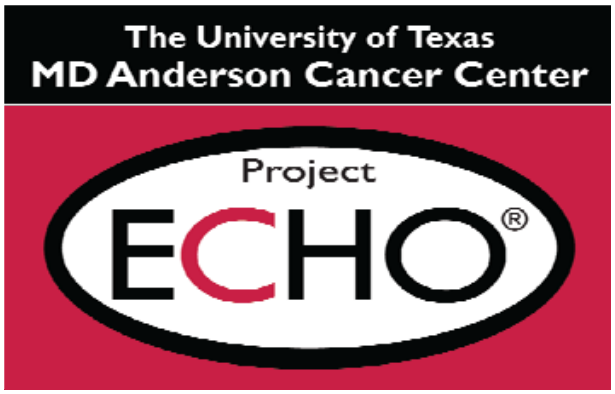
# Project ECHO
# Neurobiology of Nicotine Dependence

*Maher Karam-Hage, MD*



# Disclosure

- Have been co-investigator and study physician on two multi-site smoking cessation studies 2007 & 2014 by Pfizer, maker of: Chantix®, Zoloft® & Geodon®

- Have received medication Chantix from Pfizer for:
  - 2 NIH funded 2006-2014 and
  - 2 MD Anderson & CPRIT funded smoking cessation trials 2014-2016

# Outline

- The basic neurobiology of reward
- Addictive nature of nicotine and interplay with neuro-psych pathways
- The higher addiction potential of airway administration

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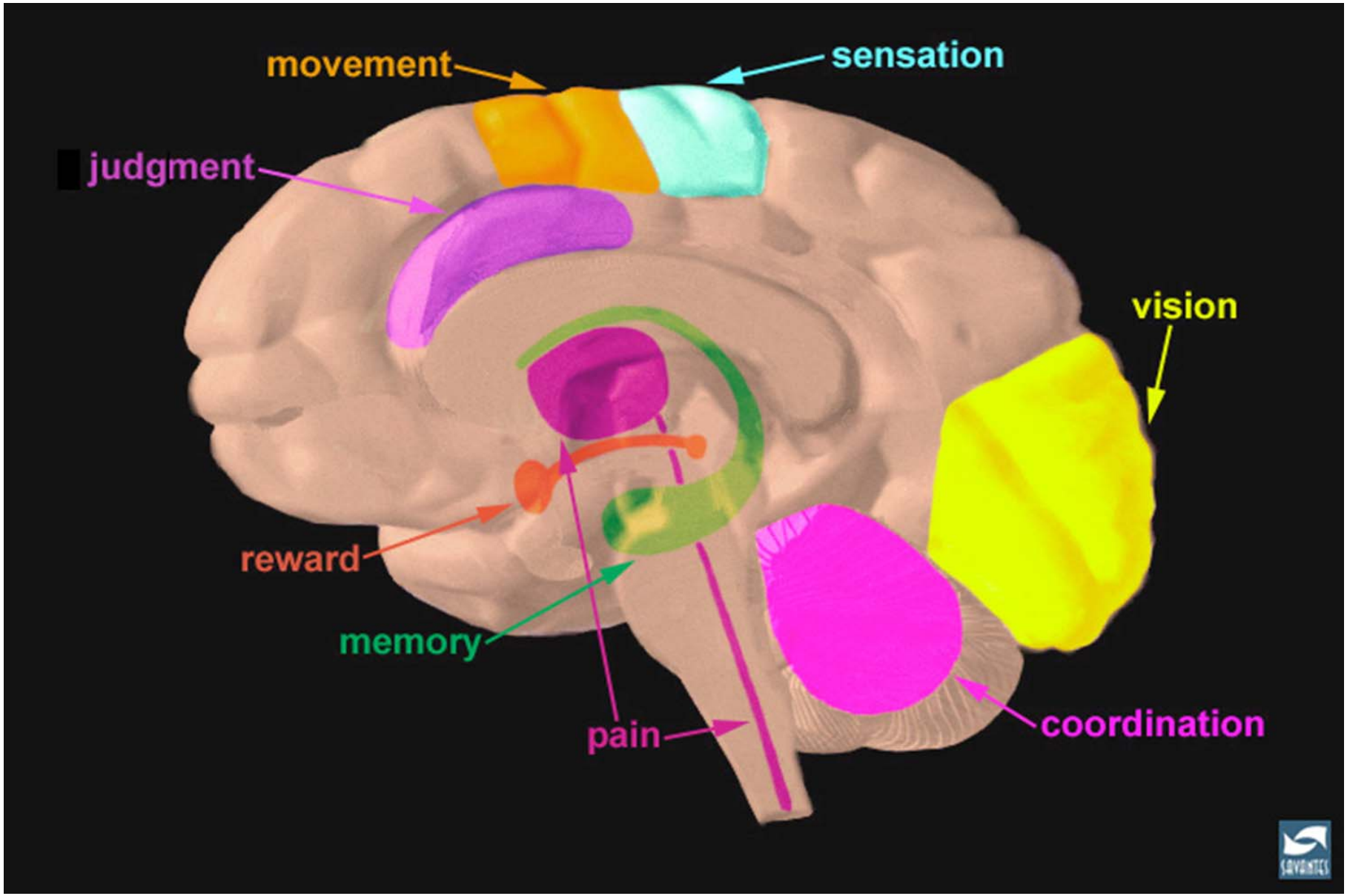
# The Reward Pathway and Addiction

