Neurobiology of Substance Use

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Board Certified American Board of Preventive Medicine in Addiction Medicine
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- Aria Wiseblatt, BA, Boston Children’s Hospital

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Acknowledgements

• SUBSTANCE USE AND ADDICTION IN CHILDREN AND ADOLESCENTS
  – ANDREA E. BONNY, M.D.
  – ASSOCIATE PROFESSOR OF PEDIATRICS
Acknowledgements

Ohio Opiate Project ECHO™: Expanding Access to Medication-Assisted Treatment

Christina M. Delos Reyes, MD
Learning Objectives

• To gain a comprehensive understanding general neurobiology and neurobiology of adolescent brain development
Short Definition of Addiction:

- Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

- Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one’s behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

https://www.asam.org/resources/definition-of-addiction
Old vs New Model of Addiction

A Biopsychosocial Illness

- Biological
- Psychological
- Social
- Use
- Addiction
- Relapse
  1. Stress
  2. Trigger (CUE)
  3. Exposure (primer)

Switch

Use

Biological

Psychological

Social

Addiction

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Activation of the reward pathway by addictive drugs

Stages of the Addiction

During intoxication, drug-induced activation of the brain’s reward regions (in blue) is enhanced by conditioned cues in areas of increased sensitization (in green). During withdrawal, the activation of brain regions involved in emotions (in pink) results in negative mood and enhanced sensitivity to stress. During preoccupation, the decreased function of the prefrontal cortex leads to an inability to balance the strong desire for the drug with the will to abstain, which triggers relapse and reinitiates the cycle of addiction. The compromised neurocircuitry reflects the disruption of the dopamine and glutamate systems and the stress-control systems of the brain, which are affected by corticotropin-releasing factor and dynorphin. The behaviors during the three stages of addiction change as a person transitions from drug experimentation to addiction as a function of the progressive neuroadaptations that occur in the brain.

Neurobiologic Advances from the Brain Disease Model of Addiction
“Adolescents Are **Not** Little Adults”
Nucleus accumbens
Toddler milestones: balance, walking, coordination

Preschool milestones: emotional regulation

School age milestones: achievement

Adolescent milestones: impulse control

Physical coordination, Sensory processing

emotion

motivation

Planning, Organizing, Impulse control

Cerebellum

Amygdala

Nucleus Accumbens

Prefrontal cortex

Toddler milestones: balance, walking, coordination

Preschool milestones: emotional regulation

School age milestones: achievement

Adolescent milestones: impulse control

Physical coordination, Sensory processing

emotion

motivation

Planning, Organizing, Impulse control

Cerebellum

Amygdala

Nucleus Accumbens

Prefrontal cortex

Slide adapted from Ken Winters, PhD.
Brain Weight by Age

Immature Brain

Synaptic Density
Blossoming

Synaptic Density
Synaptic Pruning

Myelination


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Brain Maturation


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Adolescents are *developmentally primed* to seek big rewards.
Natural Rewards Elevate Dopamine Levels

Food

NAc shell

% of Basal DA Output

Empty Box Feeding

Time (min)

Sex

DA Concentration (% Baseline)

Female Present

Sample Number

Effects of Drugs on Dopamine Release

**AMPHETAMINE**

- **Accumbens**
  - DA
  - DOPAC
  - HVA

<table>
<thead>
<tr>
<th>% of Basal Release</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5 hr</th>
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<td>DA</td>
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<td>DOPAC</td>
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<tr>
<td>HVA</td>
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</table>

**COCAIN**

- **Accumbens**
  - DA
  - DOPAC
  - HVA

<table>
<thead>
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<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5 hr</th>
</tr>
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<tr>
<td>DOPAC</td>
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<tr>
<td>HVA</td>
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</tr>
</tbody>
</table>

**NICOTINE**

- **Accumbens**
  - Caudate

<table>
<thead>
<tr>
<th>% of Basal Release</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accumbens</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MORPHINE**

- **Accumbens**
  - Dose (mg/kg):
    - 0.5
    - 1.0
    - 2.5
    - 10

<table>
<thead>
<tr>
<th>% of Basal Release</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>10</td>
<td></td>
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</tr>
</tbody>
</table>

