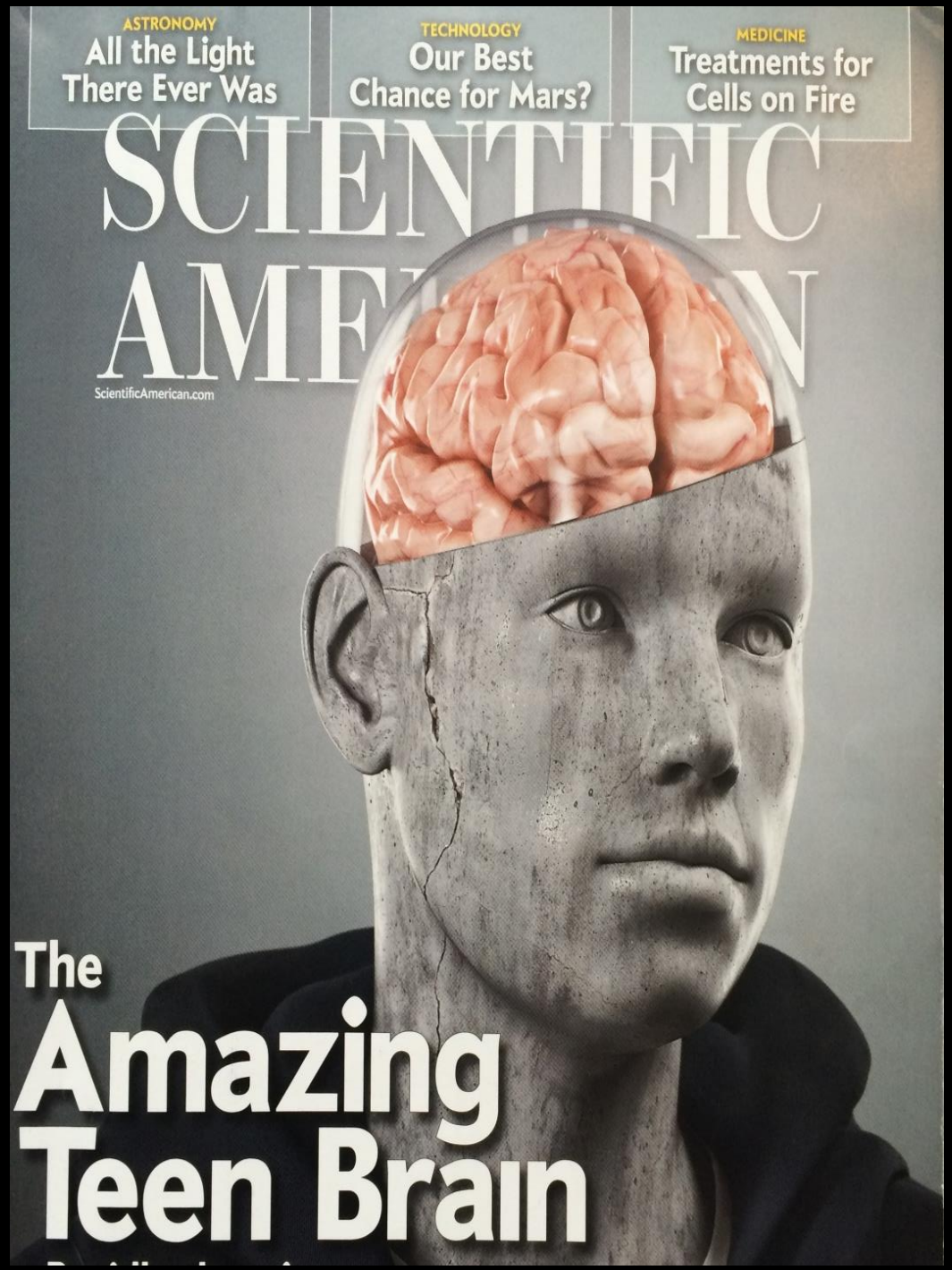
