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Child Law Practice

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Helping Lawyers Help Kids

EXPERT EXCHANGE

The Amazing Teen Brain: What Every Child Advocate Needs to Know

by Linda Burgess Chamberlain

As a child advocate, you are well aware that your teen clients think and behave differently. Recent scientific discoveries on teen brain development are helping us to better understand and respond to the sometimes unpredictable, frequently frustrating, and totally amazing teen years.

Around puberty, the teen brain begins to undergo major changes, many of which will not be completed until the early to mid-20s. The massive surges of hormones teens experience are associated with gender-specific changes in the brain that may help explain some of the differences between male and female brains. The teen brain is a work-in-progress that is far from complete.

During adolescence the brain becomes more efficient and develops more advanced skills. Brain connections that are stimulated and used repeatedly are strengthened while unused connections wither away. Similar to early childhood, this developmental window of opportunity is a period of "*use it or lose it*." Adolescence is also a time of enhanced vulnerability. Rapid changes make the teen brain more sensitive to stress and neurotoxins, such as alcohol, tobacco, and drugs. How teens spend their time influences the organization and capacity of their brains. This raises questions about whether they are engaged in activities that promote active learning and skill development, such as volunteering with community services, practicing public speaking, learning to play an instrument, engaging in physical activities, and spending quality time with adults.

While you may think teen brain development does not directly affect your advocacy with teens, you may be surprised. Every youth-serving professional should have a basic understanding of teen brain development. The implications for frontline child advocates who work with at-risk youth is even greater. Many of these teens have experienced early trauma such as child abuse or domestic violence. Trauma can impact brain development and consequently behavior.

What is going on in your teen clients' lives is influenced by their developing brains and life experiences—their behaviors, relationships, decisions, emotions, and just about everything that makes them unique. Developing a basic understanding of teen brain development can guide your interactions, enhance your communication skills, and help shape your advocacy for teens.

"What Were You Thinking?"

Challenging teen behaviors, such as sudden mood-swings, extreme risk-taking behaviors, and failure to follow instructions make sense when we understand what is happening in the teen brain. Teens lack all of the hardware in their brains to think like an adult. The outer covering of the brain, the cortex, goes through extensive remodeling during adolescence. Often referred to as the "intellectual brain," this upper region of the brain is responsible for reason, logic, and rational thinking.

The prefrontal cortex is located right behind the forehead. It has a leading role in judgment, impulse control, problem-solving, organization and planning, multitasking, goal setting, and other essential skills. Following a growth spurt around age nine or 10 when the prefrontal cortex actually thickens,

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What's Inside:

ABA *Child Law* PRACTICE

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ABA Child Law Practice (CLP) provides lawyers, judges and other professionals current information to enhance their knowledge and skills, and improve the decisions they make on behalf of children and families. Topics include: abuse and neglect, adoption, foster care, termination of parental rights, juvenile justice, and tort actions involving children and families.

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this area of the brain then goes through extensive pruning to eliminate unused brain connections. *Nature saves the best for last*—the prefrontal cortex will not mature until the early 20s when brain connections get a final coating of insulation, called myelin, which increases the brain's speed and efficiency.

Teens may not be able to respond rationally when asked "What were you thinking?" because they reacted impulsively without the benefit of a mature prefrontal cortex to think things through first. The teen brain is still developing the thought patterns and skills for rational thinking and decision making. This is new terrain for the teen brain as teens develop more advanced cognitive skills to ask "how" and "why" questions, analyze more complex issues, and evaluate alternatives in decision making.

During adolescence, short-term memory increases by approximately 30 percent. Teens have tremendous capacity for acquiring new knowledge and skills. Even so, prefrontal cortex functions such as prioritizing what is important and developing organizational skills, challenge most teens. Asking a teen to multitask (i.e., "Take these papers to your guardian and have them signed, return the signed papers to your counselor, and schedule a follow-up appointment in two weeks.") can overwhelm a teen brain that is just learning to sort and prioritize information. Add stress to the scenario, and a teen may appear defiant when really they are overwhelmed with too much information.

While part of adolescence is about seeking new experiences and independence, teens still need lots of quality time with healthy adults to help shape their brains and learn the skills to transition into adulthood. They need the guidance of adults' mature prefrontal cortexes, even more so when they have histories of trauma. Traumatized children often spend more time in the lower "survival" regions of the brain. While this shows the extraordinary ability of the brain to adapt to its environment, it comes at a high cost—spending less time in the cortex. Teens with a significant history of trauma may have deficits in cortical development and skills. Under stress, they may be more reactive and impulsive because it is harder for them to get to their upper brain/cortex. Adult mentoring can help teens model healthy behaviors and provide positive learning experiences to maximize cortical development during adolescence.

Strategies:

- Encourage activities for teens that allow time for active learning and positive social interactions (afterschool activities, sports, etc.). Teens in foster care placements should not miss out on school and extracurricular activities that are available to all students because of their foster care status.
- Educational stability is key to promoting active learning and academic success. When foster placements must change, advocate for the teen to remain in the same school to avoid disrupting the teen's education.
- Recognize trauma can impact brain development. It is important to meet each child at her developmental level rather than base expectations on age or grade in school. When a child has a long trauma history, it is not unusual to see significant developmental delays in reading, speech, social skills, and impulse control. These skills are cortical activities that require lots of energy and an ability to focus, which can be compromised when a child does not feel safe, nurtured, and stimulated in their environment.
- Create opportunities for healthy adults to spend quality time actively engaging with teens.

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Legal advocates, foster parents, caseworkers, relatives, Big Brothers/Big Sisters, mentors, teachers, coaches, pastors and other adults can positively influence a teen's life.

- When interacting with teens, communicate one task at a time and help identify priorities. Don't overwhelm teens with too many decisions at once.
- Create reminders by posting notes, setting up calendars, using erasable message boards and other strategies to help teens identify and process tasks.

Boys vs. Girls

Gender influences brain structure and function. Being aware of these differences can help you understand common behavioral patterns in boys and girls. The cerebral cortex is composed of gray and white matter. The female brain has more gray matter, which is densely packed with cell bodies. Having more gray matter may explain why girls tend to be more efficient in processing information, have stronger verbal skills, and often excel at juggling several activities. Boys have more white matter, which consists of insulated axons that form connections between brain cells. Having more white matter helps the male brain transfer information throughout the brain, which can enhance spatial skills, such as aiming at targets, navigation, and mathematical problem solving.

Several structures in the limbic system, the emotional core of the brain, grow differently in teen boys and girls. The hippocampus, which transfers new information to long-term memory, is sensitive to the female hormone, estrogen, and grows faster in girls. Scientists believe that a larger hippocampus may explain girls' strong social skills—sizing up social situations, being emotionally supportive, and coordinating complex relationships. The amygdala and the hypothalamus are sensitive to male sex hormones and grow larger in boys. Both structures are involved in the body's response to fear and danger, often called the "fight or flight" response. Enjoying contact sports, having increased sexual desires, and being more assertive are behaviors that make sense due to the male growth spurt in the amygdala and hypothalamus.

Given the differences between male and female brains, it is not surprising that boys and girls learn differently. Understanding some of these differences is relevant to anyone who is trying to reach and influence teens—

- *Boys* often learn better and have fewer impulsive behaviors when they can move around while they are learning. They typically need more variety to engage their attention and keep focused. *Girls* can typically focus on one activity or subject for longer periods and are less likely to get bored.
- *Boys* are more oriented towards spatial thinking and therefore often need more physical space to learn (spreading out their work etc.). *Girls* learn best when things are conceptualized into everyday language with examples and details.
- *Boys* tend to prefer coded language and jargon and learn more from diagrams, charts, and symbols. *Girls* are often better listeners and can absorb more details from conversations.

Strategies:

- Recognize that girls' and boys' brains develop differently, which influences how they process information and solve problems. Girls' brains mature sooner than boys.' Think about gender differences when interacting with a teen. Avoid one-size-fits-all approaches.
- Promote gender-specific enrichment activities tailored to a teen's interests. Provide additional support and learning opportunities to promote skill development in areas where a teen is particularly challenged.
- Provide opportunities for teens to develop social skills through small groups and one-on-one with adults to promote closer bonding. This especially benefits teen boys.

Managing Emotions

The core of our emotions—the limbic system—lies deep in the center of the brain. The limbic region, which includes the amygdala and the hippocampus, goes through major transformations during adolescence. It is no wonder that youth sometimes feel like they are on an emotional roller coaster as they navigate the daily drama of school, relationships, and life in general, in addition to the many changes occurring in their bodies and brains.

While adults rely on their cortexes to interpret and think through their emotions, teens rely more on the primitive limbic system. Changes in the teen brain slow teens' ability to identify emotions—their own and those of others. Teens frequently misinterpret other people's emotions. Often they confuse anger with sadness or concern. Without the advantage of a mature cortex to override the more impulsive limbic response, the teen brain is vulnerable to stress. In emotionally-charged situations, teens tend to overreact and escalate their emotions.

Lack of sleep can affect teens' brain development and their ability to manage their emotions. The brain chemicals that induce sleep also help build brain connections. Due to changes occurring in the sleep center of the teen brain, teens need more sleep than adults—approximately 9½ hours a night. Many teens are sleep deprived not only due to busy schedules but also

because melatonin, a hormone that induces sleep, is secreted two hours later at night during adolescence and stays in their systems two hours later in the morning compared to childhood.

Teens are often wide awake at bedtime and have difficulty waking up at the usual time in the morning. This can lead to chronic sleep deprivation. Sleep deprivation can look like or worsen symptoms of ADHD (attention deficit/hyperactivity disorder) in children. Sleep-deprived teens are more likely to be depressed, lack control of their emotions, and act aggressively. Adequate sleep is particularly challenging for traumatized youth because of sleep problems associated with early trauma, such as night terrors, repeated night wakings, and fear of going to sleep.

Strategies:

- When a teen seems upset or angry, respond calmly. Limit your emotions to prevent prompting or escalating an emotional (and often inaccurate) response.
- Clearly state your feelings or concerns, one at a time. Avoid communicating your emotions through facial expressions, which teens often misinterpret.
- Encourage teens to talk about their feelings by asking open-ended questions in a safe and supportive environment where their feelings can be acknowledged without judgment.
- Help teens find healthy ways to deal with stress, such as physical exercise, journaling, and peer support groups.
- Ask about sleep patterns if teens experience behavioral and/or emotional problems. Find out if they're getting enough sleep and suggest changes if not.
- Encourage teens who are having problems getting enough sleep to avoid stimulating activities, such as playing computer games, exercising, or drinking caffeinated beverages close to bedtime. Talk with them about ways to wind down when trying to go to sleep, such as reading, listening to soft music, and relaxation activities.

Resources

Web Sites:

www.cdc.gov/HealthyYouth/yrbs/ This Web site provides national data on adolescents' health and risk behaviors, including alcohol, drugs, and tobacco use from the Youth Risk Behavior Surveillance System.

www.pbs.org/wgbh/pages/frontline/shows/teenbrain/
"Inside the Teen Brain" describes what science tells us about how the teen brain works.

www.nimh.nih.gov/Publicat/teenbrain.cfm
A brief overview of research into brain development during adolescence.

Books:

Walsh, David. *Why Do They Act That Way?* New York, NY: Free Press, 2005.

Strauch, Barbara. *The Primal Teen: What the New Discoveries About the Teenage Brain Tell Us about Our Kids.* New York, NY: Doubleday, 2003.

Wolfe, David, Peter Jaffe, and Claire Crooks. *Adolescent Risk Behaviors: Why Teens Experiment and Strategies to Keep Them Safe.* New Haven, CT: Yale University Press, 2006.

Journal Articles:

Giedd, J. N. et al. "Brain Development during Childhood and Adolescence: A Longitudinal MRI Study." *Nature Neuroscience* 2(10), October 1999, 861-863.

Paus, T. et al. "Maturation of White Matter in the Human Brain: A Review of Magnetic Resonance Studies." *Brain Research Bulletin* 54(3), 2001, 255-266.

Spear, Linda Patia. "Neurobehavioral Changes in Adolescence." *Current Directions in Psychological Science* 9(4), 2000, 111-114.

Tapert, S.F. et al. "Substance Use and Withdrawal: Neuropsychological Functioning over 8 Years in Youth." *Journal of International Psychology and Sociology* 8, 2002, 873-883.

DeBellis, M. et al. "Hippocampal Volume in Adolescent-Onset Alcohol Use Disorders." *American Journal of Psychiatry* 157, 2000, 737-744.

Brown, S. A. et al. "Neurocognitive Functioning of Adolescents: Effects of Protracted Alcohol Use." *Alcoholism Clinical and Experimental Research* 24(2), 2000, 164-171.

Monti, P. M. et al. "Adolescence: Booze, Brains and Behavior." *Alcoholism Clinical and Experimental Research* 29(2), 2005, 207-220.

Abreu-Villaco, Y. et al. "Nicotine is a Neurotoxin in the Adolescent Brain: Critical Periods, Patterns of Exposure, Regional Selectivity and Dose Thresholds for Macromolecular Alterations." *Brain Research* 979, 2003, 114-128.

The Risk-Seeking Teen

What is it about adolescence that causes teens to take risks—often extreme risks—without considering the consequences? While we know what puts teens "at-risk"—poverty, neglect, violence, and substance abuse—we are less clear on why teens are more likely to take risks than adults. There is little question that puberty and the developing teen brain have a major role in teens' quests for new experiences and thrills.

To start, teens lack a mature frontal cortex to suppress those "just do it" impulses or to fully consider the consequences of their actions. Chemical changes occurring in the teen brain are also likely contributors. Levels of dopamine, the "feel good" neurotransmitter that is part of the brain's pleasure and reward circuit, are declining between childhood and adulthood. One way to get that dopamine "high" is thrill-seeking. In addition, levels of serotonin, a brain chemical that helps control impulsive behavior, fluctuate during adolescence.

Teens perceive risk differently than adults—they are more enticed by the novelty of the experience. They also have a higher sensitivity

to reward which means that when they take a risk and win the reward, they are more driven to keep taking that risk over and over again even when the strategy does not work anymore. Research shows that when other teens are present, teens' willingness to take risks increases dramatically whether it is driving a car or hanging out with a street gang.

Given teens' propensity for risk-taking, we need to create more options for positive risks under structured circumstances. Opportunities for teens to do new things and have novel experiences are essential development tasks. The types of activities depend on each teen and his/her life circumstances. It might be surfing waves in the ocean, learning to use power tools, or organizing a youth rally. There is one thing we can count on—if we do not provide them opportunities to build their confidence and independence through reasonable risk taking, they will find their own ways to take risks without adult supervision.

Drugs and the Teen Brain

The tendency towards risk-seeking and novel experiences during adolescence increases the likelihood that a teen will experiment with alcohol and drugs. Drugs such as Ecstasy and methamphetamine cause imbalances in brain chemicals and can lead to problems with impulse control and depression.

Even the nicotine in tobacco interferes with healthy brain development. Nicotine interacts with at least 20 different chemicals in the brain and can damage the hippocampus (the brain's memory maker). The neurotoxic effects of nicotine on the brain may help explain why teen smokers are more prone to infections and depression.

Alcohol is still the most common substance that teens try. According to national data, more than one out of 10 eighth graders reported heavy drinking (consuming five or more alcoholic beverages in a row) in the past two weeks. Research on the impact of alcohol on the teen brain has led to some startling discoveries:

1. Teens are more likely to black out (conscious but can't remember) than pass out and are less likely to succumb to the sedative effects of alcohol. As a result, they are less sensitive to the warning signs of inebriation and can continue consuming alcohol and engaging in other risky behaviors, such as driving while intoxicated, without recognizing their level of impairment.
2. The hippocampus is approximately 10 percent smaller in heavy teen drinkers. Young drinkers have more long-term memory impairment.
3. Teens are more prone to addiction than adults. The younger teens are when they start drinking alcohol the more quickly they become addicted.

