Understanding the Impact of Cigarette Smoking Using Brain Imaging

Angelica Morales, PhD
Postdoctoral Fellow
Developmental Brain Imaging Lab
Oregon Health & Science University
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The planning committee: Bita Moghaddam, PhD; Liz Stevenson, JD, MPH; William Wilson, MD; Neisha D’Souza, MD; Sean Stanley, MD; Micaela Sandoval, MBA, and Kevin Howden have **no financial disclosures**.
Objectives

• Identify current trends in cigarette use in the United States
• Overview of neurocircuitry implicated in substance use disorders
• Examine the evidence indicating that cigarette use is associated with abnormalities in brain structure and function in adolescent, young adult and adult smokers
• Review the association between neurobiology and response to nondrug rewards and cigarette craving
• Discuss how light and intermittent smokers differ from daily smokers
Current Cigarette Smoking Trends

MMWR, 2016
Risks Associated with Cigarette Use

• Leading cause of preventable death in the US

• Associated with 480,000 deaths per year
Benefits of Smoking Cessation

A Death from Any Cause

**Relative Risk**

**Age of Former Smokers at Cessation (yr)**

- **Current smokers**
- **Women who never smoked**

Pirie et al., 2013
Smoking Cessation is Difficult
Smoking Cessation is Difficult

- Some studies indicated that persons who start smoking at an early age are more likely to become life-long smokers and are more susceptible to nicotine addiction than adults (White et al. 2009).
- Maturational brain processes continue through early adulthood (Paus 2005).

![Brain development diagram](image)

Gogtay et al., 2004
Smoking Cessation is Difficult

• Some studies indicated that persons who start smoking at an early age are more likely to become life-long smokers and are more susceptible to nicotine addiction than adults (White et al. 2009)

• Maturational brain processes continue through early adulthood (Paus 2005)

• Tobacco use during this critical period produces neurobiological changes that promote tobacco dependence later in life (Tiffany 2008)
Development of Substance Use Disorders

Koob and Volkow, 2016
Development of Substance Use Disorders

- Nicotine reaches the brain seconds after cigarette smoking
- Nicotine binds to nicotinic acetylcholine receptors
- Release of various neurotransmitters including dopamine which is associated with reward/pleasure

Koob and Volkow, 2016

BBC, 2007
Development of Substance Use Disorders

- Cigarette use becomes paired with situations surrounding use
- Drug-associated stimuli can trigger dopamine release
- Dopamine release in response to smoking cues may motivate drug seeking behavior by increasing craving
- Cue-induced craving is intense, acute, and episodic urge to use drugs

Koob and Volkow, 2016
Development of Substance Use Disorders

- Chronic drug use produces neuroadaptations that result in withdrawal symptoms
- Smoke throughout the day to maintain levels of nicotine elevated and avoid symptoms of nicotine withdrawal

Koob and Volkow, 2016
Symptoms of Nicotine Withdrawal

• Anxiety
• Depression
• Difficulty Concentrating
• Impaired Performance
• Increased appetite and weight gain
• Irritability, frustration, and anger
• Restlessness and impatience
• Sleep disturbances
Development of Substance Use Disorders

- Chronic drug use produces neuroadaptations that result in withdrawal symptoms
- Smoke throughout the day to maintain levels of nicotine elevated and avoid symptoms of nicotine withdrawal
- Reduction in sensitivity of the brain reward system to nondrug rewards

Koob and Volkow, 2016
Development of Substance Use Disorders

• Seek substances after abstinence
• Background or tonic craving
  • Slowly change state
  • Induced by abstinence
  • Fades over time
• Insula – integrates information about motivation and emotion with interoceptive information
• Prefrontal cortex – cognitive control over tonic and cue-induced craving

Koob and Volkow, 2016
Brain function and Structure are Associated with Cigarette Craving, Craving Regulation, and Reward Processing
Task-based functional MRI

fMRI measures brain activation by indexing changes in blood oxygenation that result from changes in neuronal activity.
Assessing Cue-Induced Craving