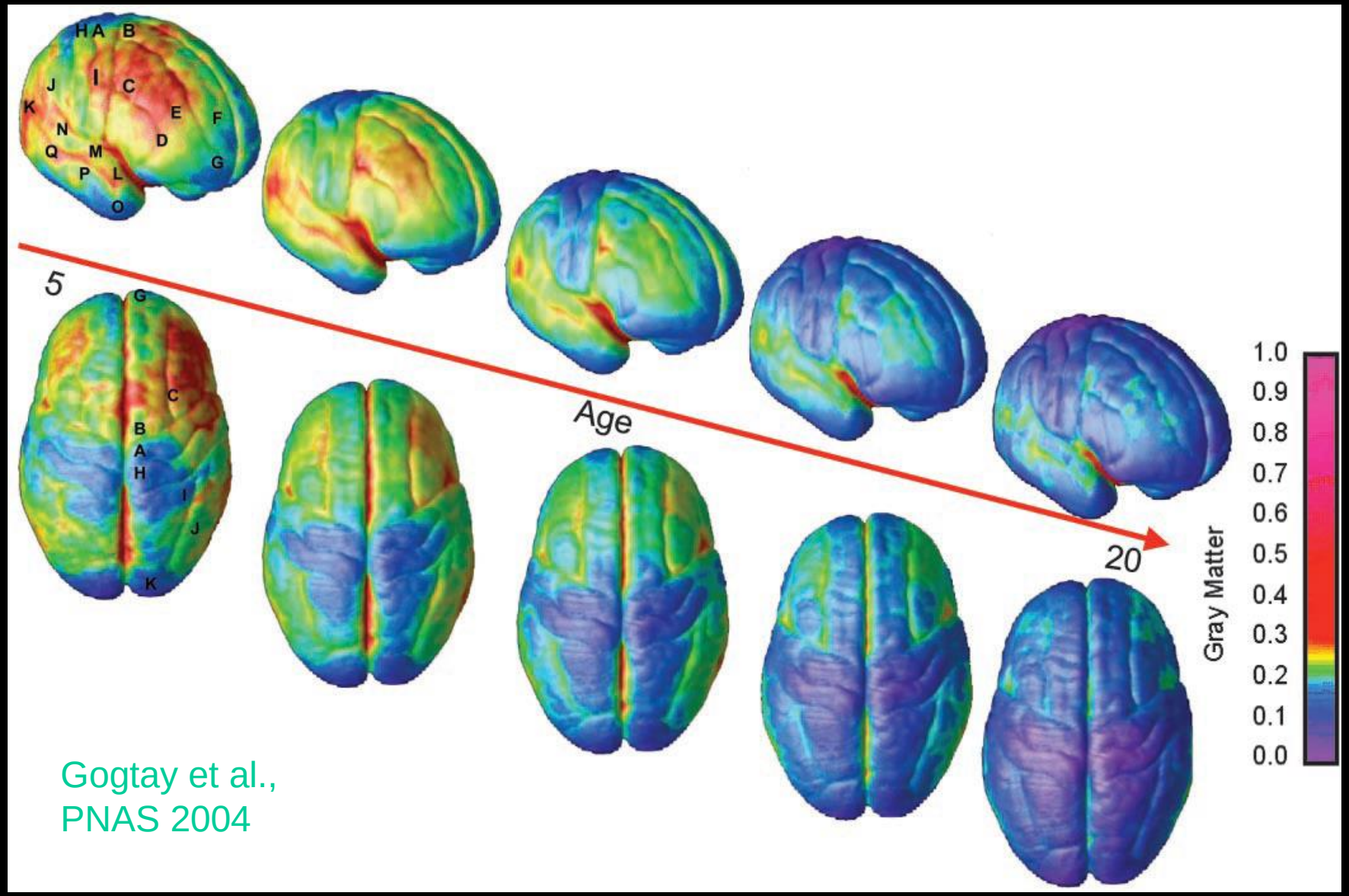