Strategies:

- When teens engage in bad or risky behavior, for example truancy, violence, and drug use, be mindful of how the teen brain is developing and transitioning. Know how these developmental changes affect teens' thought processes and behaviors so you can talk and relate to your teen client effectively, make better decisions on behalf of your client, and support positive outcomes.
- Ensure teens have opportunities for novel, challenging experiences, such as hiking, rock climbing, outdoor recreational activities, and chaperoned all-night teen events.
- Encourage caregivers to give teens an active role in discussing family rules, curfews, and consequences for their behaviors and to listen to how they evaluate risks and decide what is important.
- Recognize that teens act differently under the influence of alcohol compared to adults and that there is no known "safe" level of alcohol consumption for teen brain development.
- If a teen drives, encourage caregivers to set boundaries for driving that limit a teen driver's opportunities to take risks, such as limiting the number of friends allowed in the car.

A Peaceful Adolescence

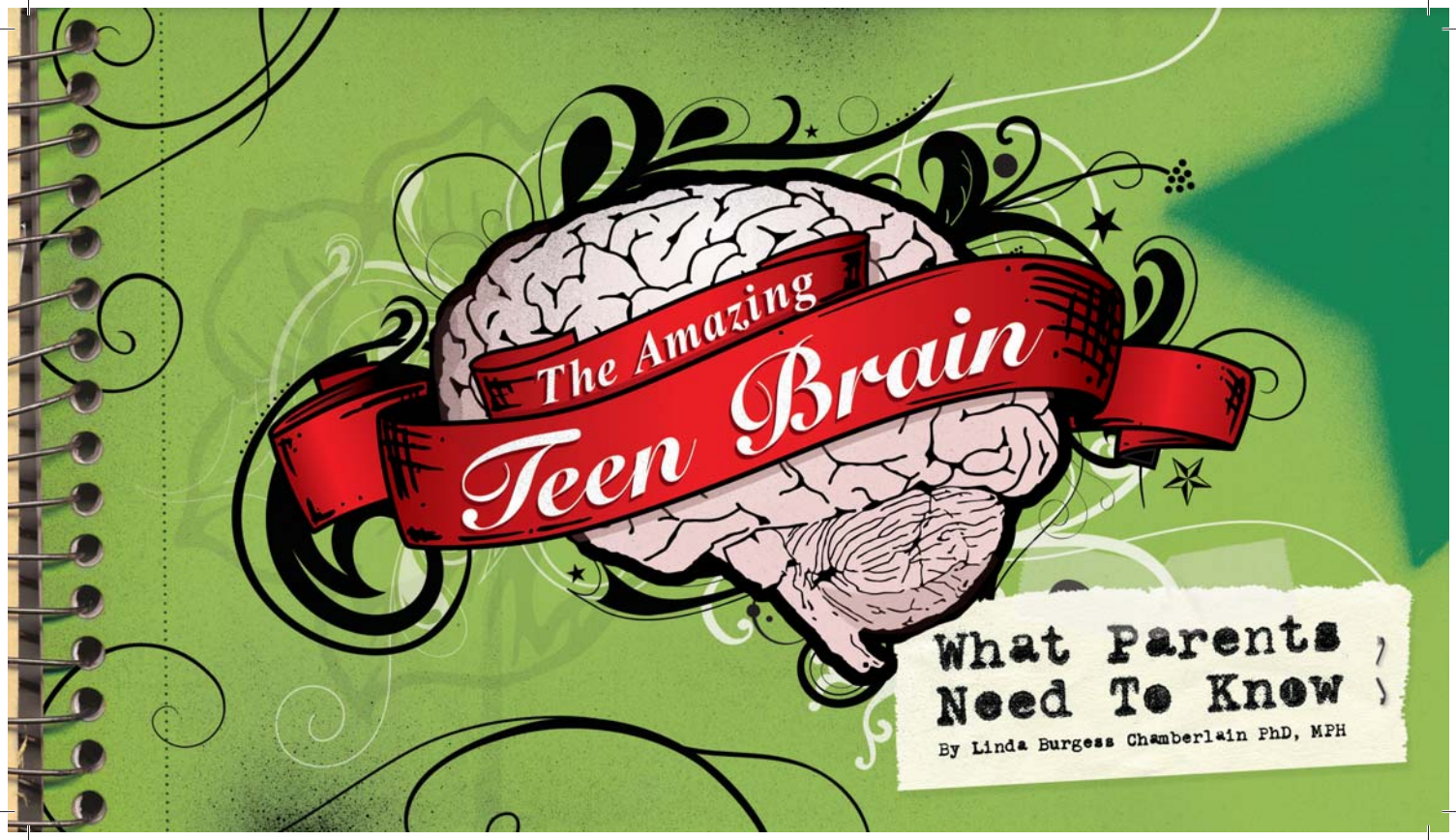
Dr. Lawrence Steinberg, an expert in teen development, compares the teenage brain to "a car with a good accelerator but a weak brake." Teens are acquiring the "hardware" in their brains to function like adults—but they are not there yet. Teens need our guidance and an enriched environment to optimize this extraordinary window of opportunity in brain development.

The importance of a stimulating and supportive learning environment is all the more important when early trauma has interfered with optimal brain development. Under the best circumstances, it is realistic to expect some chaos, conflict, emotional peaks and valleys, risk taking, and rule breaking as teens navigate the tremendous physical and neurodevelopmental changes that begin at puberty and continue into the mid-20s.

By creating opportunities for teens to practice good decision making, develop new skills, seek adventure through structured risk taking, and benefit from the experience of our mature cortexes, we can promote resilience and help teens reach their potential.

Linda Burgess Chamberlain, PhD, MPH, is the founding director of the Alaska Family Violence Prevention Project. She is a health scientist and sought-after speaker on childhood exposure to violence and brain development. Contact her through **www.drlindachamberlain.com**

An earlier version of this article was published by the Institute for Safe Families. It has been updated and expanded by the author to address issues unique to traumatized and at-risk youth.



A Work in Progress

The teen brain is still growing! During the teen years, the brain is going through lots of changes and building millions of new connections. These changes will help the brain to become faster, sharper, and smarter. Parents and other caring adults can help teens to grow healthy, strong brains. Here's how.

Encourage Your Teen to Do Things That Help the Brain to Grow

Starting around age 9 to 10, the brain has a growth spurt that lasts into the mid-20s. The outer covering of the brain (called the cortex) gets thicker. The brain follows the simple principle of use it or lose it: the brain connections that teens use again and again become stronger. The connections they do not use just fade away. How teens spend their time matters. What teens do will help to shape their brains.

One of the last areas of the brain to mature is called the prefrontal cortex. Located right behind the forehead, the prefrontal cortex helps teens to learn how to solve problems, set goals, and control their feelings.

Here are some ways you can help your teen's brain to grow:

- Encourage your teen to try a new hobby or practice a new skill like learning a musical instrument.
- Help your teen learn how to manage time and tasks. Teach your teen to make lists of things to do. Help her or him use a calendar to keep up with homework and chores.
- Help your teen to be physically active. Sports, exercise, and being outdoors are good for the brain.
- Work with your teen to set time limits for the computer and TV. Also set limits for cell phones and playing video games.
- Find ways to expand your teen's role in family decision making, how to budget money, and other tasks.

Talk with Your Teen

The teen years can be challenging. You can make it a more peaceful time by understanding how the teen brain thinks. When it comes to emotions, teens are working out of a lower area of the brain called the limbic region (the "emotional center" of the brain).

Teens often have mood swings. And they often act on how they feel before thinking things through. Changes occurring in the adolescent brain slow down a teen's ability to identify emotions. They may struggle to understand their own feelings and the feelings of others. Teens often misinterpret the look on someone's face or body language. For example, they may see anger instead of fear or concern. As their brains mature, teens will become more skilled at identifying and thinking through their emotions.

The following steps can help you talk with your teen:

- Say clearly how you feel. Use "I" statements such as "I care about you" and explain what is making you feel that way: "I am worried because you didn't call me to tell me you'd be late…" Be sure to use words – not facial expressions – to say what you mean and avoid generalizing, blaming statements ("You never do what I ask. ")
- Ask your teen how he or she feels. Remember that your teen's feelings may change a lot. Mood swings are not unusual.
- If your teen is angry or upset, stay calm. Don't lose your temper.
- Set some rules for talking about problems. Say "I want to know why you are upset. But you cannot yell, scream, or swear at me. "

Help Your Teen Get Lots of Sleep

Sleep is very important for teens and their growing brains. During these years, major changes occur in the sleep centers of the brain. The brain releases a chemical that makes teens get sleepy two hours later than when they were children. Teens do not feel tired until later at night and have a harder time waking up early. The chemicals that control teen sleep patterns also help to build important brain connections. Teens need over nine hours of sleep every night.

Here are ways you can help your teen to get enough sleep:

- Talk about why teens need more sleep. Sleep helps to build a stronger, smarter brain. Sleep helps to lower stress. Sleep helps with memory. Teens who get more sleep do better in school.
- Help your teen plan for time to sleep. Sleeping in on the weekend can be a good thing!
- Talk about ways to relax before going to bed. That means no video games, no heavy exercise, and no coffee, soda, or energy drinks late at night.

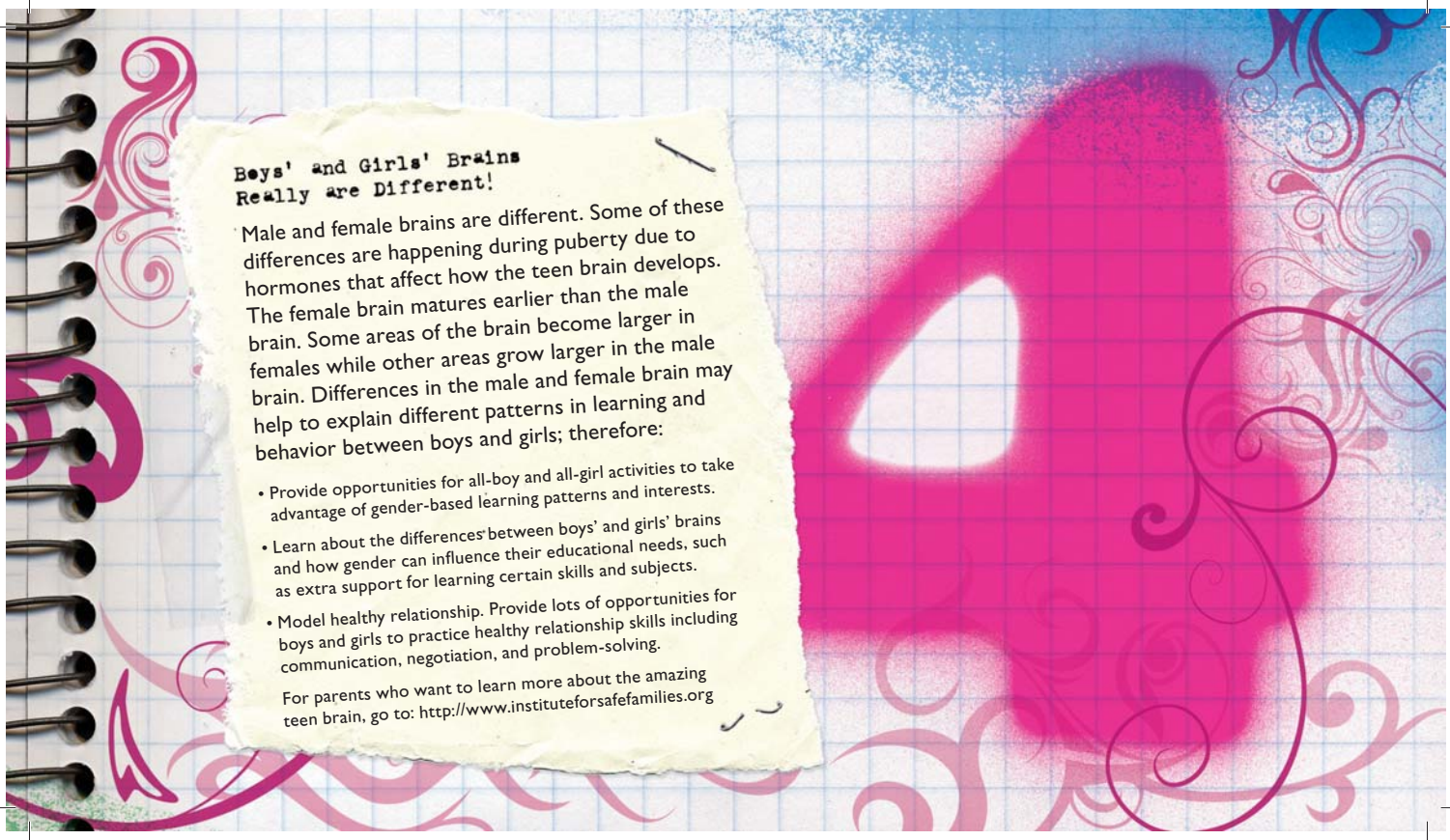
Help Your Teen Learn How to Make Good Decisions

Teens are drawn to new and exciting experiences. They want to be free and do things on their own. Chemical changes in the brain motivate teens to look for risks and challenges. This is normal. But, the part of the brain that helps teens assess risk and control impulses is still growing. This means that teens may not think about the consequences of their actions.

Teens need your help to think through the outcomes of their decisions. Teens also need practice in making decisions. You can provide chances to share responsibility, to make decisions, and to weigh the pros and cons of different types of choices. This will help your teen develop good judgment.

You Can:

- Help your teen take positive risks, like trying out for a new sport, making new friends, or visiting new places. This will build confidence and self control.
- Let your teen decide what, when, and how to do things. This will help your teen become a leader. Community service projects, summer jobs, and after school programs are good for the brain!
- Get to know your teen's friends. Together, set rules on how often your teen should check in with you. Say that you want to know what she or he is doing, where, and with whom. This builds trust between you.
- Work together to set rules and agree on curfews. Together, decide what will happen if your teen breaks the rules. Listen to what she or he wants. Talk about what you want for your teen.


Boys' and Girls' Brains
Really are Different!
Male and female brains are different. Some of these differences are happening during puberty due to hormones that affect how the teen brain develops. The female brain matures earlier than the male brain. Some areas of the brain become larger in females while other areas grow larger in the male brain. Differences in the male and female brain may help to explain different patterns in learning and behavior between boys and girls; therefore:
• Provide opportunities for all-boy and all-girl activities to take advantage of gender-based learning patterns and interests.
• Learn about the differences between boys' and girls' brains and how gender can influence their educational needs, such as extra support for learning certain skills and subjects.
• Model healthy relationship. Provide lots of opportunities for boys and girls to practice healthy relationship skills including communication, negotiation, and problem-solving.
For parents who want to learn more about the amazing teen brain, go to: http://www.instituteforsafefamilies.org

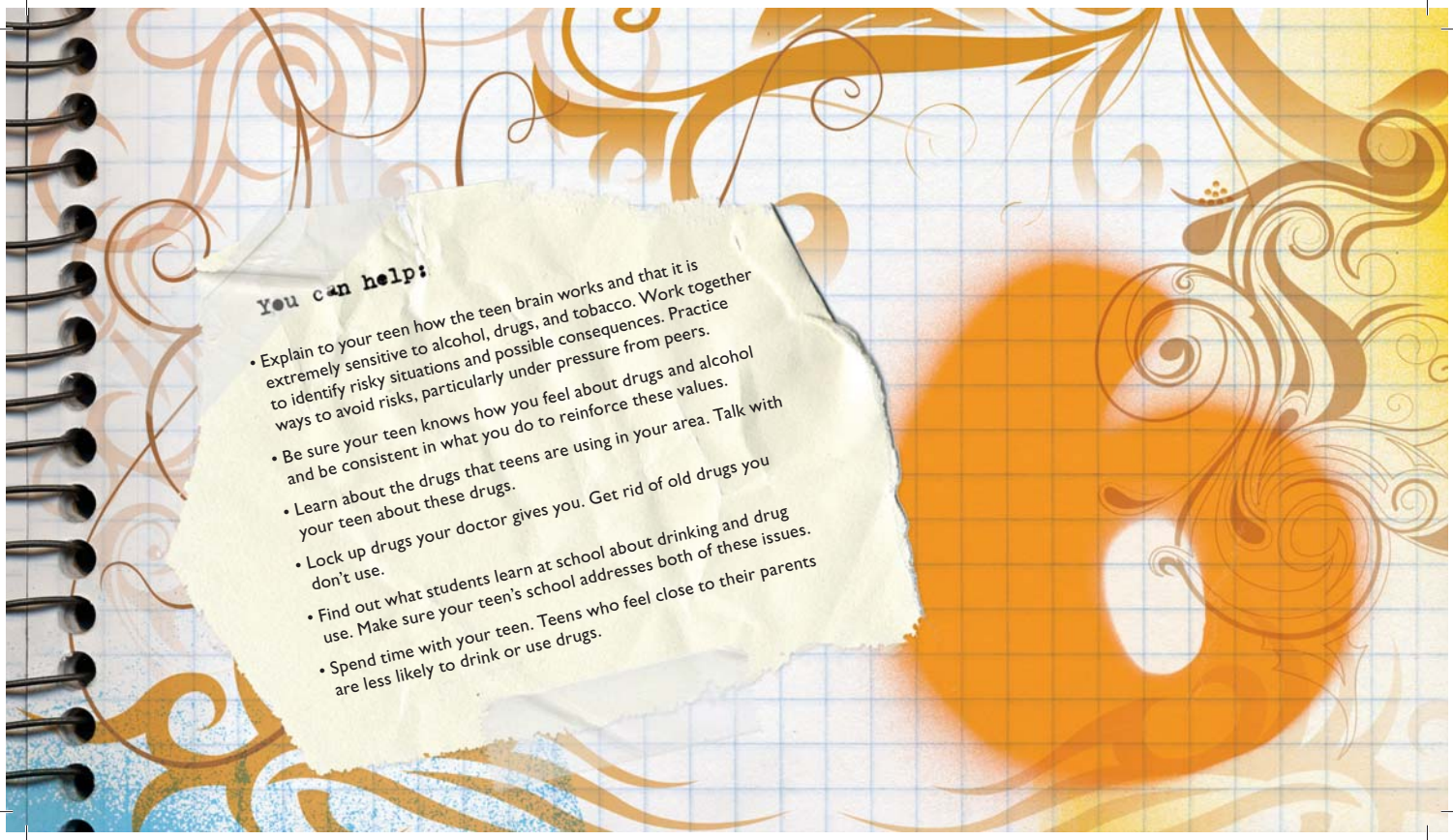

Help Your Teen Make Good Friends and Have Healthy Relationships
Teens want to be close to others. Making good friends is a big part of the teen years. This includes having girl friends and boy friends. While many parents want their teens to wait to have sex, most teens are sexually active by the time they are 20. Hormones and chemicals in the brain (called neurotransmitters) affect teens' sexual growth and desires.