# Natural Rewards

- Food
- Water
- Sex
- Nurturing

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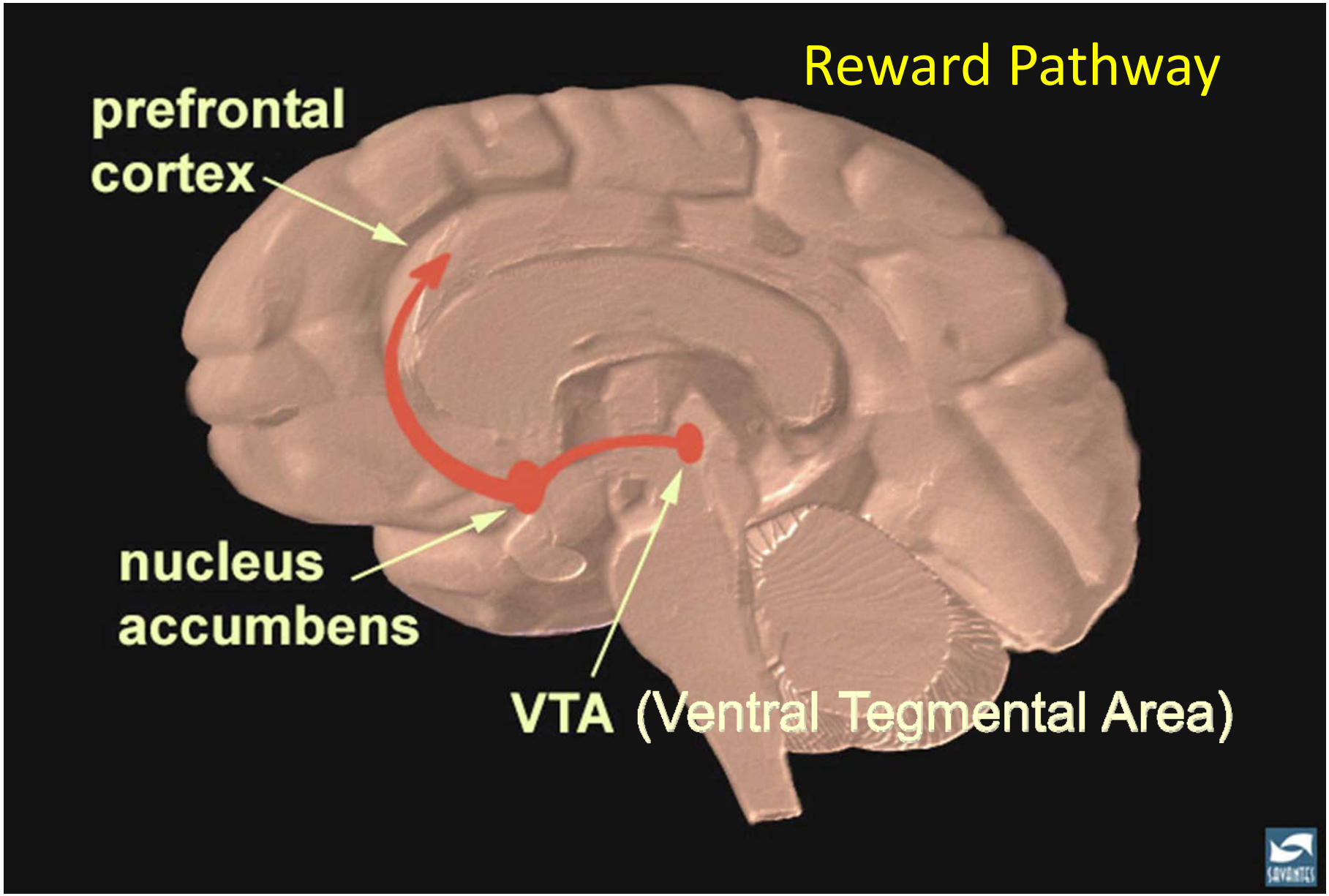