Di Chiara and Imperato, PNAS, 1988

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MORE DUMB LOVE
Adolescents Are Vulnerable

- Early substance use = high risk addiction
- Adolescent immaturity during critical development period = vulnerability
  - Impulsiveness and excitement seeking
  - Difficulty delaying gratification
  - Poor executive function and inhibitory control

The Drug Danger Zone: Most Illicit Drug Use Starts in the Teenage Years

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage of Past-Year Initiates among Those Who Have Never Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-13</td>
<td>2.9%</td>
</tr>
<tr>
<td>14-15</td>
<td>8.0%</td>
</tr>
<tr>
<td>16-17</td>
<td>11.2%</td>
</tr>
<tr>
<td>18-20</td>
<td>10.4%</td>
</tr>
<tr>
<td>21-25</td>
<td>4.5%</td>
</tr>
<tr>
<td>26 or Older</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2011 and 2012.
Age at First Use and Later Risk

## Alcohol

<table>
<thead>
<tr>
<th>Age at First Drink</th>
<th>% with Alcohol Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=13</td>
<td>47</td>
</tr>
<tr>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>15</td>
<td>38</td>
</tr>
<tr>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>17</td>
<td>28</td>
</tr>
<tr>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>&gt;=21</td>
<td>9</td>
</tr>
</tbody>
</table>

## Marijuana

<table>
<thead>
<tr>
<th>Age at First Use</th>
<th>% with Marijuana Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>21+</td>
<td>4</td>
</tr>
</tbody>
</table>

Sources:

Monitoring the Future is an annual survey of 8th, 10th, and 12th graders conducted by researchers at the Institute for Social Research at the University of Michigan, Ann Arbor, under a grant from the National Institute on Drug Abuse, part of the National Institutes of Health. Since 1975, the survey has measured how teens report their drug, alcohol, and cigarette use and related attitudes in 12th graders nationwide; 8th and 10th graders were added to the survey in 1991.

44,482 students from 392 public and private schools participated in the 2018 survey.
### Past-Year Misuse of Prescription/Over-the-Counter vs. Illicit Drugs

#### Prescription/OTC
- 5.0% Sedatives/Tranquilizers
- 4.6% Adderall®
- 3.4% Opioids
- 3.4% Cough/Cold Medicine
- 0.9% Ritalin®

#### Illicit Drugs
- 35.9% Marijuana/Hashish
- 3.5% Synthetic Cannabinoids*
- 3.2% LSD
- 2.3% Cocaine
- 2.2% MDMA (Ecstasy/Molly)
- 1.6% Inhalants
- 0.4% Heroin

**Past-year use among 12th graders**

#### Vicodin® vs. OxyContin®
- 2003: 10.5%
- 2008: 4.5%
- 2013: 1.7%
- 2018: 2.3%

Past-year misuse of Vicodin® and OxyContin® among 12th graders has dropped dramatically in the past 15 years.

**KEY**
- Vicodin®
- OxyContin®

#### Students Report Lowest Rates Since Start of the Survey

Across all grades, past-year use of illicit drugs other than marijuana holding steady at the lowest levels in over 20 years.

*Synthetic cannabinoids are called “synthetic marijuana” in the survey.

[Drugabuse.gov]
NEARLY 2 IN 5 STUDENTS IN 12TH GRADE REPORT PAST-YEAR VAPING, RAISING CONCERNS ABOUT THE IMPACT ON BRAIN HEALTH AND POTENTIAL FOR ADDICTION.
DAILY MARIJUANA USE MOSTLY STEADY

2008 – 2018

2018

8th graders 0.7%
10th graders 3.4%
12th graders 5.8%

FIVE-YEAR TRENDS IN DAILY MARIJUANA USE REMAINS STEADY FOR 10TH AND 12TH GRADERS BUT SHOWS A DECLINE IN 8TH GRADERS.
TEENS MORE LIKELY TO USE MARIJUANA THAN CIGARETTES

Past-month use among 12th graders

TEENS VAPING NICOTINE OR MARIJUANA INCREASED ACROSS ALL GRADES

Past-month use

PAST-MONTH VAPING OF NICOTINE OR MARIJUANA JUMPED ACROSS ALL GRADES. PAST-MONTH USE OF MARIJUANA IS STEADY AS CIGARETTE USE DECLINES.
Binge drinking* rates continue downward trend

*Binge drinking is defined as having 5 or more drinks in a row in the last 2 weeks.