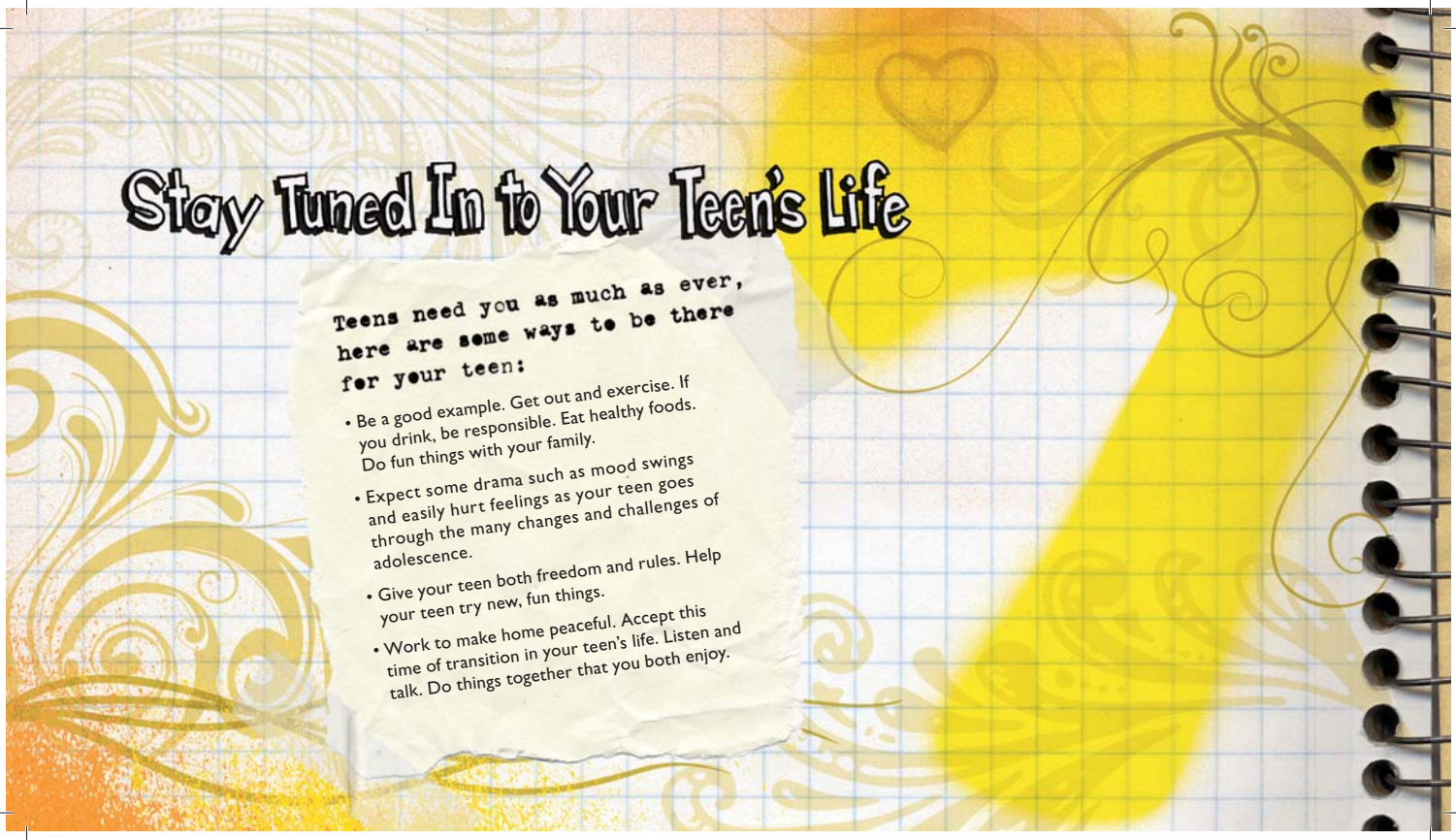
You can help your teen to have healthy relationships and make smart decisions about sex.

- Talk about the changes to the body during the teen years. These changes are a healthy, normal part of growing up.
- Let your teen ask you about love and sex. Be honest. If you don't know something, say so. Then find out the answer. Teens who talk with their parents about sex are less likely to take sexual risks. They are more likely to use condoms.
- Talk with your teen about waiting to have sex. And talk about birth control and condoms. Be sure your teen knows where to go to get them. Talking about birth control and condoms won't make your teen go out and have sex.
- Rape is too common among teens. Make sure that your teen knows that she or he has the right to say no. Make sure your teen knows that no means no. Make sure your teen knows what to do and how to get help if she or he is raped or forced into any unwanted sexual activity.
- Your teen may want to talk about private things with someone else. This might be a doctor or nurse or an aunt or a friend of yours. What you want is for your teen to be healthy and safe. So, say that it's okay for your teen to talk with someone else.

Help Your Teen Stay Away from Alcohol and Drugs

Many teens drink alcohol, use drugs, or smoke cigarettes. All of these substances can harm your teen's brain. Teens can become addicts more quickly than adults. Teen drinkers can have problems learning. Drugs like Ecstasy and Meth can cause depression.


You can help:
• Explain to your teen how the teen brain works and that it is extremely sensitive to alcohol, drugs, and tobacco. Work together to identify risky situations and possible consequences. Practice ways to avoid risks, particularly under pressure from peers.
• Be sure your teen knows how you feel about drugs and alcohol and be consistent in what you do to reinforce these values.
• Learn about the drugs that teens are using in your area. Talk with your teen about these drugs.
• Lock up drugs your doctor gives you. Get rid of old drugs you don't use.
• Find out what students learn at school about drinking and drug use. Make sure your teen's school addresses both of these issues.
• Spend time with your teen. Teens who feel close to their parents are less likely to drink or use drugs.


Stay Tuned In to Your Teen's Life
Teens need you as much as ever, here are some ways to be there for your teen:
• Be a good example. Get out and exercise. If you drink, be responsible. Eat healthy foods. Do fun things with your family.
• Expect some drama such as mood swings and easily hurt feelings as your teen goes through the many changes and challenges of adolescence.
• Give your teen both freedom and rules. Help your teen try new, fun things.
• Work to make home peaceful. Accept this time of transition in your teen's life. Listen and talk. Do things together that you both enjoy.

The Amazing Teen Brain Resources

Resources for teens and parents about healthy relationships, peer influences, and sexual risk-taking:

WHY Do They Act That Way?: A Survival Guide to the Adolescent Brain for You and Your Teen by David Walsh PhD (2004). Published by Free Press, NY, NY.

The Primal Teen: What the New Discoveries about the Teenage Brain Tell Us About Our Kids by Barbara Strauch (2003). Published by Doubleday, NY, NY.

www.advocatesforyouth.org
Provides information about adolescent sexual and reproductive health to parents, health care providers, educators, and advocates. The Parent's Sex Ed Center contains tips and resources to help parents communicate effectively with their teens.

www.shelternet.ca
Offers teens information and a quiz to help build healthy relationships. Provides suggestions for how to talk to a friend who is in an abusive relationship and explores options for how to get help and safety planning.

www.freevibe.com
Provides information and resources to teens using drugs and alcohol and offers support for those who have parents with substance abuse problems. Sponsored by the Federal government.

www.empowered.org
Provides prevention education to address bullying and peer aggression.

www.focusas.com
Serves as a clearinghouse for information, resources, and support. Large volume of resources dealing with teen and family issues including state resources.

http://au.reachout.com
Provides information about a number of mental health concerns including depression, loss and grief, and substance abuse, as well as other teen issues such as friendship.

www.teenshealth.org
Addresses a wide range of teen health concerns including cutting, tattoos, sexual health, personal safety, and diseases.

www.reachout.asn.au
Provides information about a number of mental health concerns including depression, loss and grief, and substance abuse as well as other teen issues such as friendship.

www.teenshealth.org
Addresses a wide range of teen health concerns including cutting, tattoos, sexual health, personal safety, and diseases.

www.loveisrespect.org
Targeted to 13- to 18-year-olds, this national teen dating violence resource offers teens who are experiencing dating abuse the opportunity to log in and get help from trained associates in a one-on-one private chat room. This website is co-sponsored by the National Domestic Violence Hotline and Liz Claiborne Inc.

There are a growing number of resources for learning and socioemotional development that integrate information and strategies from new research about brain development. For example:

http://www.brainwise-plc.org/
http://www.copingskills4kids.net/

The Amazing Teen Brain: What Parents Need To Know, 2009, Philadelphia, PA. This brochure was written by Linda Burgess Chamberlain, PhD, MPH with support from the Institute for Safe Families and Multiplying Connections of the Health Federation of Philadelphia and Advocates for Youth.

Linda Burgess Chamberlain is the founding director of the Alaska Family Violence Prevention Project. An epidemiologist specializing in domestic violence, she is an internationally recognized speaker on the effects of violence on children and brain development. She lives on a rural homestead outside of Homer, Alaska with her dog team. A national Kellogg Leadership Fellow, Dr. Chamberlain is also a motivational speaker and uses "lessons from the trail" to promote key strategies for teamwork and leadership.
howlinghusky@gci.net

The Institute for Safe Families (ISF) is a non-profit organization whose mission is to prevent family violence and promote the health and well being of each member of the family and their community. Since the early 1990's, ISF has developed innovative programming and built coalitions that unite health care providers with social service, policy experts, researchers, academicians, and victim/survivors. One of ISF's unique strengths has been to create forums for cross-systems dialogue aimed at building greater capacity for more effective prevention and response to family violence.
www.instituteforsafefamilies.org

Multiplying Connections of The Health Federation of Philadelphia is a cross system collaborative whose mission is to translate the research on early childhood brain development into better practice through professional training and organizational and policy change. Multiplying Connections is developing materials and strategies to promote trauma informed and developmentally appropriate care across the public child and family service system in the City of Philadelphia. This capacity building initiative is funded by the William Penn Foundation.
www.multiplyingconnections.org

Advocates for Youth is dedicated to creating programs and advocating for policies that help young people make informed and responsible decisions about their reproductive and sexual health. Advocates provides information, training, and strategic assistance to youth-serving organizations, policy makers, youth activists, and the media in the United States and the developing world.
www.advocatesforyouth.org

Design and Illustration: Peter Camburn,
About Face Design, www.aboutfacedesign.net

The Amazing Adolescent Brain: Opportunities and Vulnerabilities

Linda Chamberlain PhD MPH

www.drlindachamberlain.com

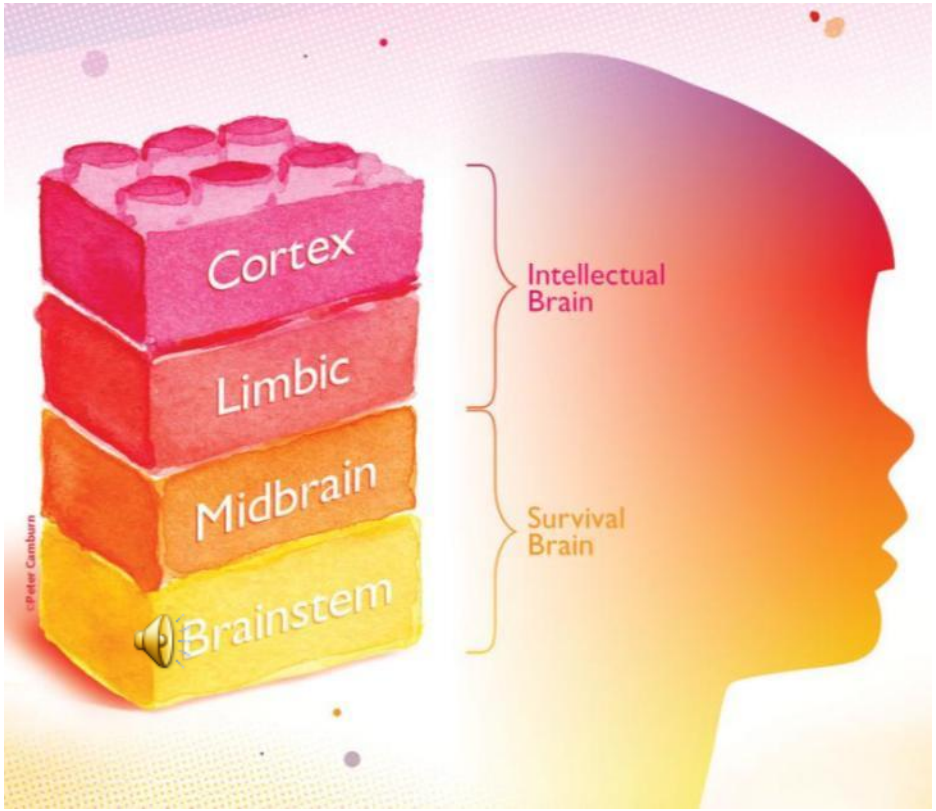
Brain-Body Strategies are integrated into this presentation.
Everything is an invitation.