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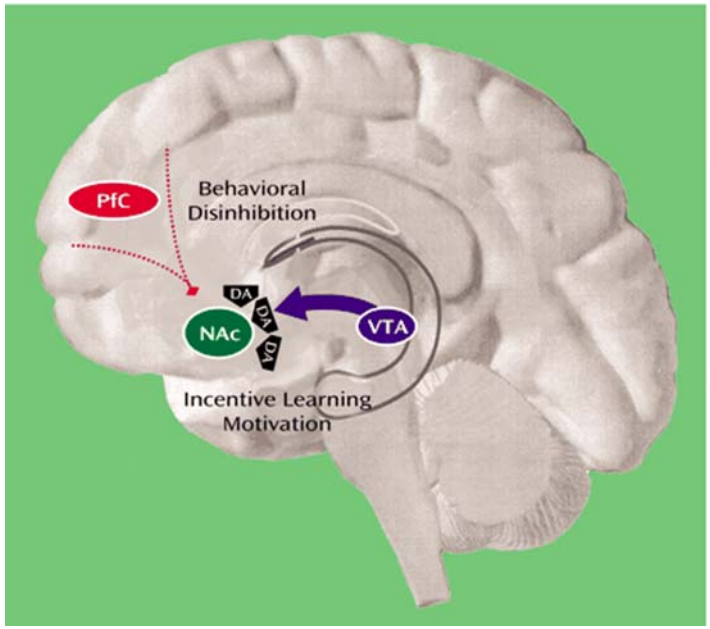
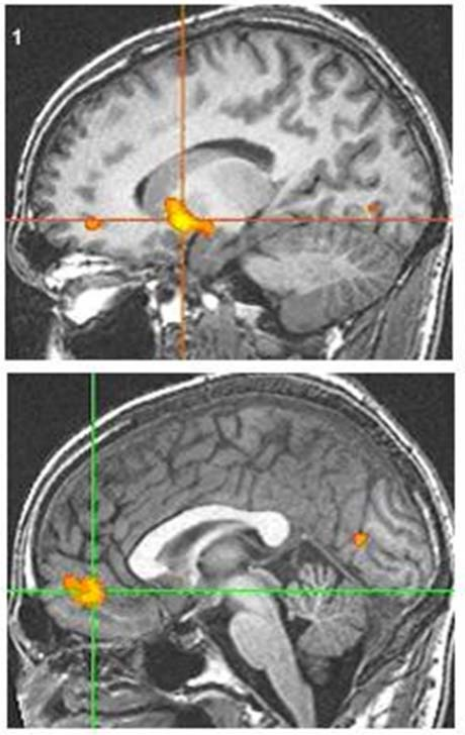
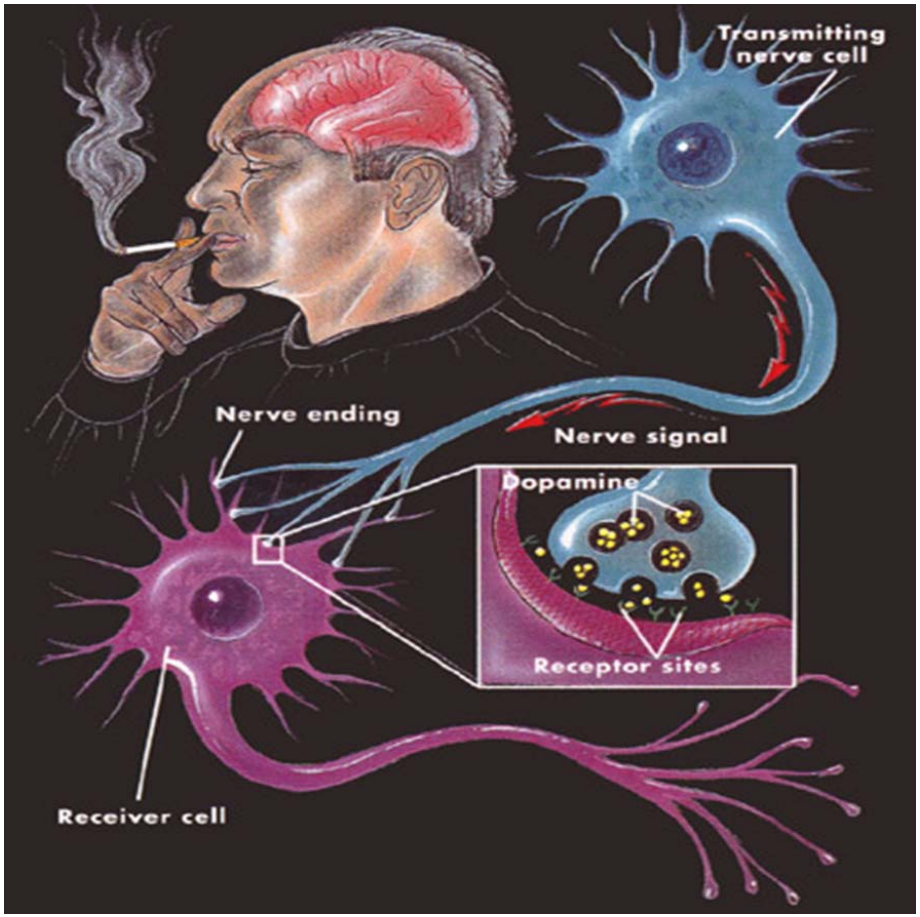
# fMRI of Nicotine's Effect on Blood Flow