“Rapidly changing wiring leads to mental agility – and risky behavior”

By Jay N. Giedd

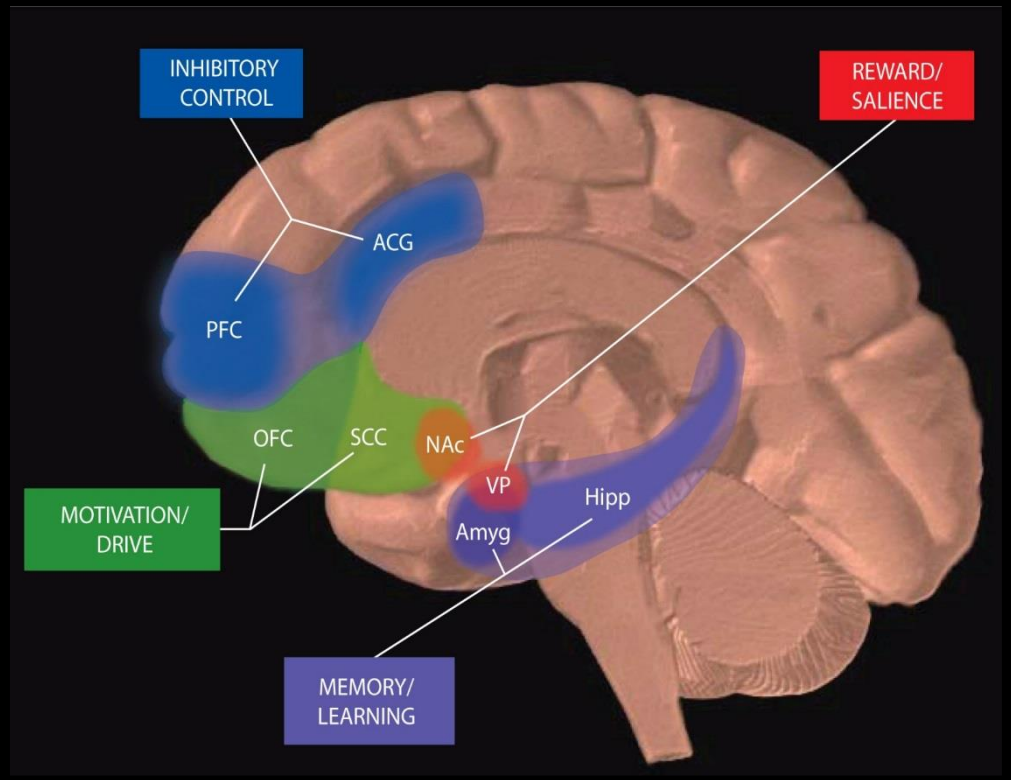
Healthy brain development

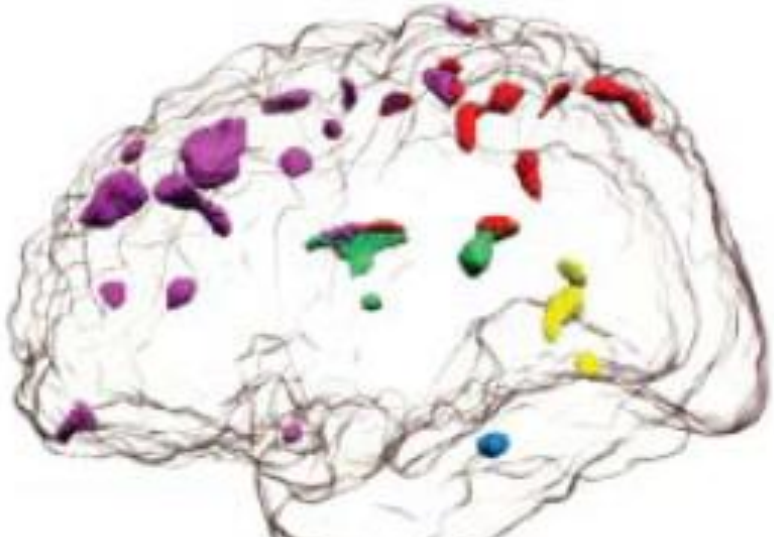


Gogtay et al.,
PNAS 2004

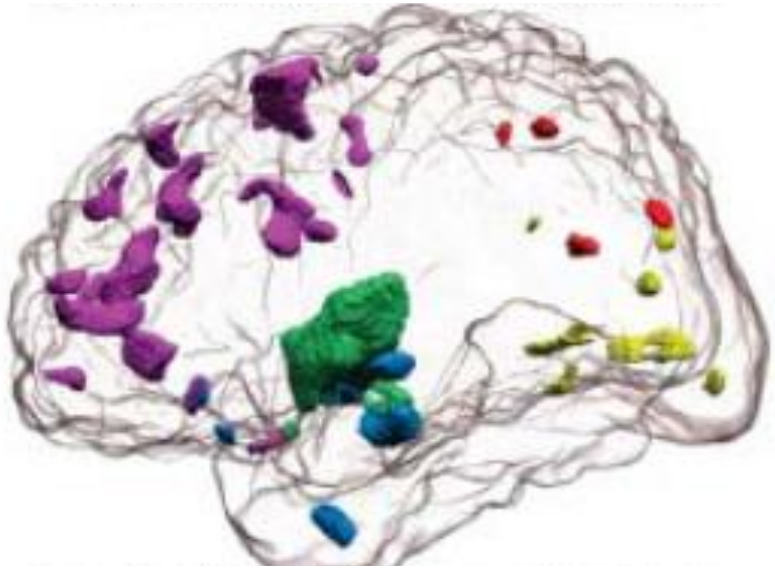
Patterns of cortical maturation during development

Sowell et al. The Neuroscientist, 2004.