Smolka et al., 2006
Exposure to Smoking Cues Increases Brain Activation

Engelmann et al, 2005

David et al, 2005
Brain Activation During Cue-Induced Craving Correlates with the Subject Experience

Brody et al., 2007
Brain Reactivity to Smoking Cues Predicts Treatment Outcomes

Subjects who slipped showed greater brain activation to smoking vs neutral images

Janes et al., 2010
Craving Regulation

• Loss of control over craving contributes to compulsive drug taking
• Treatment strategies help identify and regulate craving
• Cognitive Behavioral Therapy – Use cognitive strategies such as focusing on the long term consequences of smoking
  • “If I smoke this cigarette my lungs will fill with tar”
• Mindfulness Based Interventions – Notice craving and accept them as they are
  • “Craving is impermanent and I don’t have to act on it or avoid it”
Craving Regulation

- NOW = respond naturally and focus on immediate response
- LATER = the about the negative consequences associated with drug use or eating

Kober et al., 2010
Cognitive Strategies for Craving Regulation

Kober et al., 2010
Mindfulness-Based Regulation

- **LOOK** or **MINDFULLY ATTEND**
- **Strength of Craving**
  - 1--2--3--4--5

**LOOK** = view the picture as naturally as possible

**MINDFULLY ATTEND** = focus on their responses to the picture while maintaining a nonjudgmental attitude toward those responses

Westbrook et al., 2013
Mindful attention reduced self-reported cigarette craving in response to cues

Less mPFC activity during mindful attention

Less mPFC connectivity during mindful attention

Westbrook et al., 2013
Resting State Functional Connectivity to Assess Abstinence-Induced Craving

Identifies the functional organization of brain systems by measuring temporal correlations of intrinsic brain activity.
Connectivity of the anterior insula in adult cigarette smokers

Stoeckel et al., 2015
Abstinence Induced-Craving In Young Adults

Bi et al., 2017
Brain Structure and Craving
Structural Abnormalities in Adult Smokers

Fritz et al., 2014

Morales et al., 2012

Franklin et al., 2014
Greater Striatal Volume Associated with Greater Abstinence-Induced Craving

Janes et al., 2015
Brain Structure Relates to Abstinence-Induced Cigarette Craving in Young Adults

Morales et al., 2014
Craving and Craving Regulation: Take Home Points

• Abstinence-induced and cue-induced craving are related to abnormalities in brain structure and function in brain regions implicated in interoceptive awareness, reward processing, and executive functioning.

• Longitudinal studies are needed to determine whether structural and functional abnormalities observed in adolescents or young adults reflect pre-existing risk factors for substance use or a consequence of drug use.

• Different craving regulation strategies may rely on different neurobiological mechanisms.

• More research is needed to determine whether individual differences in neurobiology influence the success of various craving reduction strategies.
Measuring Neurobiological Response to Monetary Reward in Smokers
Blunted Mesocorticolimbic Responses During Reward Anticipation in Adult Smokers

Fedota et al., 2015

Wilson et al., 2014
Nondrug Reward Processing in Adolescent Smokers

Peters et al., 2011
Nondrug Reward Processing: Take Home Points

• Smokers show blunted neurobiological responses in mesolimbic circuitry in response to nondrug reward
• The potent response to cigarette use may bias the individual toward smoking behavior
• Pre-existing risk factor for various form of psychopathology?
• In adolescents, prospective studies show that blunted mesolimbic responses during reward anticipation predict future symptoms of depression (Morgan et al., 2013) and anxiety (Forbes et al., 2010)
Current Cigarette Smoking Trends

MMWR, 2016
Current Cigarette Smoking Trends

MMWR, 2016
Defining Light / Intermittent Smoking

• No consistent definition
  • Light Smokers – smoke daily but smoke few cigarettes per day
  • Occasional / Nondaily Smokers – smoke fewer than 30 days a month
  • Social Smoker – nondaily smoking limited to social contexts