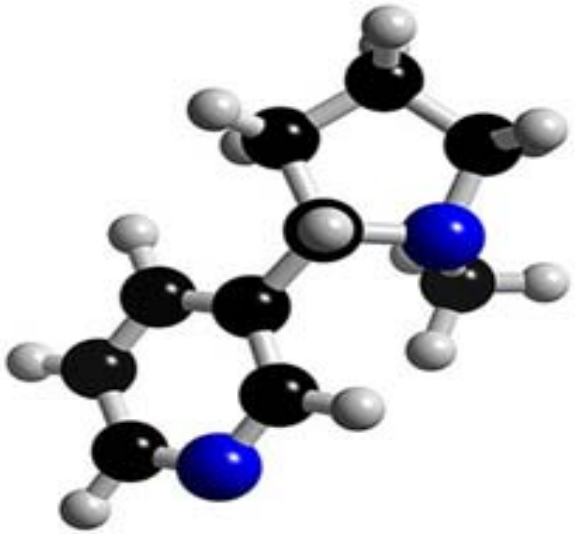




Interplay of reward/appetitive system with behavioral control/executive system

# Nicotine: Primary Psychoactive Substance in Cigarette Smoke

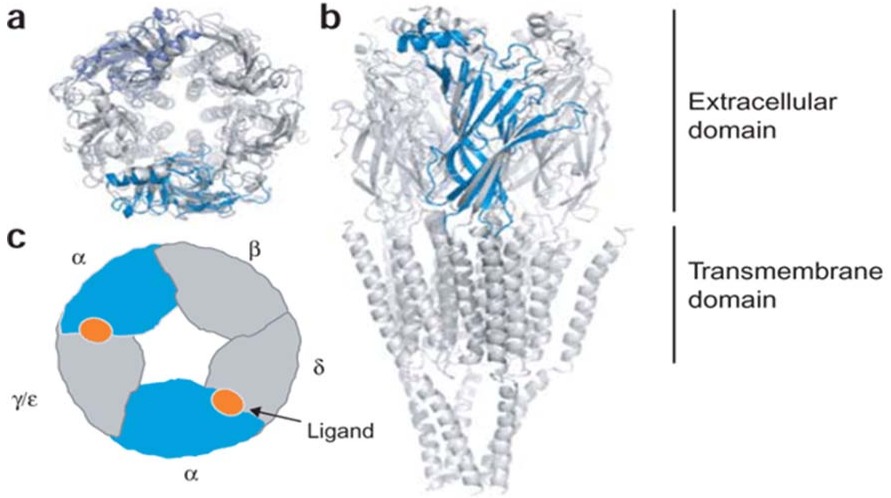


# Nicotine & Nicotinic Receptors



Nicotine Molecule

# Nicotine & Nicotinic Receptors




Nicotine Receptor Structure

# Outline

- The basic neurobiology of reward
- **Addictive nature of nicotine and interplay with neuro-psych pathways**
- **The higher addiction potential of airway administration**

