Project ECHO
Neurobiology of Nicotine Dependence
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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
Reward Pathway

prefrontal cortex

nucleus accumbens

VTA (Ventral Tegmental Area)
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
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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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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

![Graph showing plasma nicotine concentrations over time for different products including Cigarette, Moist snuff, Nasal spray, Inhaler, Lozenge (2mg), Gum (2mg), and Patch.](image)
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


4. Henningfield et al. (1933). Drug Alcohol Depend 33:23-29