• Who is engaging in light / intermittent smoking?
  • Young
  • Educated
  • Women
  • Minorities

Schane et al., 2010
Increased Prevalence of Light / Intermittent Smoking

- Smoking bans in public places
- Increased price of cigarettes
- Increased in initiation of smoking among those over the age of 19
- Perception of harm

Institute of Medicine, 2007

Adapted from Amrock et al, 2015
Negative Consequences of Light / Intermittent Smoking

• Light and intermittent smoking increases risk for:
  • Cardiovascular disease (occasional smoking)
  • Cancer
  • Respiratory Diseases
  • Other disease (e.g. reproductive issues)
  • All cause mortality

• Nondaily smokers and social smokers may not self-identify as smokers and are not likely to perceive a need to quit

• Understanding the ways in which nondaily smokers are similar to and different from daily and non-smokers is important for the development of targeted interventions.

Schane et al, 2010
Smoking Motives Among Intermittent Smokers

• With abstinence intermittent smokers experience fewer symptoms of craving and withdrawal than daily smokers (Shiffman et al., 2015)
• Adult intermittent smokers are less likely to make quit attempts and 73-82% fail in their attempts (Tindle et al., 2011)
Smoking Motives Among Intermittent Smokers

Koob and Volkow, 2016
Smoking Motives Among Intermittent Smokers

• With abstinence intermittent smokers experience fewer symptoms of craving and withdrawal than daily smokers (Shiffman et al., 2015)

• Adult intermittent smokers are less likely to make quit attempts and 73-82% fail in their attempts (Tindle et al., 2011)

• Among intermittent smokers, cigarette use more strongly associated with situational triggers (Shiffman et al., 2014):
  • Being away from home
  • Social interaction
  • Others smoking
  • Drinking alcohol
Strong Association Between Alcohol and Nondaily Cigarette Use Among Young Adults

• Nondaily smokers are more likely to engage in hazardous drinking (Harrison et al., 2008)

• The majority of smoking occasions occur under the influence of alcohol (McKee et al., 2004)

• Smoking typically occurs after 2-3 drinks suggesting that the effects of alcohol intoxication promote cigarette use (Harrison et al., 2008)
Acute Alcohol Intoxication Increases Cigarette Craving in Nondaily Smokers

King et al., 2010
Alcohol Intoxication Increases NAcc Response to Cigarette Cues in Young Nondaily Smokers

King et al., 2010
What factors determine future cigarette use?

• Smoking patterns are unstable during young adulthood (Caldeira et al., 2012)
Cigarette Smoking Trajectories Among College Students

Caldeira et al., 2012

Number of smoking days in the past month

- High Stable
- Low-increasing
- High-decreasing
- Low-stable
What factors determine future cigarette use?

• Smoking patterns are unstable during young adulthood (Caldeira et al., 2012)
• Individual differences in response to smoking cues during placebo?
• Individual differences in response to smoking cues during alcohol intoxication? With friends?
• Responses to nondrug rewards?
• No existing longitudinal studies
Drug vs Nondrug Reward Processing in Adult Occasional Smokers

Buhler et al., 2010
Occasional Smokers Have Stronger Responses to Nondrug Rewards

Buhler et al., 2010
Drug vs Nondrug Reward Processing in Occasional Smokers

Buhler et al., 2010
Light / Intermittent Cigarette Use: Take Home Points

• We need to raise awareness about the health risks of ANY smoking.

• Since nondaily smokers and social smokers may not self-identify as smokers, clinicians may want ask “Do you use any tobacco products on a daily, weekly, or on a social basis?”

• Behavior modification techniques which focus on situational cues, such as alcohol use, may be useful with curbing cigarette use among nondaily smokers.

• More research is necessary to understand the neurobiological markers that promote risk and resilience for varies trajectories of future cigarette use among young adults.
QUESTIONS

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Please limit your questions to 30 seconds or less to allow everyone to participate.

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