Binge drinking: significant drop in past five years across all grades.
Alcohol
Parts of the brain affected by alcohol
Behavioral Effects of Alcohol on the Adolescent Rat

The Water Maze Test

<table>
<thead>
<tr>
<th>Intoxicated Adult Rat</th>
<th>Swimming Speed</th>
<th>Time to Platform</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decreased</td>
<td>Increased</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intoxicated Adolescent Rat</th>
<th>Swimming Speed</th>
<th>Time to Platform</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unchanged</td>
<td>Increased</td>
</tr>
</tbody>
</table>

### Leading Causes of Mortality Ages 10-24, United States, 2013

<table>
<thead>
<tr>
<th>Cause</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Vehicle Crashes</td>
<td>22.1%</td>
</tr>
<tr>
<td>Other Unintentional Injuries</td>
<td>17.4%</td>
</tr>
<tr>
<td>Homicides</td>
<td>16.8%</td>
</tr>
<tr>
<td>Suicides</td>
<td>14.3%</td>
</tr>
<tr>
<td>Other</td>
<td>29.4%</td>
</tr>
</tbody>
</table>

The 4 leading causes of death are all associated with alcohol consumption.

Percentages calculated using data from National Center for Health Statistics (NCHS) Vital Statistics System.
Impact of chronic alcohol exposure
Hippocampal Size by MRI

Marijuana’s effects on the brain
Delta-9 tetrahydrocannabinol (THC)

- Primary psychoactive ingredient in marijuana
- Fat-soluble; crosses the blood-brain barrier and the placenta
- Accumulates in adipose tissue resulting in long elimination half-life (several days to 1 week)
- Acts on the body’s endogenous cannabinoid receptors, present in the central and peripheral nervous system
In 1988 researchers Allyn Howlett and William Devane discovered cannabinoid receptors in the brain and called them cannabinoid 1 receptors (CB1) (Devane et al., 1988). In 1992 researchers discovered an endogenous cannabinoid and called it anandamide (Devane et al., 1992).
Endocannabinoid System Functions

• The neuron’s “volume control” system: dials down neuron activity when too strong

• Regulates neurotransmitters affecting pleasure, mood, pain, appetite, motivation, memory (e.g., dopamine, glutamate, endorphins, serotonin)
Endocannabinoid System cont’d.

• Shapes *brain development* ...
  
  – Guides neurons to grow to the right places in the brain for correct function
  
  – Controls neuron activity, thereby shaping brain wiring and pruning
  
  – Supports myelin growth on neurons
THC vs. Anandamide

- Both **dial down** neuron activity to change neurotransmitter release

- **THC** has a MUCH STRONGER, LONGER effect than anandamide on brain cells
  - Sledge hammer versus scalpel analogy

- **THC** interferes with cell function and growth
**Receptor binding in brain tissue**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Potency relative to THC</th>
</tr>
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<tbody>
<tr>
<td>(-)-Delta9-THC</td>
<td>1</td>
</tr>
<tr>
<td>Anandamide</td>
<td>.47*</td>
</tr>
</tbody>
</table>

*The affinity of anandamide for cannabinoid receptors ranges from about one-fourth to one-half that of THC. The differences depend on the cells or tissue that are tested and on the experimental conditions, such as the binding assay used.

Content of THC in marijuana has increased over time

Long-term effects associated with marijuana use in adolescence

<table>
<thead>
<tr>
<th>Effect</th>
<th>References</th>
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<tbody>
<tr>
<td>Psychosis</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>2, 3, 4</td>
</tr>
<tr>
<td>Anxiety</td>
<td>4</td>
</tr>
<tr>
<td>Diminished life satisfaction and achievement</td>
<td>5, 6, 7</td>
</tr>
<tr>
<td>Cognitive decline</td>
<td>8, 9</td>
</tr>
<tr>
<td>Addiction</td>
<td>10, 11</td>
</tr>
</tbody>
</table>

Impact of chronic THC exposure

- THC reduces hippocampal neuron activation
- With chronic THC exposure, neurons are gradually lost due to continual suppression
- THC users have smaller hippocampuses, and poorer memory

The Dunedin Study
N=1,037

Assessment ages

13 yrs (Pre-initiation)  18 yrs  21 yrs  32 yrs  38 yrs

1  2  3  4  5

Assessment ages


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Average IQ change:

- “Never used”
  - 99.8 to 100.6
- “Mj dependent 3+ yrs”
  - 99.7 to 93.9

Regular marijuana use during adolescence found to increase risk 2 to 5 times of developing psychosis, schizophrenia, anxiety, and depression in adulthood.