What We're Talking About

- Adolescence is a critical period in brain development
- Attraction to novel experiences, risk-taking, and impulsivity are neurodevelopmentally driven
- Implications & opportunities for juvenile justice system
- Teen brain is uniquely vulnerable to stress, substance use & addiction
- Strategies to strengthen communication

Sequential Development: From the Bottom-Up

Abstract Thought
Problem solving
Affiliation
Attachment
Emotional Reactivity
Motor Regulation
Sleep
Digestion
Blood Pressure
Heart Rate
Respiration
Body Temperature



NEUROPLASTICITY

Peter Camburn

Neuroplasticity= Risk and Resilience

- Brain adapts and changes in response to experience and environment

- Adolescent brains are **fantastically "plastic!"**

The Adolescent Brain is a Work in Progress

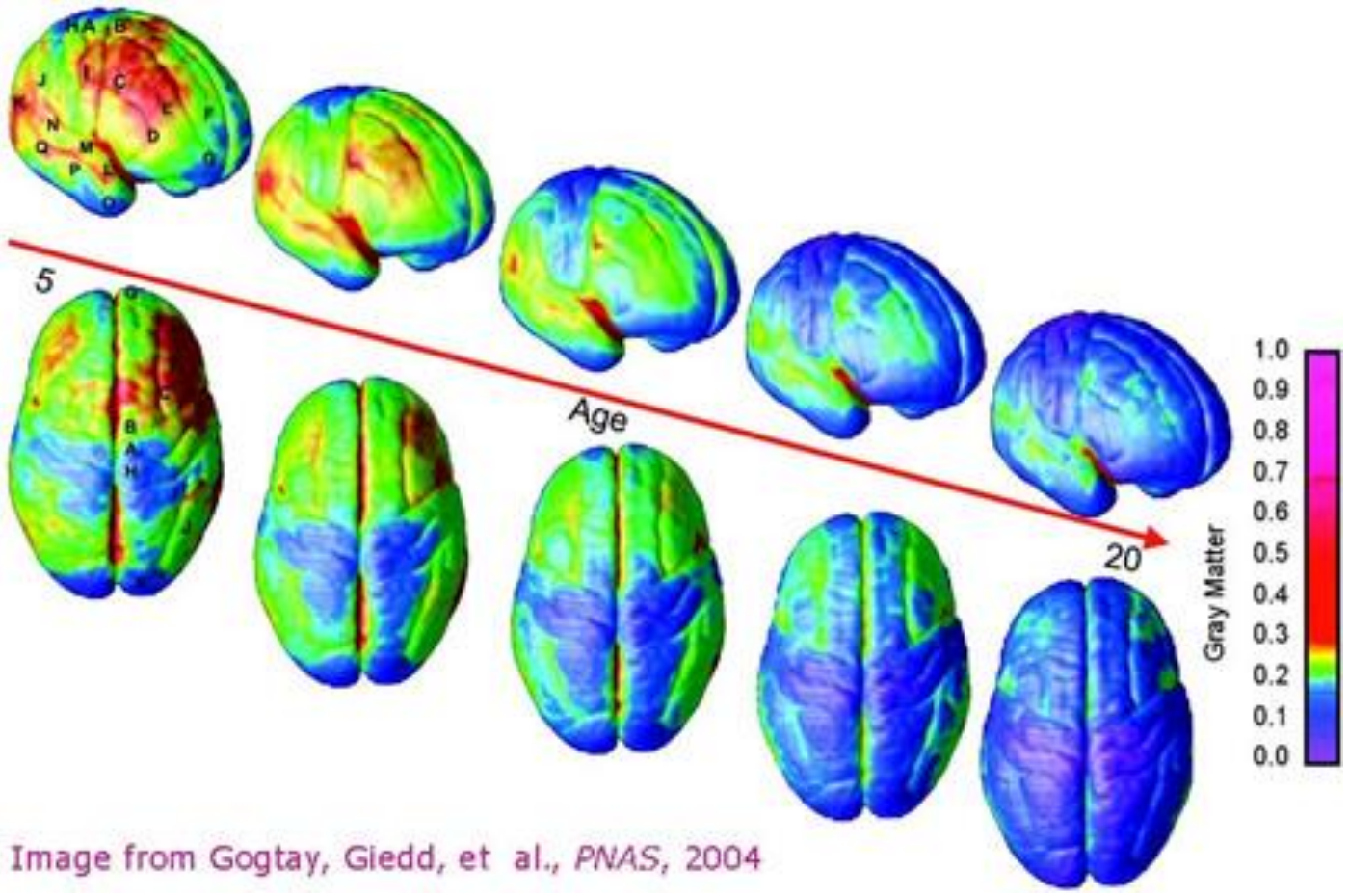


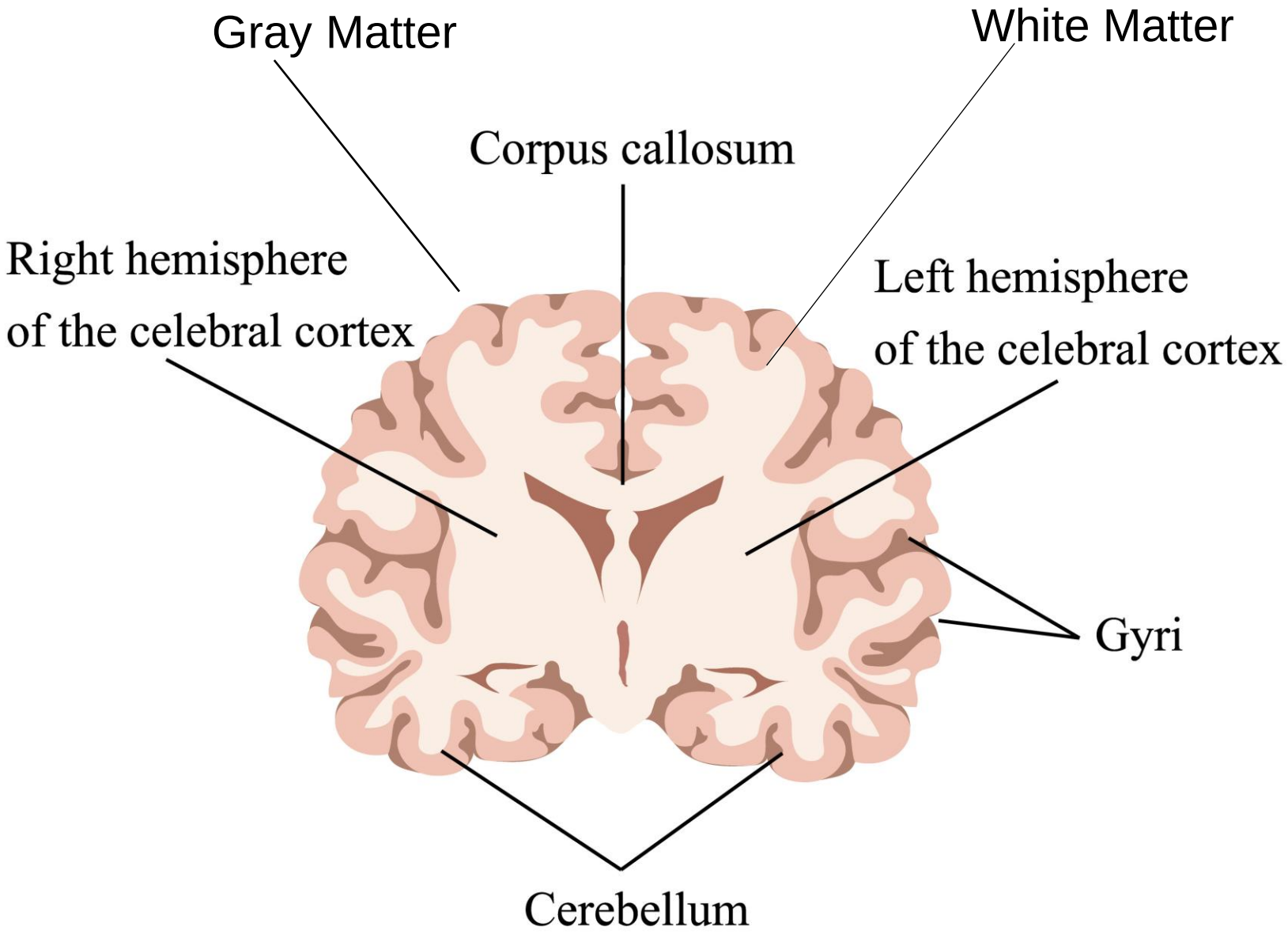
Image from Gogtay, Giedd, et al., *PNAS*, 2004

www.nytimes.com/interactive/2008/09/15/health/20080915-brain-development.html?

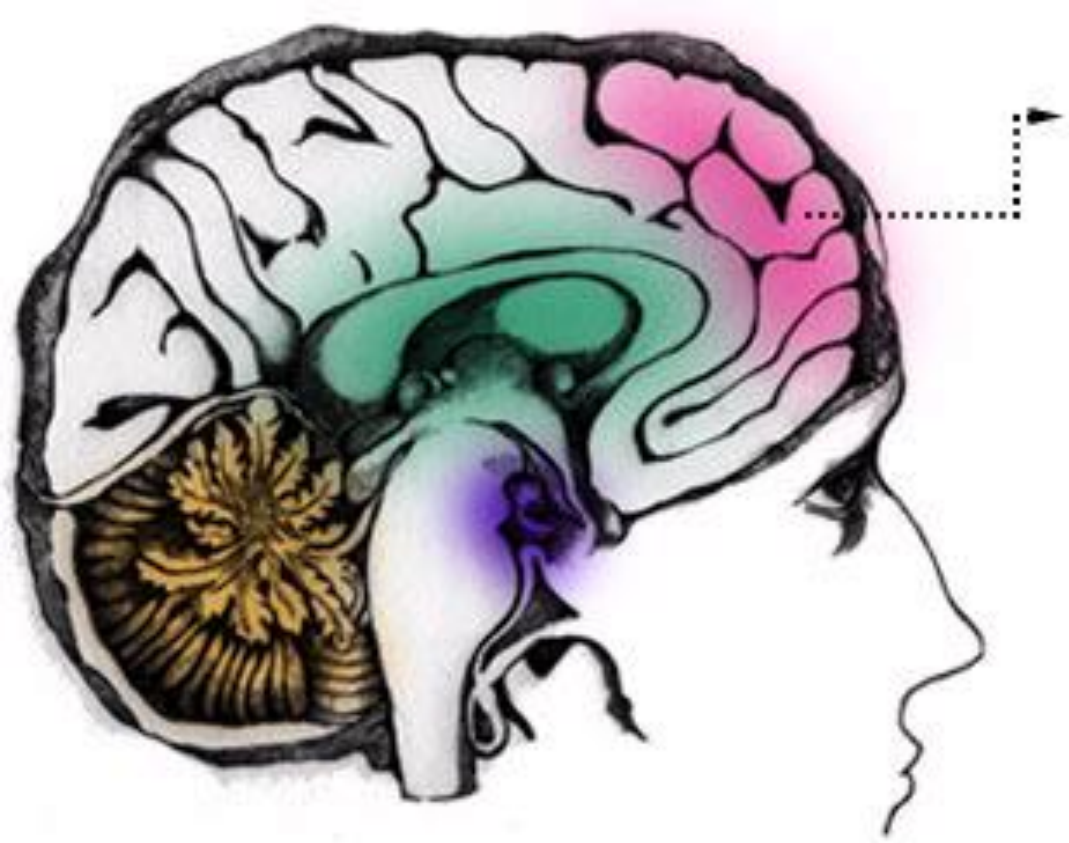
Adolescent brain science is in its infancy!

Changes in Structure and Function

- **Second surge of synaptogenesis (making new connections) & pruning→ efficiency and specialization**
- **Gray matter (=cell bodies) peaks around puberty & then decreasing**
- **Myelination (white matter=insulation) accelerates→ speed & integration**


Gray Matter
White Matter
Corpus callosum
Right hemisphere
of the celebral cortex
Left hemisphere
of the celebral cortex
Gyri
Cerebellum

THE BRAIN'S CEO

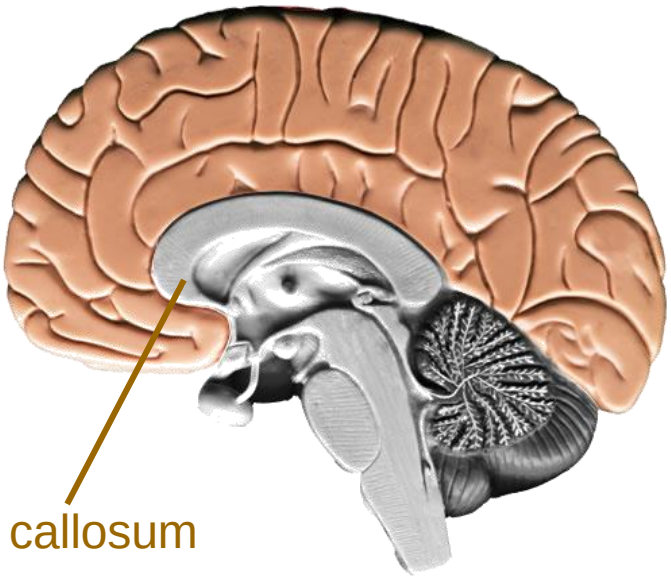


Prefrontal Cortex

- Impulse control
- Judgment
- Problem solving
- Emotional processing
- Organization & planning
- Motivation
- Goal-setting behaviors

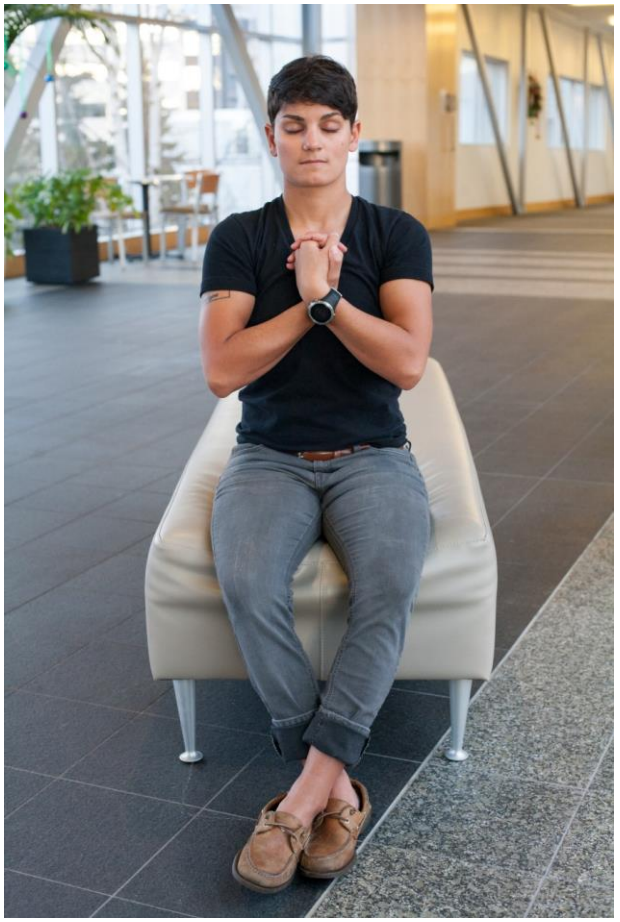
WHILE PREFRONTAL CORTEX IS STILL MATURING…

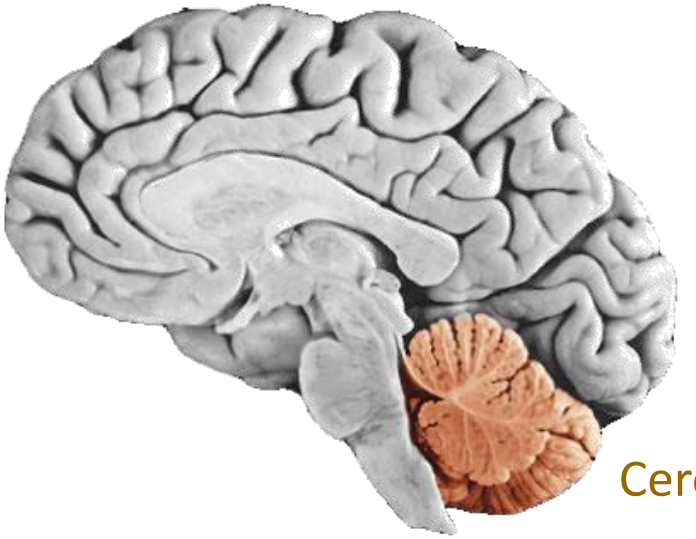
- **More rigid thinking** so harder to see options →
- Maturing brain must work harder to integrate information until it gets all the connections
- Decision-making and working memory hyper-sensitive to emotional content/context
  - Good decision-making comes from experience



- Communicates information from one side of brain to the other
- Creativity & higher thinking