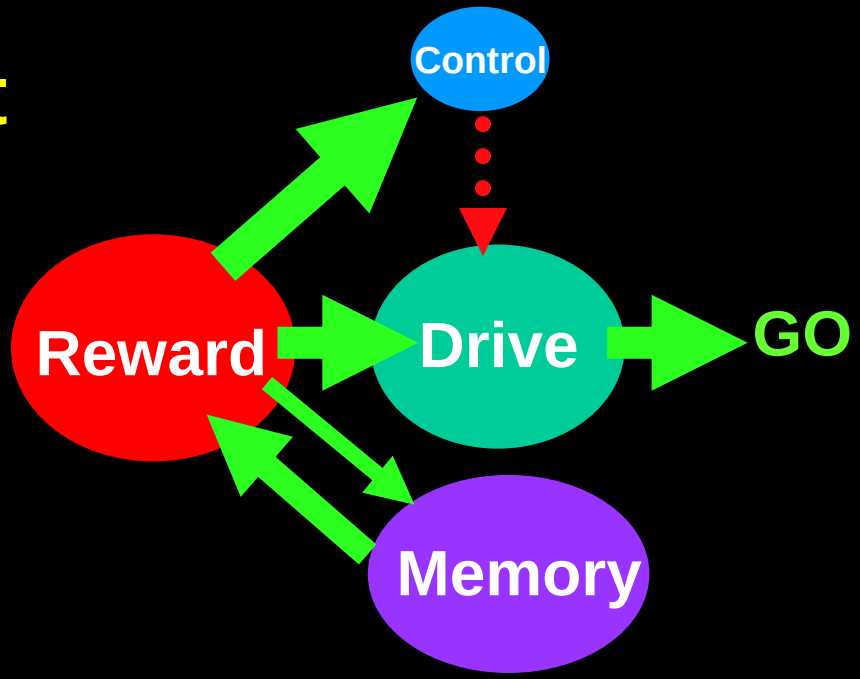
Child to Adolescent

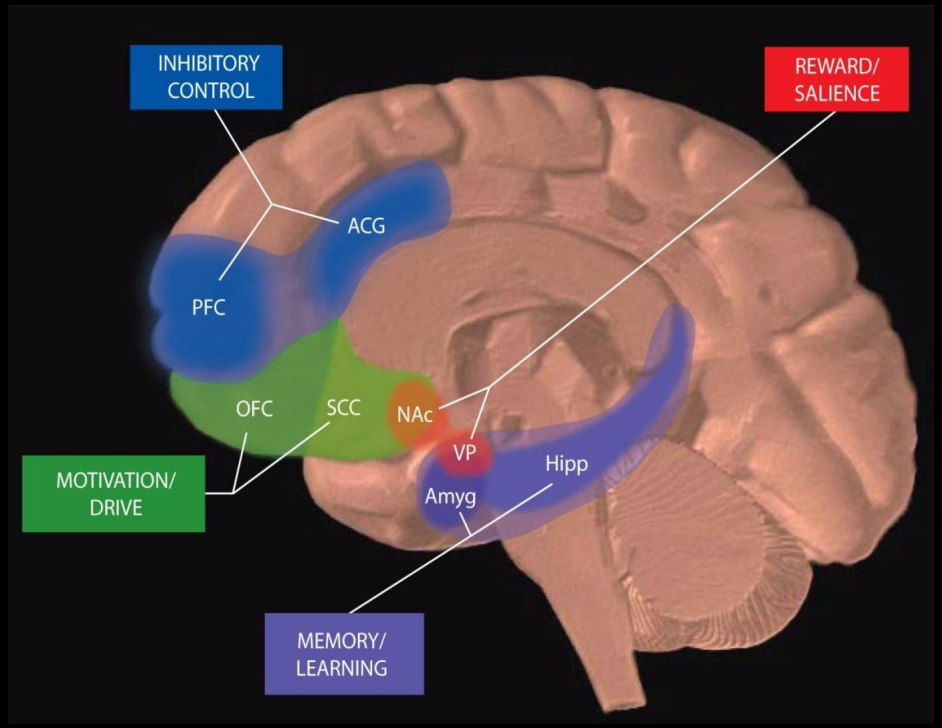


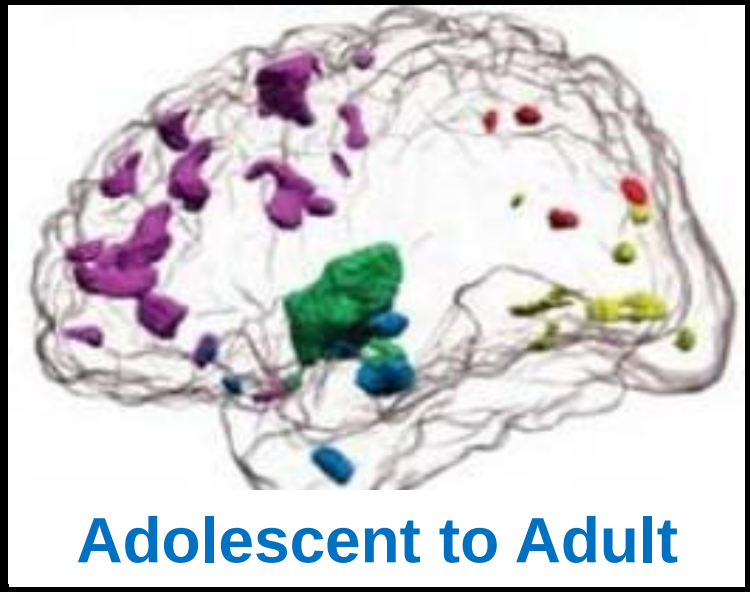
Adolescent to Adult

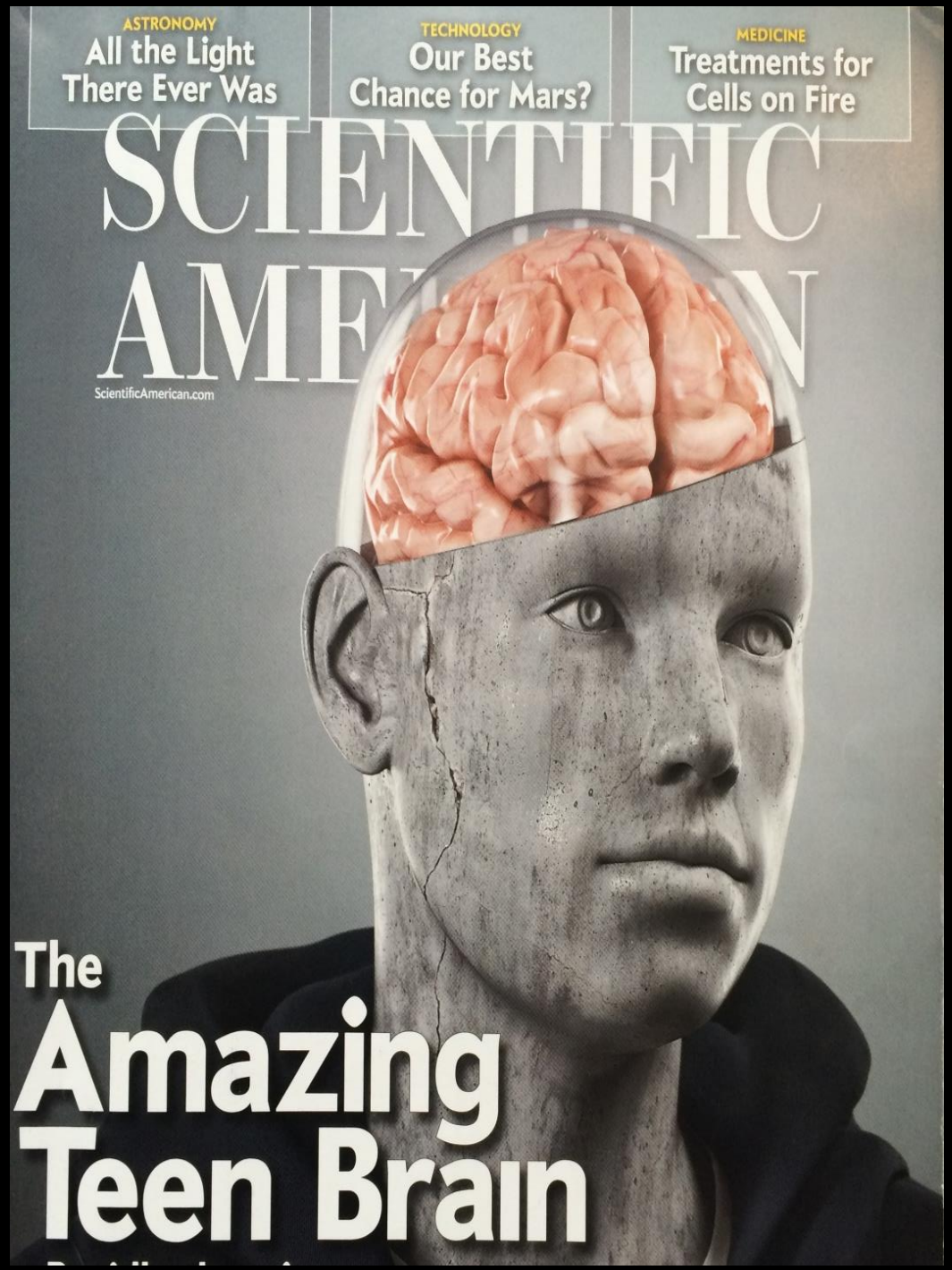
Cortical development and decision making

Sowell et al. The Neuroscientist, 2004.









"Rapidly changing wiring leads to mental agility – and risky behavior"

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Time of increased vulnerability to developing substance use disorders. With potential for long-term consequences.

In Conclusion, It is Important to:

- Understand the neuroscience of drug abuse
- Understand risk factors and protective factors
- Teach coping skills that allow good decision making
- Treatment does work!

NIDA Public Information:

www.nida.nih.gov

www.drugabuse.gov