# The Addictive Nature of Nicotine

- The addictive characteristics of nicotine are believed to be a result of its rapid, intense and short-acting effects on dopamine release in the brain. More so when smoked.

# The Addictive Nature of Nicotine

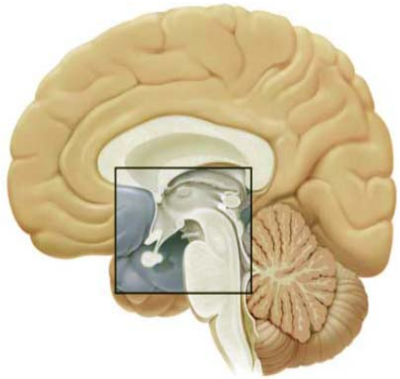
- Similar to addictions associated with cocaine, amphetamines and opiates, nicotine dependence (addiction) is a chronic, relapsing medical condition and warrants clinical intervention

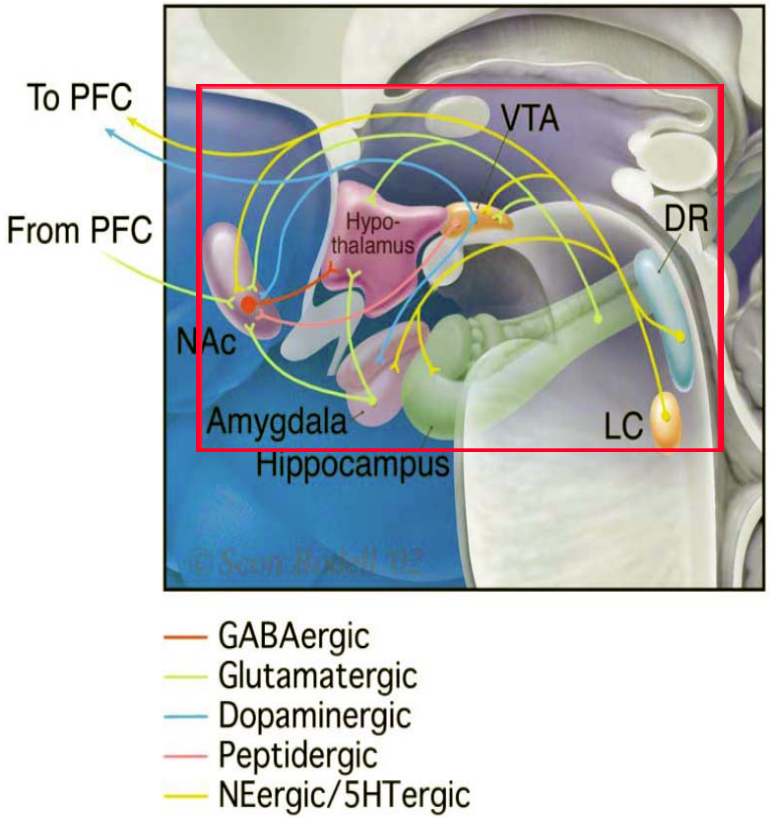
# The Addictive Nature of Nicotine

- Nicotine, cocaine, amphetamines and morphine act on different areas within the dopamine reward system that encompasses the mesolimbic portion of the brain.