Cross-Lateral Movement



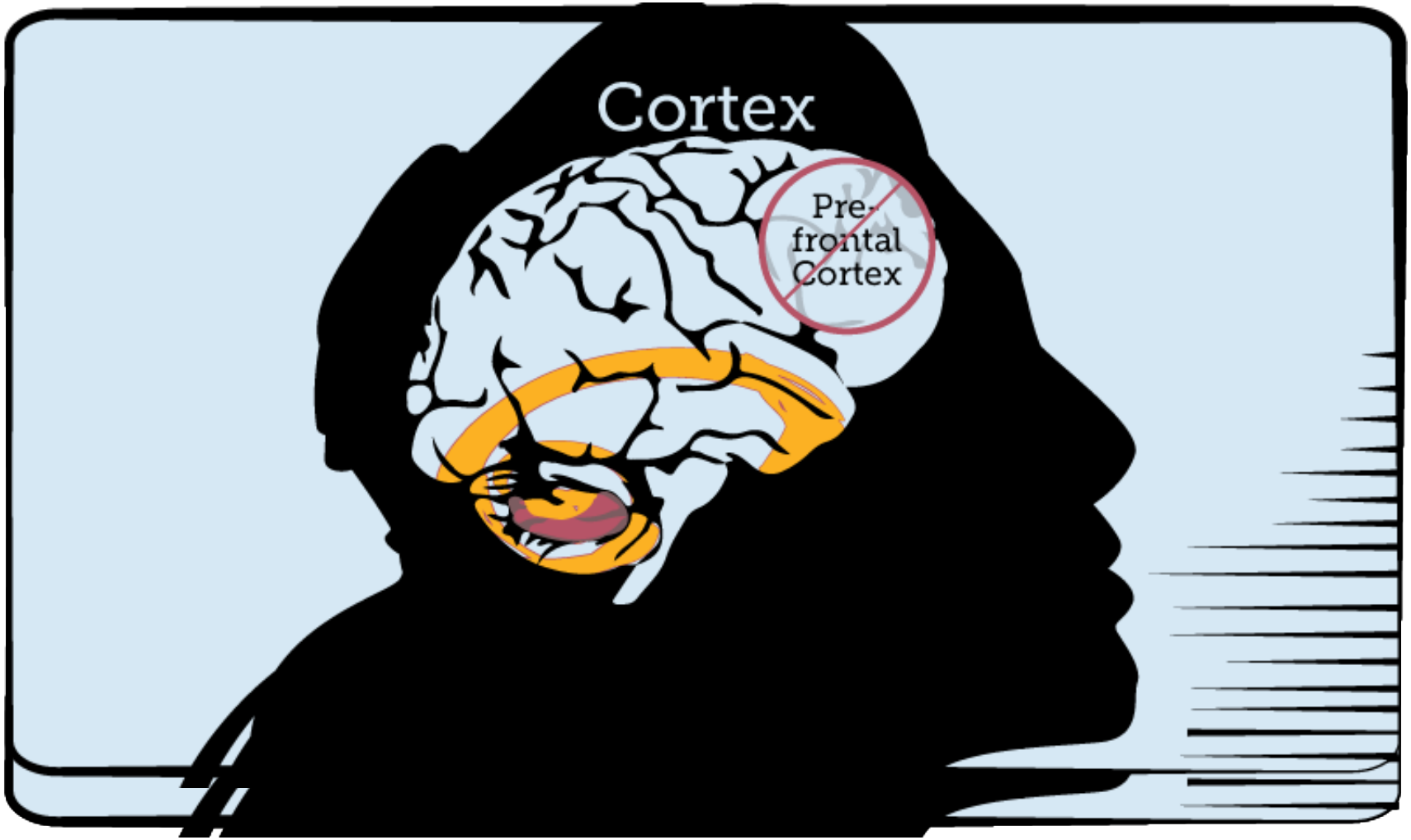


Cerebellum

- **Movement, balance, & complex cognitive processes**
- **Greatest changes during adolescence**
- **Physical exercise boosts development**

Corpus Callosum and Cerebellum continue to develop into 20s

The Brain On Stress

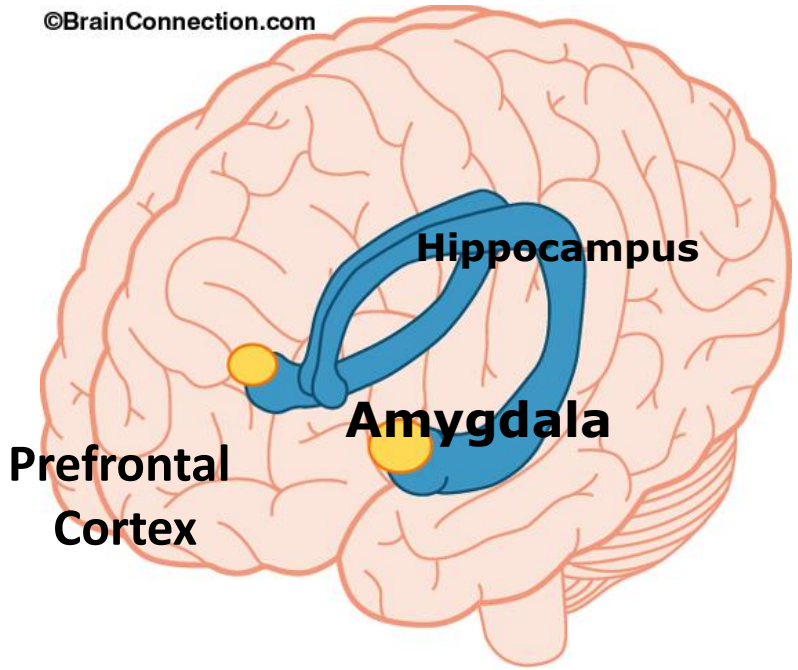


Alaska Native Tribal Health Consortium (ANTHC)

Linda Chamberlain PhD, MPH

Teen Brain is *Exquisitely* Sensitive to Stress

- Key areas of brain involved in stress response—**hippocampus, amygdala & prefrontal cortex**—undergoing major changes



17.3 percent increase in the use of anxiety medications among adolescents during first two years of the pandemic

Adolescent Mental Health

- Half of lifetime mental health disorders start by age 14
- Strong association between trauma and depressive symptoms among adolescents
- Depression is linked to **adolescent risk behaviors**

Mental Health First Aid, 2019; Blum et al, 2019;
https://www.mhanational.org/issues/2020/mental-health-america-youth-data#two

Trauma, Mental Health & Detention

- 75% of youth in juvenile justice system have experienced trauma
- 65% of youth in JJS have a diagnosable mental health disorder
    - 60% of these youth have co-occurring substance abuse disorder

Data sources: OJJDP and National Child Traumatic Stress Network, Justice Policy Institute

Opportunities for Juvenile Justice System

- Research-informed assessment tools for youth
  - Massachusetts Youth Screening Instrument-2 (MYSI-2) → mental health in JJ settings
  - Child and Adolescent Trauma Screen (CATS)
  - Structured Assessment of Violence Risk in Youth (SAVRY)
- Diversion strategies for youth with mental health needs
  - For youth who enter JJ system, refer to community-based MH services
- Brief, evidence-based interventions for adolescents with complex trauma

See *Better Solutions for Youth with Mental Health Needs in the Juvenile Justice System, National Center on Mental Health and Juvenile Justice*

Brain-Building During Sleep

- Need minimum of 9 to 9 ½ hours of sleep
- Brain sleep centers are in transition
- Melatonin secreted up to 2 hours later at night

Sleep assessment if struggling in school, behavioral problems, and/or mental health issues

Linda Chamberlain PhD, MPH

Sleep Assessment as Part of Mental Health Screening

Adolescent Sleep Deprivation:

Compromises REM sleep and learning
Mimics symptoms of ADHD
Increases symptoms of depression
Decreases ability to control emotions
Increases aggressive behaviors
Increases risk of obesity

Poor Self-Regulation Skills During Adolescents Increases Risk of:

- Substance use
- Sexual risk-taking
- Juvenile delinquency

Self-regulation = skills to manage thoughts & feelings, control impulses & problem solve

Self-Regulation and Adolescence

- Temporary regression during **"LIMBIC SURGE"**
- Window of opportunity for self-regulation interventions (OPRE Report, 2017)
- Poor self-regulation and executive function (EF) deficits are common effects of trauma

EF is like air traffic controller at an airport-mental processes that enable us to plan, focus attention, self-regulate, and juggle multiple tasks.

Resilience-Building Toolkit for Youth with Developmental Trauma

1. Emotional Regulation
2. Executive Control/Function
3. Self-Awareness
4. Relational Skills
5. Life Skills

When Age Doesn't Match Stage,
Trauma-Informed Care, 2015, v. 29

Linda Chamberlain PhD, MPH

Child and Youth Resilience Measure (CYRM-12)

I am able to solve problems without harming myself or others	I know where to go in the community to get help	Getting an education is important to me	I try to finish what I start
I have people to look up to	My parents/caregivers know a lot about me	My family stands by me during difficult times	My friends stand by me during difficult times
I have opportunities to develop skills that will be useful later in life	I am treated fairly in my community	I feel I belong at my school	I enjoy my cultural and family traditions

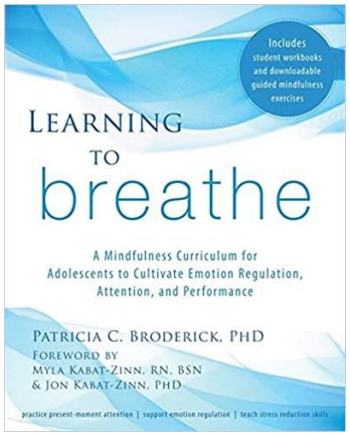
www.resilienceresearch.org

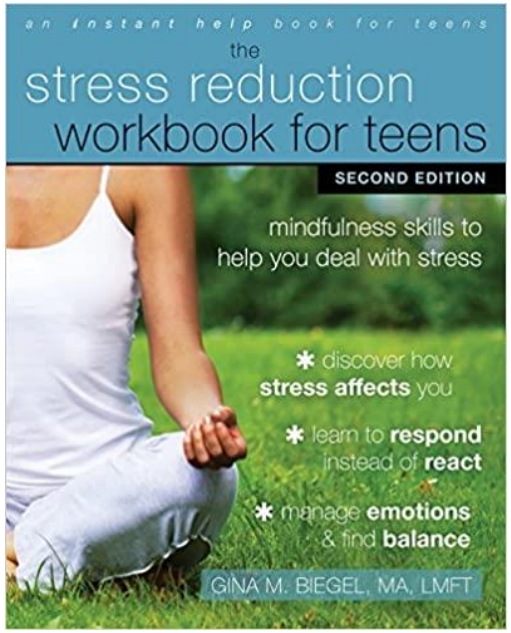
Linda Chamberlain PhD, MPH

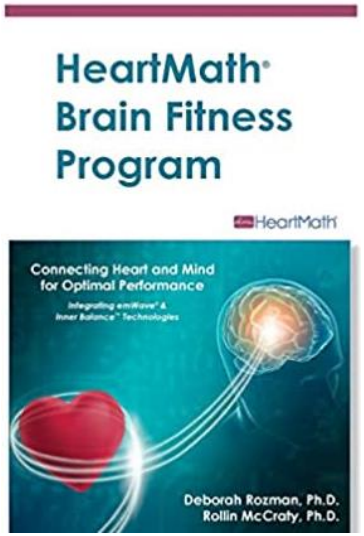
"Neuroscience suggests that mediating the impact of adverse childhood experiences involves not only education and emotional and practical support but also the introduction and application of neurological repair methods such as mindfulness training."

Bryck et al, 2012

People always tell us not to stress out, but nobody tells us how…







Self-regulatory skills open door for cognitive “top-down” treatments for trauma and substance use

Online Searchable Database and Publication

- Trauma & Grief Component Therapy for Adolescents **(TGCT-A)**
- Skills Training in Affective and Interpersonal Regulation/Narrative Story-Telling **(STAIR/NST)**
- Integrative Treatment of Complex Trauma for Adolescents **(ITCT-A)**
- Celebrating Families **(CF!)**
- Cue-Centered Treatment **(CCT)**

www.promising.futureswithoutviolence.org

Getting "SMART" About Sensory Spaces & Tools

MOVEABLE
LIGHTING

WEIGHTED BLANKET

ANKLE WEIGHTS/
BAG OF BEANS

"CRASH" PILLOWS
BEAN BAG CHAIRS

FITNESS BALLS

EXERCISE/GYM MATS ON FLOOR

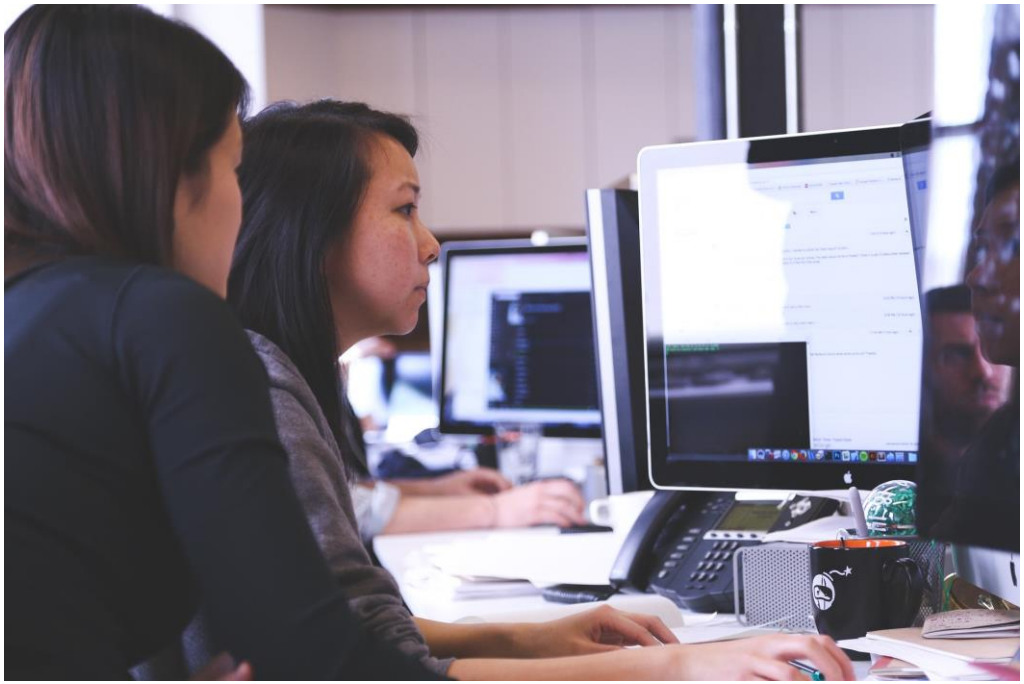
TEEN "BROGLIE BOX" FOR IDEAS

- Tactile (therapy dough, roller ball)
- Affirmations, mindfulness cues
- *Oral-Motor*
- *Auditory*
- *Scent…*

Sensory Motor Arousal Regulation Treatment (SMART)
"Transforming Trauma in Children and Adolescents: An Embodied Approach to Somatic Regulation, Trauma Processing, and Attachment-Building" 2020