### Association between cannabis use and schizoaffective disorder

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cases</th>
<th>HR Crude</th>
<th>HR adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never used cannabis</td>
<td>39,978</td>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td>Ever used cannabis</td>
<td>5,109</td>
<td>12</td>
<td>2.1 (1.1-3.8)</td>
</tr>
<tr>
<td>&gt;50 times</td>
<td>855</td>
<td>7</td>
<td>7.5 (3.4-16.7)</td>
</tr>
</tbody>
</table>

*Adjustments for: prior personality disorders at conscription, IQ, disturbed behavior in childhood, social adjustment, risky use of alcohol, smoking, early adulthood socioeconomic position, use of other drugs, brought up in a city. The category “Ever used cannabis” includes all individuals who reported cannabis use, including those who reported “>50 times”.

**Sources:** Griffith-Lendering, Addiction, 108(4), 733-740. Manrique-Garcia, BMC Psychiatry, 12, 112.
E-Cigarettes

• Most e-cigarettes consist of four different components, including:
  – a cartridge or reservoir, which holds a liquid solution (e-liquid or e-juice) containing varying amounts of nicotine, flavorings, and other chemicals
  – a heating element (atomizer)
  – a power source (usually a battery)
  – a mouthpiece that the person uses to inhale

• In many e-cigarettes, puffing activates the battery-powered heating device, which vaporizes the liquid in the cartridge. The person then inhales the resulting aerosol or vapor (called vaping).

THE EVOLUTION OF E-CIGS

FIRST GENERATION
The Cigalike - an early vaping device made to resemble a traditional cigarette. Poor battery life and an overall unsatisfying experience. Many people using them as an aid to quit smoking cigarettes found them less useful than later devices.

SECOND GENERATION
Vape Pens - so called because they resemble pens. Much larger than the first generation devices and with an improved battery life. Many second generation devices are still available, often used as a 'starter kit' for those new to vaping.

THIRD GENERATION
Much bulkier devices, with a clear tank and a larger battery, or a chunkier pen style, looking somewhat like Dr Who's 'Sonic Screwdriver.' Devices of this generation introduced a higher degree of control over the individual's vaping experience.

FOURTH GENERATION
Light years ahead of the earliest devices, the latest generation offer considerable advances in technology, and the ability to modify and adjust devices to the user’s specifications - coils, wicks etc - giving the best experience possible.

“Vape Mod” vs. “Pod Mod”

• Vape mod
  – Refillable tank, customizable coils, etc.
  – Used by enthusiasts (cloud chasers, tricksters, etc.) → people that want to tinker with and improve the performance of their vaporizers

• Pod mod
  – Closed system where vape juice is stored in disposable pods
  – Popular with people that want a simple, easy to use device (e.g. former smokers)

http://blog.misticecigs.com/vape-mods-vs-pod-mods-how-are-they-different
“Juuling”

Juul and Similar Products

Juul

KandyPen’s Rubi

MLV’s Phix

Mylé

ITG Brands’ myblu

Altria’s MarkTen Elite

What’s in a Juul Pod?

1-2 packs of cigarettes, or 20-40 cigarettes are equal to 1 juul pod

Source: Vox.com

UNDER THE RADAR

The sleek Juul device is the market leader. But the features that make it so attractive to the general public also make it easy for teens to conceal.