# The Addictive Nature of Nicotine

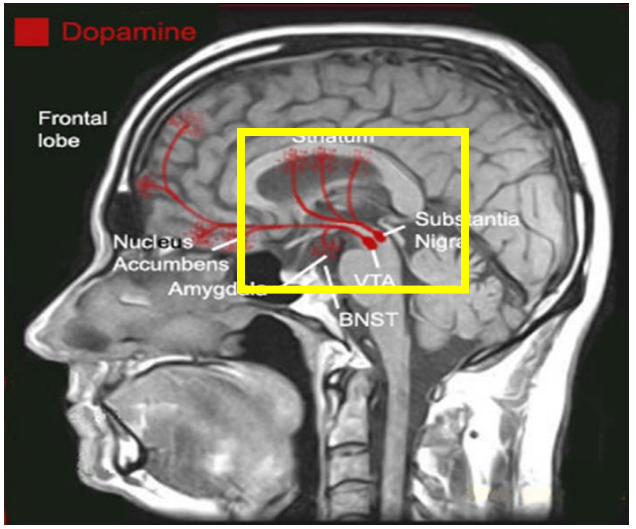
- Among users of tobacco, alcohol, cannabis, and cocaine: Tobacco users were more likely to be nicotine dependent (28%) than alcohol (5.2%), cannabis (8.2%) or cocaine (11.6%) users






Nicotine stimulates dopamine, serotonin & norepinephrine release, which may help smokers modulate their mood.

GABAergic and glutamatergic activity are intimately involved in the process



# National Geographic Video

http://video.nationalgeographic.com/video/magazine/focal-point/170822-ngm-focal-point-addiction

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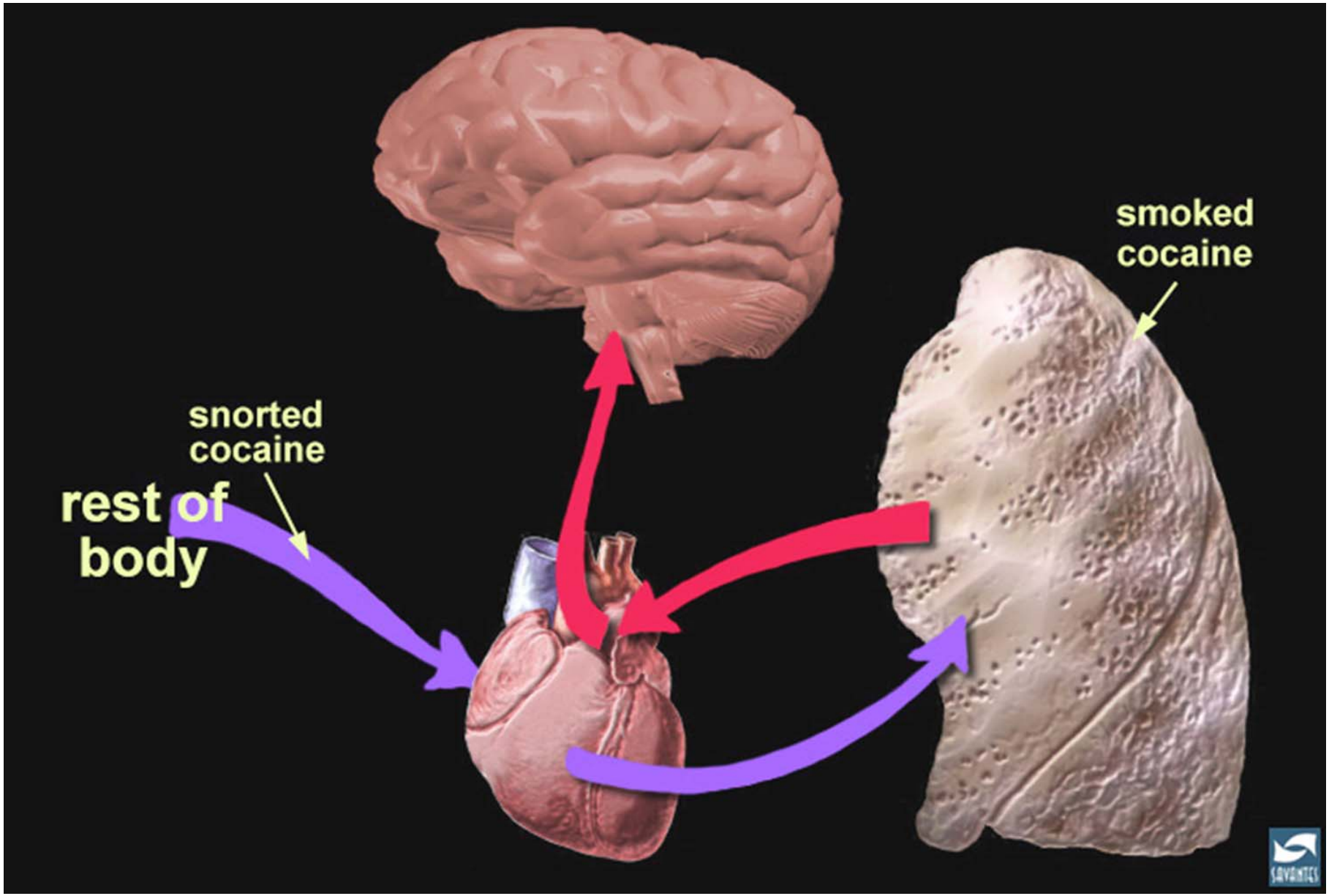