Linda Chamberlain PhD, MPH

Mindful Movement Break for Tech Neck

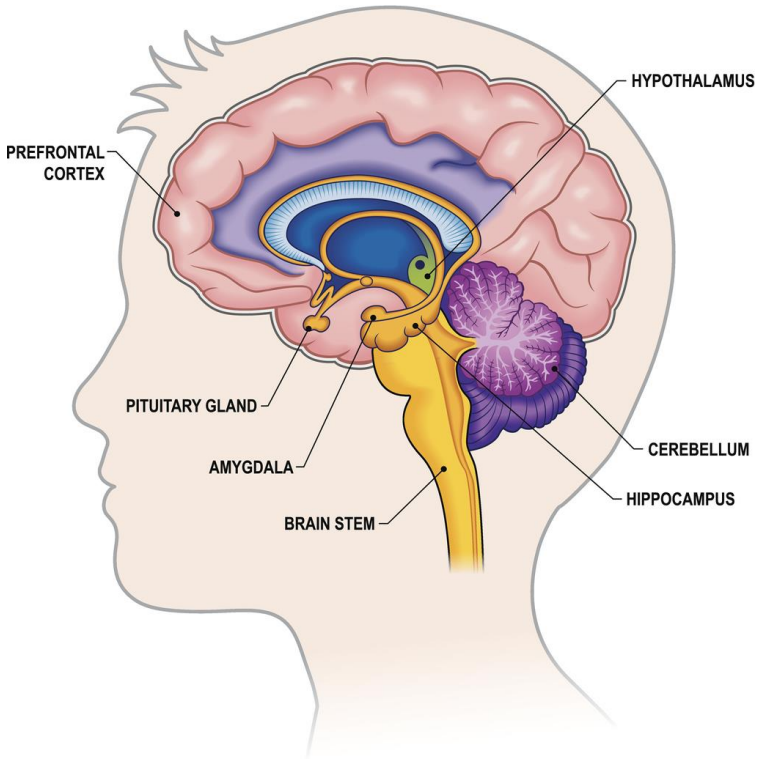


Linda Chamberlain PhD, MPH

Three Most Consistent Adolescent Behavioral Changes Across Cultures

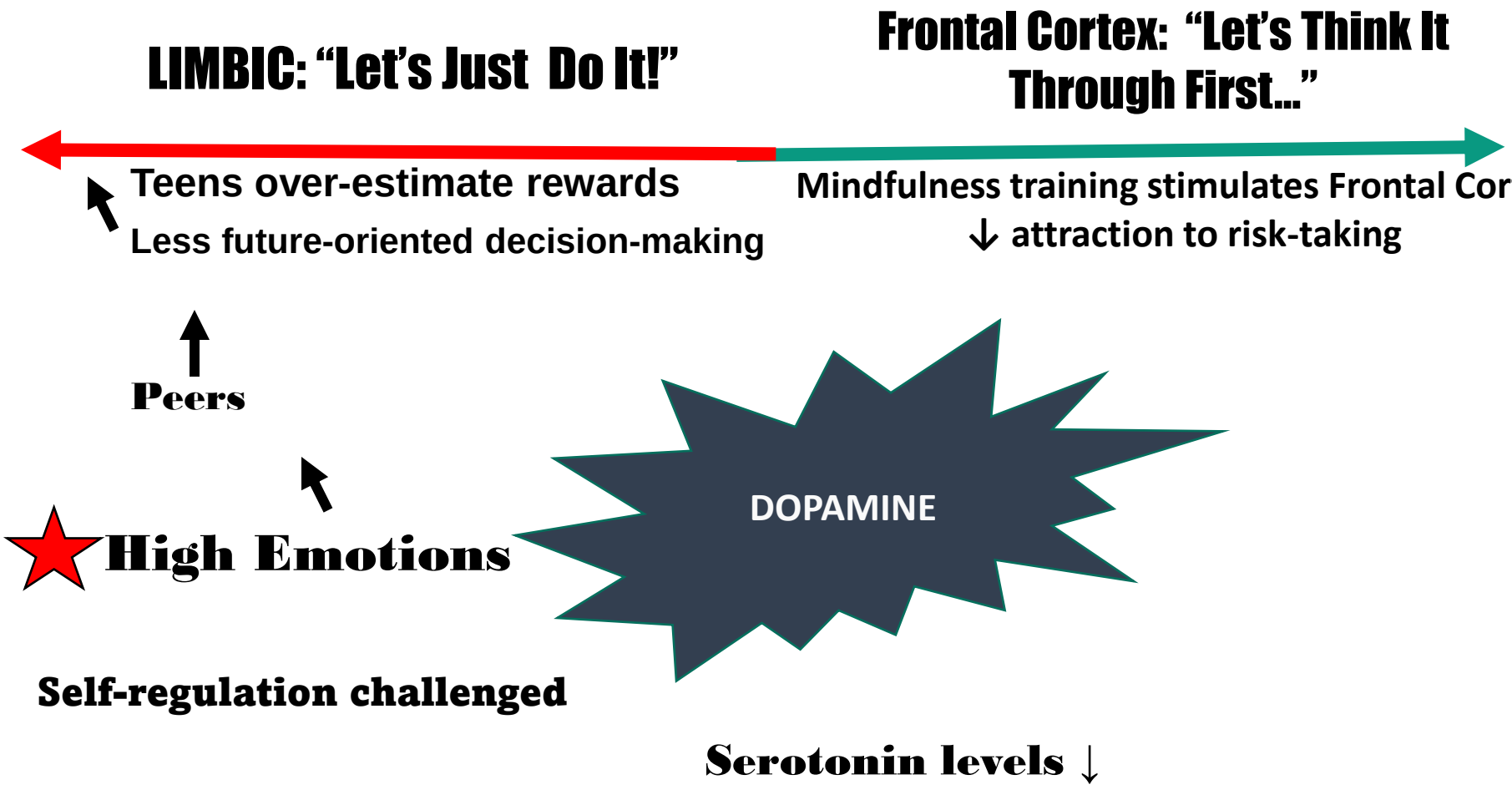
- Novelty seeking
- Focus on peer relationships
- Attraction to risk-taking

The Limbic Challenge



- Matures before Prefrontal Cortex
- Influences emotion, reward, novelty-seeking, memory & impulsivity
- *Feel good sensation* with substances use happens here *(and so does addiction)*

Adolescents Evaluate Risk Differently
Neurodevelopmental Tug-of-War

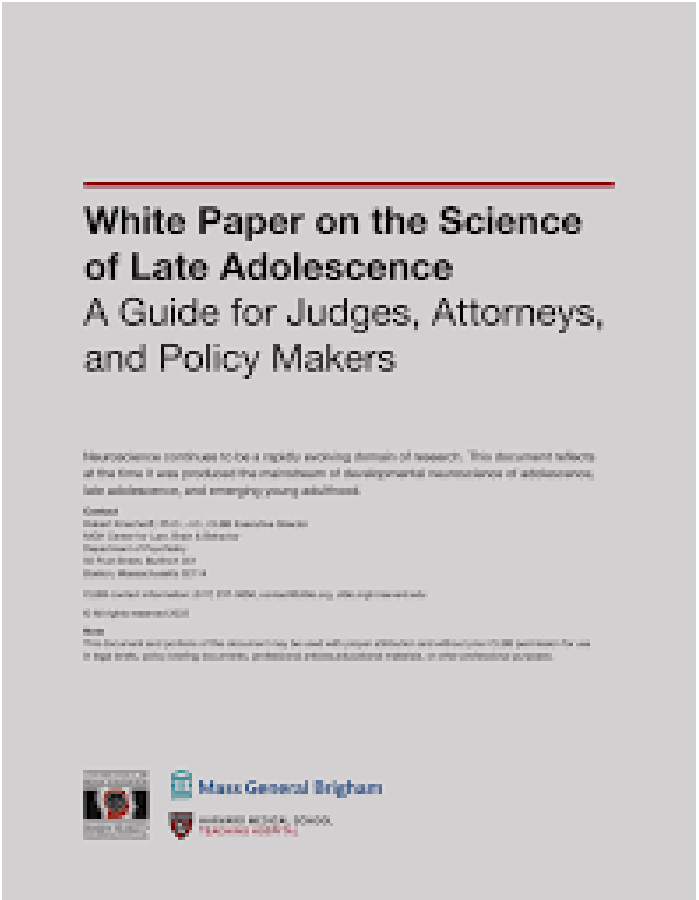


Linda Chamberlain PhD, MPH

Due to differences in brain development, late adolescents (18-21 y.o.) are more likely than young adults (22-25 y.o.) to respond to immediate outcomes and are less likely to delay gratification

Implications for:

- Susceptibility to false confessions
- Waiving Miranda rights
- Plea decisions



The Adolescent Brain and Substance Use

THE BIG THREE*

- **Cognitive impairment**
- **Mental health problems**
- **Future substance abuse**

*DOSE & AGE MEDIATE IMPACT

Substance Use During Adolescence

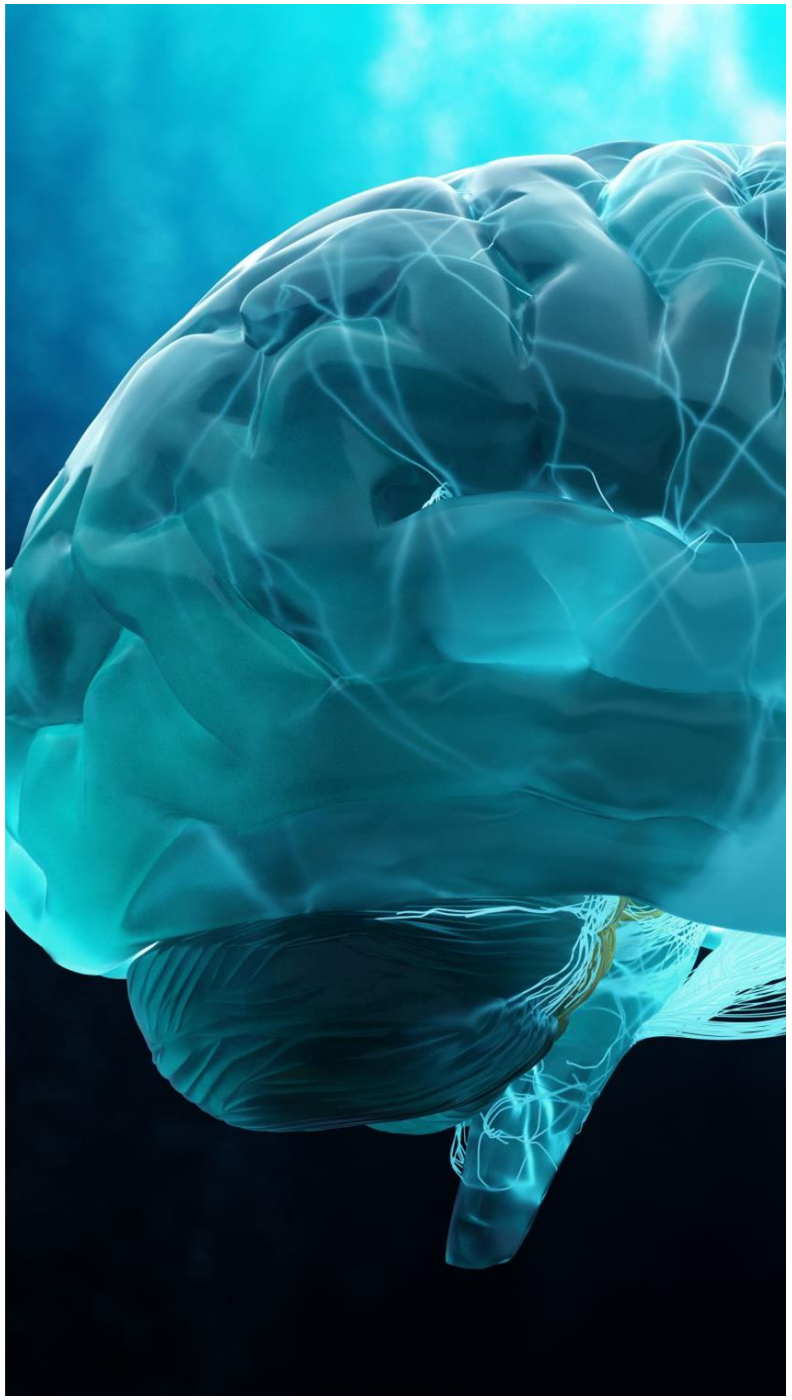
1. **At the same blood alcohol levels, adolescents are less likely to show the effects of intoxication on muscle coordination compared to adults.**

2. **At the same blood alcohol levels, adolescents are more likely to black-out than pass-out compared to adults.**

3. **The impact of marijuana on the brain suggests that some of the same areas of the brain that affected by alcohol are also affected by marijuana.**

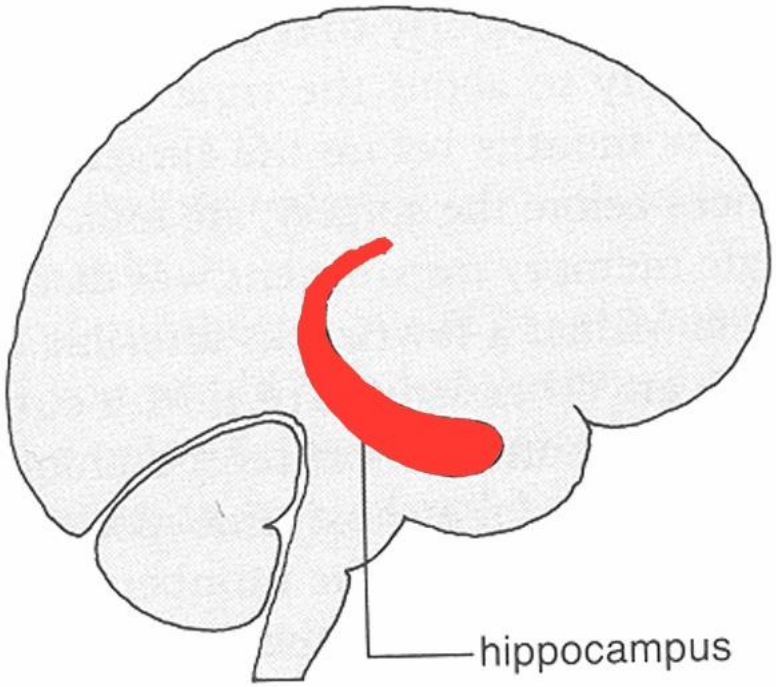
Impact of Alcohol on Teen Brain

- Smaller prefrontal cortices
- ↓ white matter development, especially Corpus Collosum
- Cognitive impairments
  - Attention
  - Memory



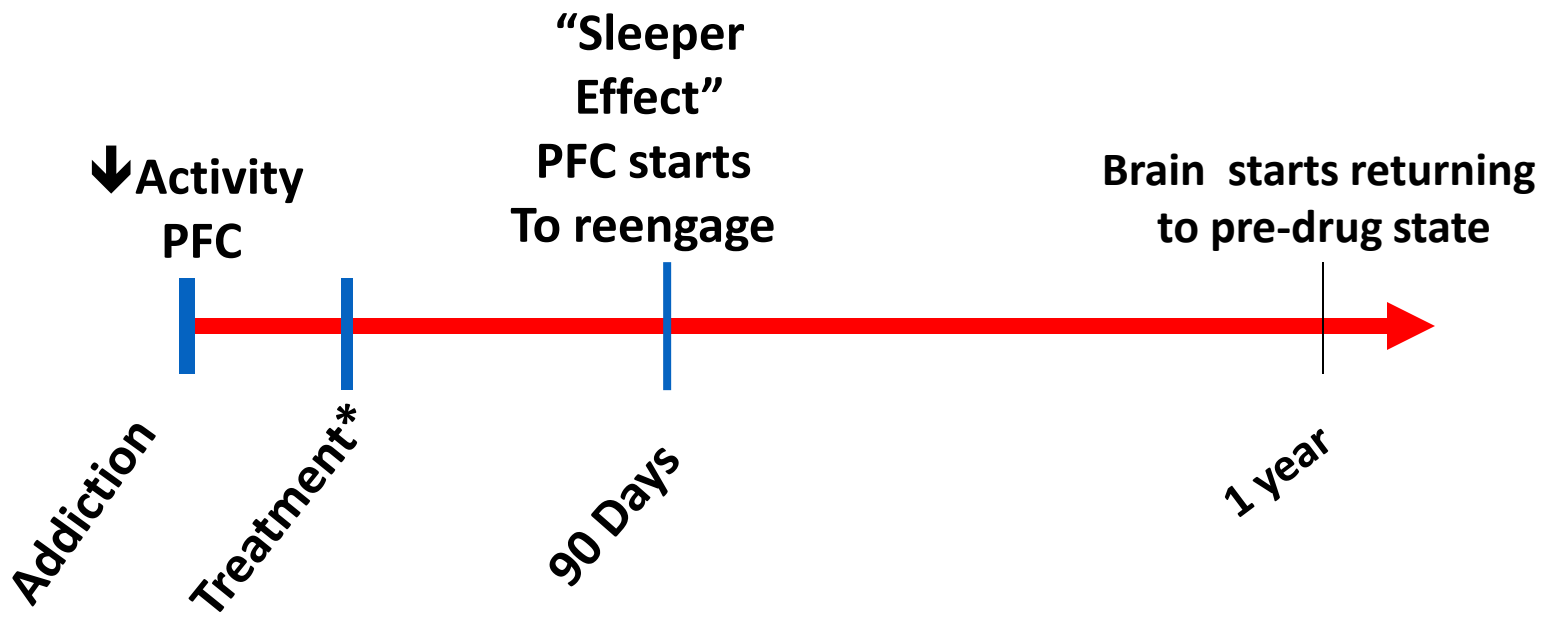
Hippocampus

- "Switchboard" between short- and long-term memory = gateway to learning
- Alcohol impairs ability to create new neurons in hippocampus
- Studies show that interruption of binge-drinking patterns led to partial cognitive recovery