- The exhaled aerosol is less visible than cigarette emissions
- Pre-packaged pods come in flavors like mango and crème brûlée
- The device resembles a flash drive
- Battery charges in an hour via a USB port

THE TREND

Percentage of high schoolers who, in the past month, have:

- Smoked: 16%
- Vaped: 12%
- 8%
- 2%


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Freebase vs. Nic-salt

• Freebase nicotine treated with benzoic acid creates a nicotine salt
Phillip morris vs. Pax Labs (JUUL)

• Phillip Morris stripped away the naturally occurring nicotine salts in leaf tobacco with ammonia to create freebase nicotine

• In 2015, Pax Labs (Juul) turned this strategy on its head, taking the freebase nicotine and adding benzoic acid to create nicotine-salt e-juice
  – Benzoic acid ↓ alkalinity in freebase nicotine allowing manufacturers to increase the nicotine level in nic-salts
  – Benzoic acid nic-salts cross the blood brain barrier faster than freebase nicotine for a smoother throat hit
  – Nic-salt ejuices can be vaped at a lower temperature, bringing cheaper and less powerful devices back in the game again

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Nic-SALT E-juice more similar to combustible Cigarette

https://www.vapor4life.com/blog/salt-nic-ejuice-guide/
“Dripping” vs. “Dabbing”

• **Dripping (nicotine)** ➔ adolescents modify e-cigarette by dripping nicotine refill liquid directly onto the coil to increase the “nicotine hit”
  
  (ASAM Principles, Chap 20)
  
  – 25% of adolescents who use e-cigarettes have engaged in “dripping” in a recent survey
  
  – manufacturers are reportedly making their coils more accessible to enable this practice

• **Dabbing (THC)** ➔
  
  – “dab rig” is the water-filled device through which user inhales vapor
  
  – Affixed to the dab rig is a domeless nail ➔ heated with blowtorch until it is red-hot
  
  – Wait 20-40 seconds, then touch a piece of “MJ wax” to nail, producing vapor that is inhaled through the rig

https://vapevetstore.com/blogs/vaporizer-learning-center/vaping-vs-dabbing-vs-smoking-key-differences
E-cig increase risk to cigarettes

• A study showed that students who had used e-cigarettes by the time they started 9th grade were more likely than others to start smoking cigarettes and other smokable tobacco products within the next year.

• Another study has shown an association between e-cigarette smoking and progression to smoking actual cigarettes.
  • This study suggests that e-cigarettes may actually encourage cigarette smoking in adolescents.

• Another study shows that high school students who used e-cigarettes in the last month were about 7 times more likely to report that they smoked cigarettes when asked approximately 6 months later, as compared to students who said they didn't use e-cigarettes.


FOUR-FOLD INCREASE IN CIGARETTE SMOKING INITIATION AMONG TEENS

Youth who used e-cigarettes were more likely to be smoking combustible cigarettes the next time they were observed.

Those who smoked combustible cigarettes were not more likely to be smoking e-cigarettes at a later time.
How do e-cigarettes affect the brain?

• The nicotine in e-liquids is readily absorbed from the lungs into the bloodstream when a person uses an e-cigarette. Upon entering the blood, nicotine stimulates the adrenal glands to release the hormone epinephrine (adrenaline).

• Epinephrine stimulates the central nervous system and increases blood pressure, breathing, and heart rate.
  – As with most addictive substances, nicotine activates the brain’s reward circuits and also increases levels of a chemical messenger in the brain called dopamine, which reinforces rewarding behaviors.

• Pleasure caused by nicotine’s interaction with the reward circuit motivates some people to use nicotine again and again, despite risks to their health and well-being.
ADOLESCENTS USING E-CIGS ARE AT HIGHER RISK TO PROGRESS TO MARIJUANA USE

Dai, Pediatrics, 2018

<table>
<thead>
<tr>
<th>Marijuana Never Users at Wave 1</th>
<th>E-cigarette Ever Use at Wave 1</th>
<th>Marijuana P12M Use at Wave 2</th>
<th>Marijuana Heavy Use at Wave 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Weighted % (95% CI)</td>
<td>aOR*</td>
</tr>
<tr>
<td>Aged 12–14 (n = 5901) b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n = 5703)</td>
<td>321</td>
<td>5.5 (4.9–6.2)</td>
<td>REF</td>
</tr>
<tr>
<td>Yes (n = 177)</td>
<td>52</td>
<td>29.2 (23.0–36.2)</td>
<td>2.7 (1.7–43)**</td>
</tr>
<tr>
<td>Aged 15–17 (n = 4463) b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n = 4117)</td>
<td>438</td>
<td>10.6 (9.5–11.9)</td>
<td>REF</td>
</tr>
<tr>
<td>Yes (n = 334)</td>
<td>85</td>
<td>25.3 (21.0–30.3)</td>
<td>1.6 (1.2–2.3)**</td>
</tr>
<tr>
<td>Interaction between age group and e-cigarette ever use</td>
<td>—</td>
<td>—</td>
<td>2.1 (1.3–3.3)**</td>
</tr>
</tbody>
</table>