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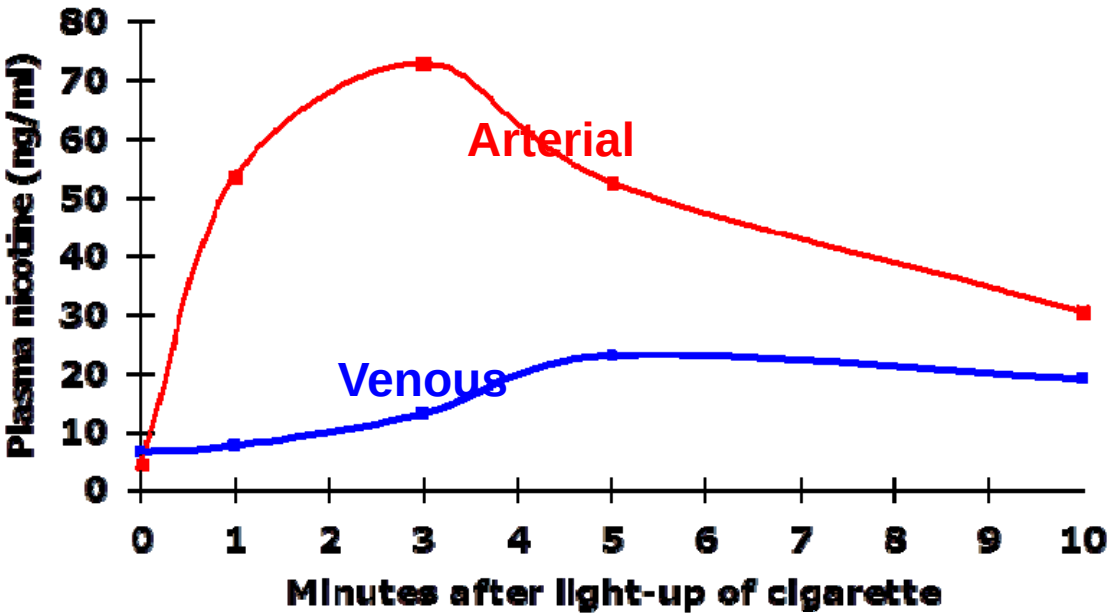
# The Addictive Nature of Nicotine