ALCOHOL BLOCKS GLUTAMATE RECEPTORS WHICH ARE KEY FOR BUILDING NEW SYNAPSES→ MEMORY IMPAIRMENT (Jensen, 2015)

Lessons being learned from Adult Alcohol Addiction, Brain Changes, & Intervention



Treatment: Over-ride "impulsive brain"-Amygdala➔
Strengthen Prefrontal Cortex

Marijuana Slows Adolescent Brain Development

- THC disrupts development of neural pathways→ greater potential harm for developing brain
  - ↓gray matter
  - ↓ white matter
- Most significant factor between marijuana use and impact on brain is **AGE (before 15 y.o.)**

There is no known safe limit

Linda Chamberlain PhD, MPH

Higher doses of THC are more likely to produce anxiety, agitation, paranoia & psychosis

Poorer connections between limbic system & prefrontal cortex

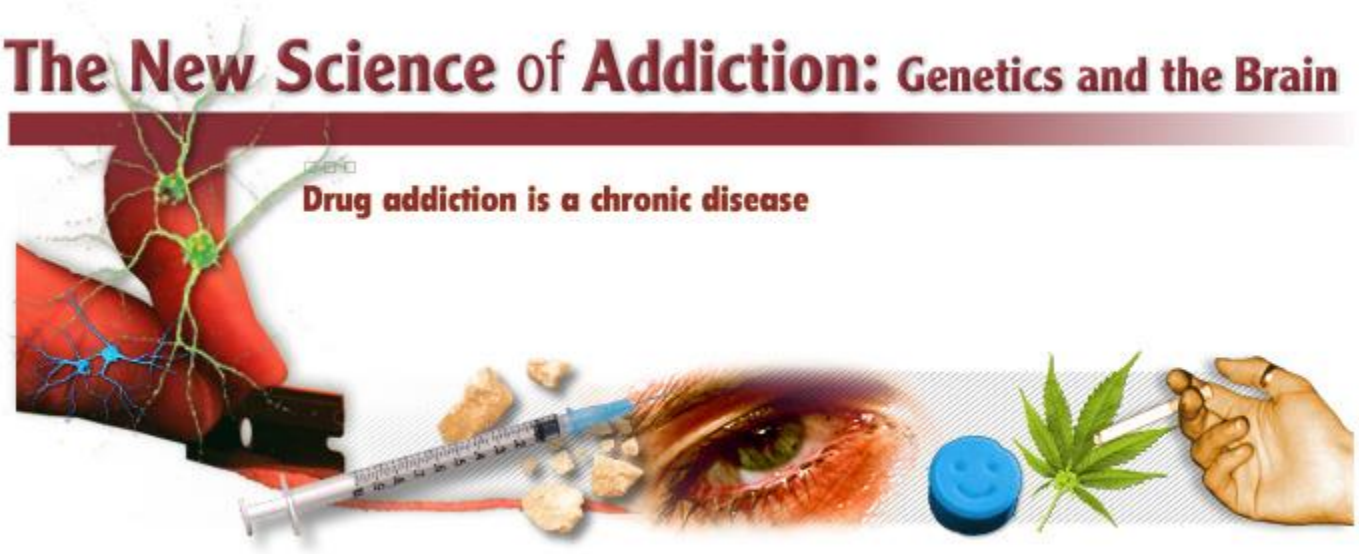
Difficulties with impulse control, attention, memory, learning and problem solving

Implications

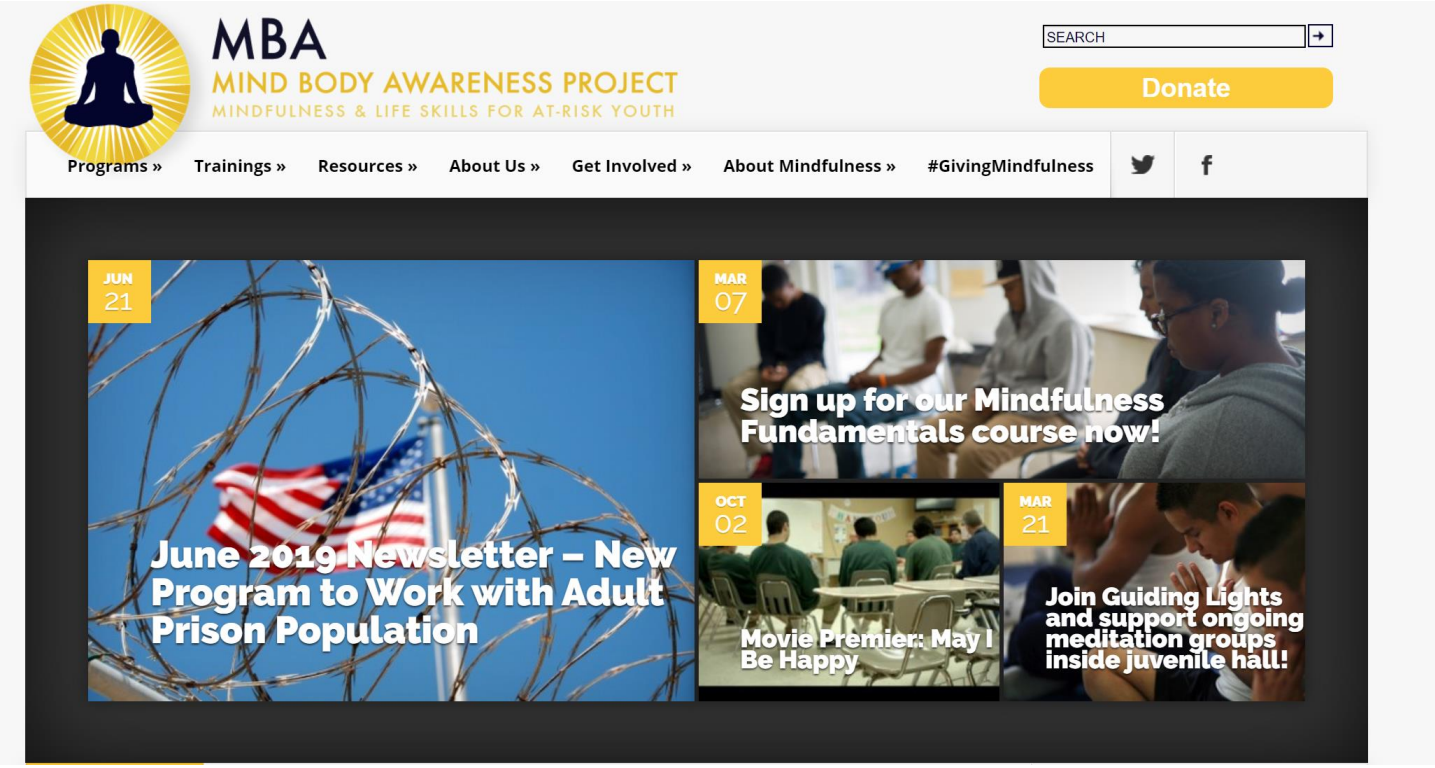
Increased risk of psychotic symptoms & disorders in young adulthood, especially schizophrenia-hastens onset & amplifies severity

Cannabinoid Hyperemesis Syndrome

How Substances Affect The Adolescent Brain



http://learn.genetics.utah.edu/content/addiction/



- MBA Curriculum (usually once weekly for 10-15 weeks) for high-risk and incarcerated populations (focus has been youth with substance abuse issues)
  - Modules include Impulse Regulation, Emotional Awareness, Emotional Intelligence, Cause and Effect and Interpersonal Relationships

See research at https://www.mbaproject.org/

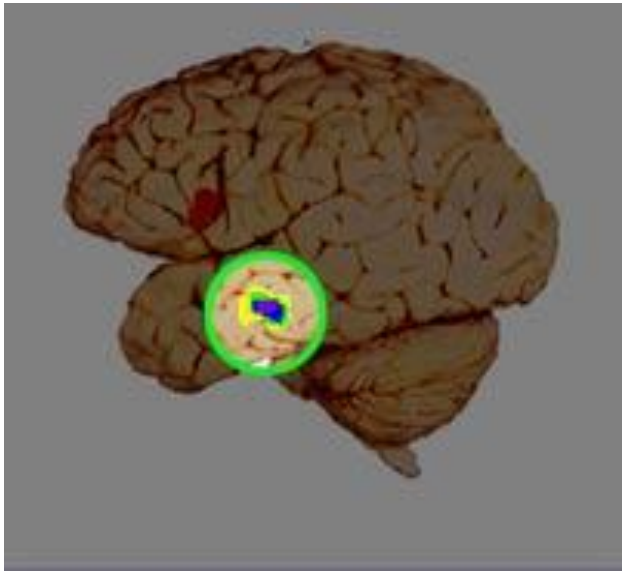
Communicating More Effectively with Teens

Linda Chamberlain PhD, MPH

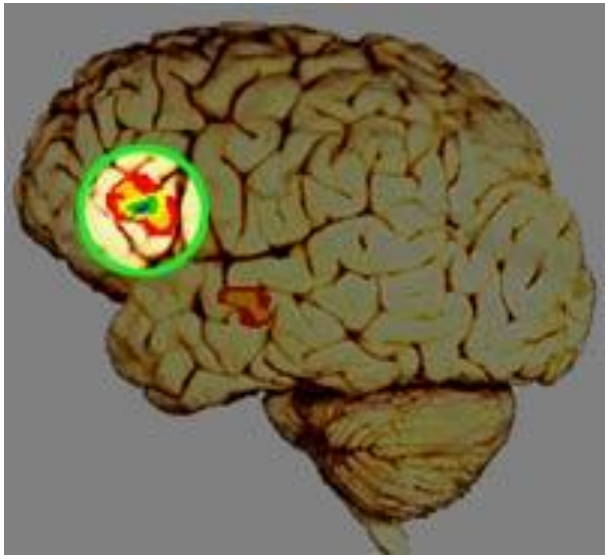
What emotion do you see?

Permission to use photo from Dr. Yurgelun-Todd

Teens Use Less of the Prefrontal Region compared to Adults



Adolescent



Adult

Yurgelun-Todd, D. Frontline Interview; permission to use graphics from Dr. Yurgelin-Todd
http://www.pbs.org/wgbh/pages/frontline/shows/teenbrain/interviews/todd.html

= Communication Gap

The teen brain:

- **Processes more in amygdala**
  - **Reacts more quickly**
  - **Sees anger when it isn't intended**
- **Uses less of prefrontal cortex to interpret facial expressions so ↑ likely to misinterpret**

Frontline Interview with Dr. Yurgelin-Todd

IMPLICATIONS

- Immature prefrontal cortex goes "limbic"
- Doesn't focus attention on behavior that needs to change
- Weakens relationship → isolation & less likely to ask for help
- Strategy: **Right brain-to-right brain**
- Tool: **FETI** (Forensic Experiential Trauma Interview)

What Do Teen Brains Need?

1. Hands-on, skill-based learning

2. Novel experiences & opportunities to practice decision-making and build sense of agency

3. At least 9 hours of sleep for brain-building

4. Tools to build brain connectivity & manage stress

5. To understand how their brains are changing.

National Institute on Drug Abuse
Advancing Addiction Science

Research Report
Revised July 2020

Cannabis (Marijuana) Research Report

Table of Contents

Cannabis (Marijuana) Research Report

Explores the latest research on marijuana, including the scope of marijuana use in the U.S., health consequences, its effects on everyday activities, and available treatments.

Letter From the Director

Photo by NIDA

Changes in marijuana policies across states legalizing marijuana for medical and/or recreational use suggest that marijuana is gaining greater acceptance in our society. Thus, it is particularly important for people to understand what is known about both the adverse health effects and the potential therapeutic benefits linked to marijuana.

Because marijuana impairs short-term memory and judgment and distorts perception, it can impair performance in school or at work and make it dangerous to drive. It also affects brain systems that are still maturing through young adulthood, so regular use by teens may have negative and long-lasting effects on their cognitive development, putting them at a competitive disadvantage and possibly interfering with their well-being in other ways. Also, contrary to popular belief, marijuana can be addictive, and its use during adolescence may make other forms of problem use or addiction more likely.

Whether smoking or otherwise consuming marijuana has therapeutic benefits that outweigh its health risks is still an open question that science has not resolved. Although many states now permit dispensing marijuana for medicinal purposes and there is mounting anecdotal evidence for the efficacy of marijuana-derived compounds, the U.S. Food and Drug Administration has not approved "medical marijuana." However, safe medicines based on cannabinoid chemicals derived from the marijuana plant have been available for decades and more are being developed.

This Research Report is intended as a useful summary of what the most up-to-date science has to say about marijuana and its effects on those who use it at any age.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

See Also:

- Message from the NIDA Director - Marijuana's Lasting Effects on the Brain, (Archives) (March 2013)

What is marijuana?

Image by ©iStock.com/nicoolay

Marijuana—also called *weed, herb, pot, grass, bud, ganja, Mary Jane*, and a vast number of other slang terms—is a greenish-gray mixture of the dried flowers of *Cannabis sativa*. Some people smoke marijuana in hand-rolled cigarettes called *joints*; in pipes, water pipes (sometimes called *bongs*), or in *blunts* (marijuana rolled in cigar wraps).[1] Marijuana can also be used to brew tea and, particularly when it is sold or consumed for medicinal purposes, is frequently mixed into foods (*edibles*) such as brownies, cookies, or candies. Vaporizers are also increasingly used to consume marijuana. Stronger forms of marijuana include sinsemilla (from specially tended female plants) and concentrated resins containing high doses of marijuana's active ingredients, including honeylike *hash oil*, waxy *budder*, and hard amberlike *shatter*. These resins are increasingly popular among those who use them both recreationally and medically.

The main *psychoactive*(mind-altering) chemical in marijuana, responsible for most of the intoxicating effects that people seek, is *delta-9-tetrahydrocannabinol* (THC). The chemical is found in resin produced by the leaves and buds primarily of the female cannabis plant. The plant also contains more than 500 other chemicals, including more than 100 compounds that are chemically related to THC, called *cannabinoids*.[2]

What is the scope of cannabis (marijuana) use in the United States?

All data refer to the United States population.

How many people use cannabis ?

- Among people aged 12 or older in 2020, 17.9% (or about 49.6 million people) reported using cannabis in the past 12 months.
  Source: 2020 National Survey on Drug Use and Health

How many young students use cannabis?

- In 2021, an estimated 7.1% of 8th graders, 17.3% of 10th graders, and 30.5% of 12th graders reported using cannabis/hashish in the past 12 months.
  Source: 2021 Monitoring the Future Survey

How many people have a cannabis use disorder?

- Among people aged 12 or older in 2020, an estimated 5.1% (or about 14.2 million people) had a cannabis use disorder in the past 12 months.
  Source: 2020 National Survey on Drug Use and Health

What are marijuana's effects?

When marijuana is smoked, THC and other chemicals in the plant pass from the lungs into the bloodstream, which rapidly carries them throughout the body to the brain. The person begins to experience effects almost immediately (see "How does marijuana produce its effects?"). Many people experience a pleasant euphoria and sense of relaxation. Other common effects, which may vary dramatically among different people, include heightened sensory perception (e.g., brighter colors), laughter, altered perception of time, and increased appetite.