*aOR: adjusted odds ratio; **p < 0.01; ***p < 0.001.
ADOLESCENTS USING E-CIGS ARE AT HIGHER RISK TO PROGRESS TO MARIJUANA USE

Table 3. Association of Baseline Multiple Tobacco Product Use and Covariates with Multiple Marijuana Product Outcomes at a 24-month Follow-up

<table>
<thead>
<tr>
<th>Baseline Regressors Ever Use</th>
<th>Outcome at 24-Month Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Combustible Marijuana</td>
</tr>
<tr>
<td>Adjusted models(^c)</td>
<td>1.90 (1.01, 3.57)†</td>
</tr>
<tr>
<td>Combustible cigarettes</td>
<td>3.15 (2.14, 4.64)†</td>
</tr>
<tr>
<td>E-cigarettes</td>
<td>3.91 (2.56, 5.97)†</td>
</tr>
<tr>
<td>Hookah</td>
<td>3.79 (2.73, 5.27)†</td>
</tr>
<tr>
<td>Any product</td>
<td>2.55 (2.01, 3.24)†</td>
</tr>
</tbody>
</table>

E-cigarette and hookah use at age 14 was associated with a 3.6 to 4-fold increase in the odds of initiating and currently using marijuana two years later.

Audrain-McGovern, Pediatrics, 2018
What are the health effects of e-cigarettes? Are they safer than tobacco cigarettes?

- Research suggests Nicotine can prime the brain’s reward system, putting vapers at risk for addiction to other drugs.9
- Also, e-cigarette use exposes the lungs to a variety of chemicals, including those added to e-liquids, and other chemicals produced during the heating/vaporizing process. A study of some e-cigarette products found the vapor contains known carcinogens and toxic chemicals,
  - as well as potentially toxic metal nanoparticles from the device itself.
  - Certain brands contain high levels of nickel and chromium, which may come from the heating coils of the vaporizing device.
  - May also contain low levels of cadmium, a toxic metal that can cause breathing problems and disease.
  - More research is needed on the health consequences of repeated exposure to these chemicals.

Nicotine and Brain Reward System

• Because nicotine affects the development of the brain's reward system, continued e-cigarette use can not only lead to nicotine addiction, but it also can make other drugs such as cocaine and methamphetamine more pleasurable to a teen's developing brain.

• Nicotine also affects the development of brain circuits that control attention and learning.
  – Other risks include mood disorders and permanent problems with impulse control—failure to fight an urge or impulse that may harm oneself or others.

77% of vaping-related illnesses linked to THC products, CDC says

- About three-fourths of patients with vaping-related illnesses nationwide reported using products containing THC, according to CDC's *Morbidity and Mortality Weekly Report* published Sept. 27.
- The investigation into the source of the illnesses is ongoing. However, the CDC report provides the first national data regarding the sex, age and type of vaping products used in the cases reported to CDC.
- Of the 514 patients who self-reported data on their vaping habits, 76.9 percent used products containing THC. Thirty-six percent said they used THC products exclusively, while 16 percent used solely nicotine products.
- A separate *Morbidity and Mortality Weekly Report* containing information on 86 patients in Wisconsin and Illinois found that most THC products were packaged cartridges obtained through informal sources such as friends, family or illicit dealers. Though more information is needed to know the exact cause of the lung injuries, CDC recommends people refrain from using e-cigarettes or vaping products, specifically those containing THC.
- As of September 24, the CDC has reported 805 confirmed and probable cases of vaping-related illnesses in 46 states and the U.S. Virgin Islands. Among those cases, there have been 12 deaths.

• Thank You
• Questions?
• If you think your Child may have a problem, contact Akron Children’s Addiction Service Program at

• 330-543-3343