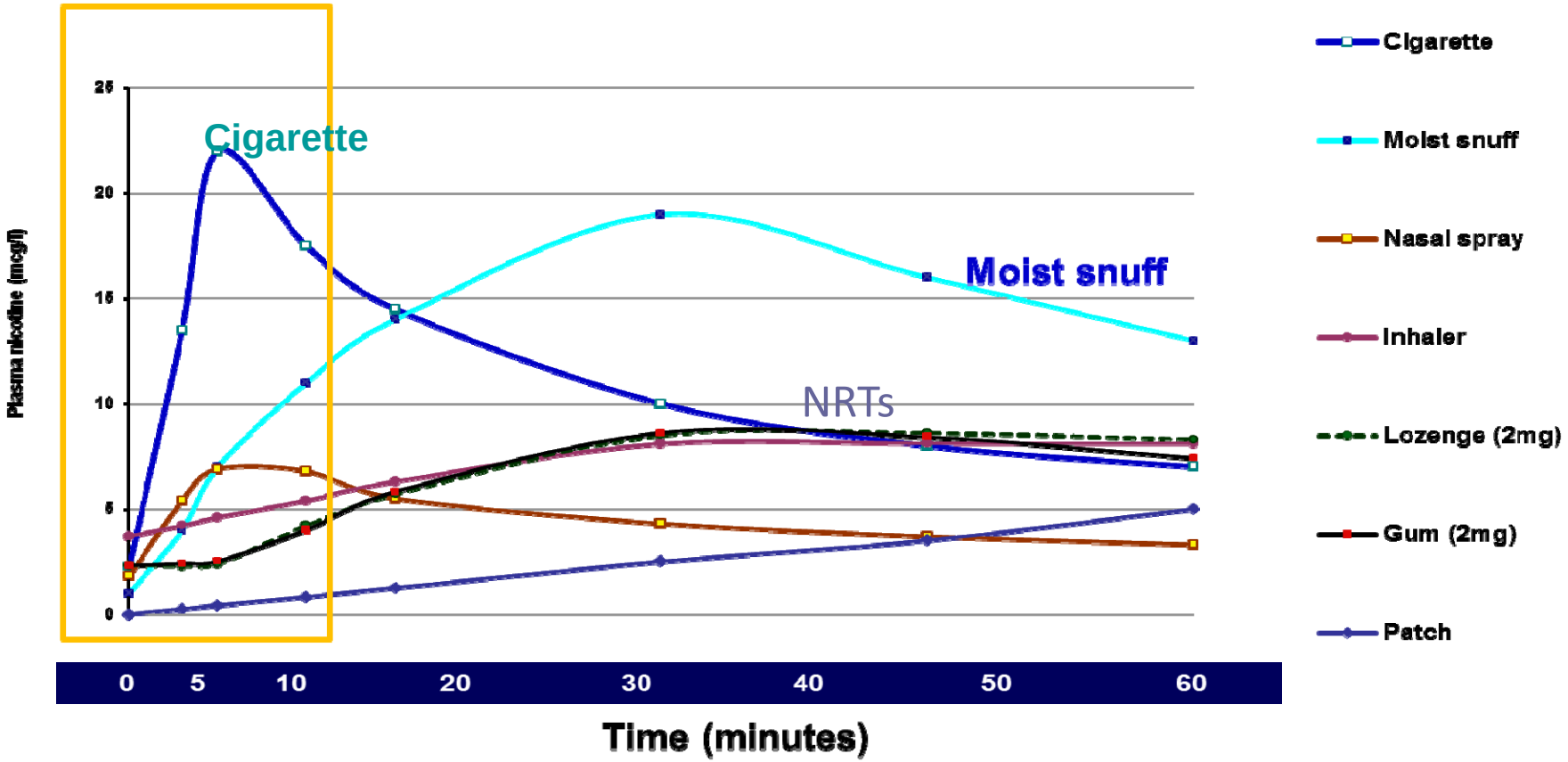
- When inhaled, nicotine reaches the brain within 7-10 seconds
- Via oral mucosa nicotine reaches brain around 5-10 min, transdermal 10-15 min
- Nicotine's half-life is approximately 2 hours

# Nicotine Distribution in Blood After Smoking a Cigarette




**Arterial Nicotine reaches the brain within 7-10 seconds**

# Plasma Nicotine Concentrations for Nicotine-Containing Products

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# Bupropion and Varenicline

Bupropion:

- A nicotine receptor antagonist within the first 1-2 weeks of taking it
- Weak norepinephrine and dopamine re-uptake inhibitor

# Bupropion and Varenicline

Varenicline:

- A *strong* partial agonist on alpha4-Beta2 nicotinic receptors, within days

- Very high affinity for the receptors that is not displaced by nicotine administration


If God wanted you to
smoke you would have a
chimney!

# References


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