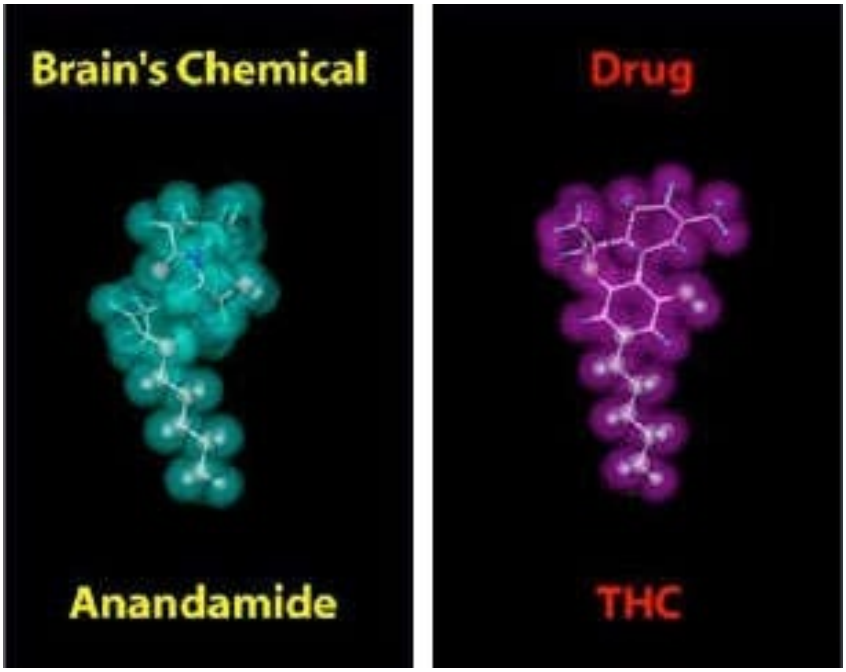
If marijuana is consumed in foods or beverages, these effects are somewhat delayed—usually appearing after 30 minutes to 1 hour—because the drug must first pass through the digestive system. Eating or drinking marijuana delivers significantly less THC into the bloodstream than smoking an

equivalent amount of the plant. Because of the delayed effects, people may inadvertently consume more THC than they intend to.

Pleasant experiences with marijuana are by no means universal. Instead of relaxation and euphoria, some people experience anxiety, fear, distrust, or panic. These effects are more common when a person takes too much, the marijuana has an unexpectedly high potency, or the person is inexperienced. People who have taken large doses of marijuana may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity. These unpleasant but temporary reactions are distinct from longer-lasting psychotic disorders, such as schizophrenia, that may be associated with the use of marijuana in vulnerable individuals. (See "Is there a link between marijuana use and psychiatric disorders?")

Although detectable amounts of THC may remain in the body for days or even weeks after use, the noticeable effects of smoked marijuana generally last from 1 to 3 hours, and those of marijuana consumed in food or drink may last for many hours.

How does marijuana produce its effects?



Courtesy of NIDA

THC’s chemical structure is similar to the brain chemical *anandamide*. Similarity in structure allows the body to recognize THC and to alter normal brain communication.

> THC’s chemical structure is similar to the brain chemical anandamide. Similarity in structure allows drugs to be recognized by the body and to alter normal brain communication.

Endogenous cannabinoids such as anandamide (see figure) function as *neurotransmitters* because they send chemical messages between nerve cells (*neurons*) throughout the nervous system. They affect brain areas that influence pleasure, memory, thinking, concentration, movement, coordination, and sensory and time perception. Because of this similarity, THC is able to attach to molecules called *cannabinoid receptors* on neurons in these brain areas and activate them, disrupting various mental and physical functions and causing the effects described earlier. The neural communication network that uses these cannabinoid neurotransmitters, known as the *endocannabinoid system*, plays a critical role in the nervous system’s normal functioning, so interfering with it can have profound effects.

For example, THC is able to alter the functioning of the hippocampus (see "Marijuana, Memory, and the Hippocampus") and orbitofrontal cortex, brain areas that enable a person to form new memories and shift his or her attentional focus. As a result, using marijuana causes impaired thinking and interferes with a person’s ability to learn and perform complicated tasks. THC also disrupts functioning of the cerebellum and basal ganglia, brain areas that regulate balance, posture, coordination, and reaction time. This is the reason people who have used marijuana may not be able to drive safely (see "Does marijuana use affect driving?") and may have problems playing sports or engaging in other physical activities.

> People who have taken large doses of the drug may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity.

THC, acting through cannabinoid receptors, also activates the brain’s reward system, which includes regions that govern the response to healthy pleasurable behaviors such as sex and eating. Like most other drugs that people misuse, THC stimulates neurons in the reward system to release the signaling chemical *dopamine* at levels higher than typically observed in response to natural rewarding stimuli. The surge of dopamine “teaches” the brain to repeat the rewarding behavior, helping account for

marijuana’s addictive properties.

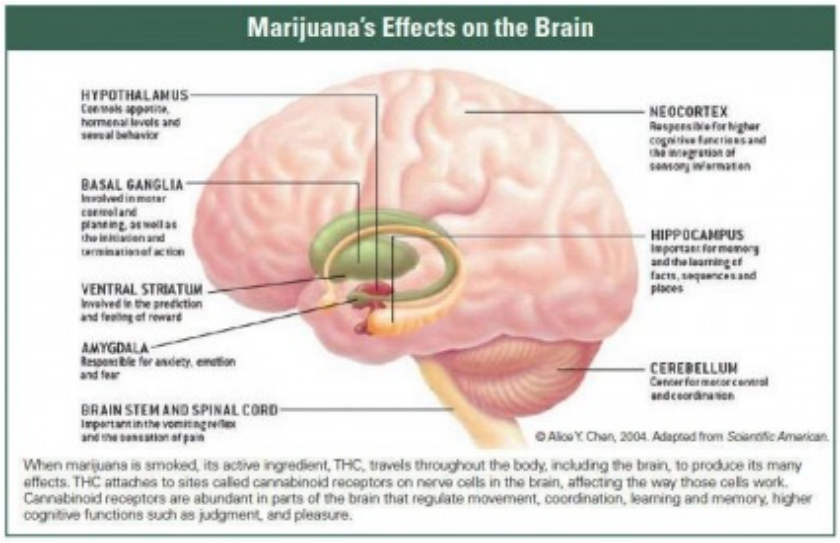


Diagram showing different parts of the brain and describing marijuana's effects on the brain

Does marijuana use affect driving?

Marijuana may impair judgment, motor coordination, and reaction time, and studies have found a direct relationship between blood THC concentration and impaired driving ability.[7–9]

Photo by ©iStock.com/MadCircles

Marijuana is the illicit drug most frequently found in the blood of drivers who have been involved in vehicle crashes, including fatal ones.[10] Two large European studies found that drivers with THC in their blood were roughly twice as likely to be culpable for a fatal crash than drivers who had not used drugs or alcohol.[11’12] However, the role played by marijuana in crashes is often unclear because it can be detected in body fluids for days or even weeks after intoxication and because people frequently combine it with alcohol. Those involved in vehicle crashes with THC in their blood, particularly higher levels, are three to seven times more likely to be responsible for the incident than drivers who had not used drugs or alcohol. The risk associated with marijuana in combination with alcohol appears to be

greater than that for either drug by itself.[8]

Several meta-analyses of multiple studies found that the risk of being involved in a crash significantly increased after marijuana use[13]—in a few cases, the risk doubled or more than doubled.[14–16] However, a large case-control study conducted by the National Highway Traffic Safety Administration found no significant increased crash risk attributable to cannabis after controlling for drivers' age, gender, race, and presence of alcohol.[17]

Is marijuana addictive?

Marijuana use can lead to the development of problem use, known as a marijuana use disorder, which takes the form of addiction in severe cases. Recent data suggest that 30% of those who use marijuana may have some degree of marijuana use disorder.[18] People who begin using marijuana before the age of 18 are four to seven times more likely to develop a marijuana use disorder than adults.[19]

Marijuana use disorders are often associated with *dependence*—in which a person feels withdrawal symptoms when not taking the drug. People who use marijuana frequently often report irritability, mood and sleep difficulties, decreased appetite, cravings, restlessness, and/or various forms of physical discomfort that peak within the first week after quitting and last up to 2 weeks.[20,21] Marijuana dependence occurs when the brain adapts to large amounts of the drug by reducing production of and sensitivity to its own endocannabinoid neurotransmitters.[22,23]

Marijuana use disorder becomes addiction when the person cannot stop using the drug even though it interferes with many aspects of his or her life. Estimates of the number of people addicted to marijuana are controversial, in part because epidemiological studies of substance use often use dependence as a proxy for addiction even though it is possible to be dependent without being addicted. Those studies suggest that 9% of people who use marijuana will become dependent on it,[24,25] rising to about 17% in those who start using in their teens.[26,27]

In 2015, about 4.0 million people in the United States met the diagnostic criteria for a marijuana use disorder;[3] 138,000 voluntarily sought treatment for their marijuana use.[28]

Rising Potency

Marijuana potency, as detected in confiscated samples, has steadily increased over the past few decades. In the early 1990s, the average THC content in confiscated marijuana samples was less than 4%.[2] In 2018, it was more than 15%.[29] Marijuana concentrates can have much higher levels of THC (see Marijuana Concentrates DrugFacts). The increasing potency of marijuana, combined with the use of high-THC concentrates, raises concerns that the consequences of marijuana use today could be worse than in the past, particularly among those who are new to marijuana use and in young people, whose brains are still developing (see "What are marijuana's long-term effects on the brain?").

Researchers do not yet know the full extent of the consequences when the body and brain (especially the developing brain) are exposed to high concentrations of THC or whether the recent increases in emergency department visits by people testing positive for marijuana are related to rising potency. The extent to which people adjust for increased potency by using less or by smoking it differently is also unknown. Recent studies suggest that experienced people may adjust the amount they smoke and how much they inhale based on the believed strength of the marijuana they are using, but they are not able to fully compensate for variations in potency.[30,31]

What are marijuana's long-term effects on the brain?

Substantial evidence from animal research and a growing number of studies in humans indicate that marijuana exposure during development can cause long-term or possibly permanent adverse changes in the brain. Rats exposed to THC before birth, soon after birth, or during adolescence show notable problems with specific learning and memory tasks later in life.[32–34] Cognitive impairments in adult rats exposed to THC during adolescence are associated with structural and functional changes in the hippocampus.[35–37] Studies in rats also show that adolescent exposure to THC is associated with an altered reward system, increasing the likelihood that an animal will self-administer other drugs (e.g., heroin) when given an opportunity (see "Is marijuana a gateway drug?").

Imaging studies of marijuana's impact on brain structure in humans have shown conflicting results. Some studies suggest regular marijuana use in adolescence is associated with altered connectivity and reduced volume of specific brain regions involved in a broad range of executive functions such as memory, learning, and impulse control compared to people who do not use.[38,39] Other studies have not found significant structural differences between the brains of people who do and do not use the drug.[40]

Several studies, including two large longitudinal studies, suggest that marijuana use can cause functional impairment in cognitive abilities but that the degree and/or duration of the impairment depends on the age when a person began using and how much and how long he or she used.[41]

Among nearly 4,000 young adults in the Coronary Artery Risk Development in Young Adults study tracked over a 25-year period until mid-adulthood, cumulative lifetime exposure to marijuana was associated with lower scores on a test of verbal memory but did not affect other cognitive abilities such as processing speed or executive function. The effect was sizable and significant even after eliminating those involved with current use and after adjusting for confounding factors such as demographic factors, other drug and alcohol use, and other psychiatric conditions such as depression.[42]

Some studies have also linked marijuana use to declines in IQ, especially when use starts in adolescence and leads to persistent cannabis use disorder into adulthood. However, not all of the studies on the link between marijuana and IQ have reached the same conclusion, and it is difficult to prove that marijuana causes a decline in IQ when there are multiple factors that can influence the results of such studies, such as genetics, family environment, age of first use, frequency of use, having a cannabis use disorder, duration of use, and duration of the study. Key research in this area to date is described below.

A large longitudinal study in New Zealand found that persistent marijuana use disorder with frequent use starting in adolescence was associated with a loss of an average of 6 or up to 8 IQ points measured in mid-adulthood.[43] Those who used marijuana heavily as teenagers and quit using as adults did not recover the lost IQ points. People who only began using marijuana heavily in adulthood did not lose IQ points. Two shorter-duration prospective longitudinal twin studies found that youth who used marijuana showed significant declines in verbal ability (equivalent to 4 IQ points) and general knowledge between the preteen years (ages 9 to 12, before use) and late adolescence/early

adulthood (ages 17 to 20); however those who went on to use marijuana at older ages already had lower scores on these measures at the start of the study, before they started using the drug. Also, no predictable difference was found between twins when one used marijuana and one did not.[44]

More research will be needed to answer definitively whether marijuana use causes long-term IQ losses and whether factors that weren't measured in the prior research, such as the increasing amounts of THC in cannabis and the emergence of new cannabis products, are relevant.

Also, the ability to draw definitive conclusions about marijuana's long-term impact on the human brain from past studies is often limited by the fact that study participants use multiple substances, and there is often limited data about the participants' health or mental functioning prior to the study. Over the next decade, the National Institutes of Health is funding the Adolescent Brain Cognitive Development (ABCD) study—a major longitudinal study that will track a large sample of young Americans from late childhood (before first use of drugs) to early adulthood. The study will use neuroimaging and other advanced tools to clarify precisely how and to what extent marijuana and other substances, alone and in combination, affect adolescent brain development.

Marijuana, Memory, and the Hippocampus

Image by NIDA

Distribution of cannabinoid receptors in the rat brain. Brain image reveals high levels (shown in orange and yellow) of cannabinoid receptors in many areas, including the cortex, hippocampus, cerebellum, and nucleus accumbens (ventral striatum).

Memory impairment from marijuana use occurs because THC alters how the hippocampus, a brain area responsible for memory formation, processes information. Most of the evidence supporting this assertion comes from animal studies. For example, rats exposed to THC *in utero*, soon after birth, or during adolescence, show notable problems with specific learning/memory tasks later in life. Moreover, cognitive impairment in adult rats is associated with structural and functional changes in the

> hippocampus from THC exposure during adolescence.
>
> As people age, they lose neurons in the hippocampus, which decreases their ability to learn new information. Chronic THC exposure may hasten age-related loss of hippocampal neurons. In one study, rats exposed to THC every day for 8 months (approximately 30% of their lifespan) showed a level of nerve cell loss at 11 to 12 months of age that equaled that of unexposed animals twice their age.

Is marijuana a gateway drug?

Some research suggests that marijuana use is likely to precede use of other licit and illicit substances [45] and the development of addiction to other substances. For instance, a study using longitudinal data from the National Epidemiological Study of Alcohol Use and Related Disorders found that adults who reported marijuana use during the first wave of the survey were more likely than adults who did not use marijuana to develop an alcohol use disorder within 3 years; people who used marijuana and already had an alcohol use disorder at the outset were at greater risk of their alcohol use disorder worsening.[46] Marijuana use is also linked to other substance use disorders including nicotine addiction.

Early exposure to cannabinoids in adolescent rodents decreases the reactivity of brain dopamine reward centers later in adulthood.[47] To the extent that these findings generalize to humans, this could help explain the increased vulnerability for addiction to other substances of misuse later in life that most epidemiological studies have reported for people who begin marijuana use early in life.[48] It is also consistent with animal experiments showing THC's ability to "prime" the brain for enhanced responses to other drugs.[49] For example, rats previously administered THC show heightened behavioral response not only when further exposed to THC but also when exposed to other drugs such as morphine—a phenomenon called *cross-sensitization*.[50]

These findings are consistent with the idea of marijuana as a "gateway drug." However, the majority of people who use marijuana do not go on to use other, "harder" substances. Also, cross-sensitization is not unique to marijuana. Alcohol and nicotine also prime the brain for a heightened response to other

drugs[51] and are, like marijuana, also typically used before a person progresses to other, more harmful substances.

It is important to note that other factors besides biological mechanisms, such as a person's social environment, are also critical in a person's risk for drug use. An alternative to the gateway-drug hypothesis is that people who are more vulnerable to drug-taking are simply more likely to start with readily available substances such as marijuana, tobacco, or alcohol, and their subsequent social interactions with others who use drugs increases their chances of trying other drugs. Further research is needed to explore this question.

How does marijuana use affect school, work, and social life?

Research has shown that marijuana's negative effects on attention, memory, and learning

Image by ©iStock.com/AntonioGuillem

can last for days or weeks after the acute effects of the drug wear off, depending on the person's history with the drug.[52] Consequently, someone who smokes marijuana daily may be functioning at a reduced intellectual level most or all of the time. Considerable evidence suggests that students who smoke marijuana have poorer educational outcomes than their nonsmoking peers. For example, a review of 48 relevant studies found marijuana use to be associated with reduced educational attainment (i.e., reduced chances of graduating).[53] A recent analysis using data from three large studies in Australia and New Zealand found that adolescents who used marijuana regularly were significantly less likely than their non-using peers to finish high school or obtain a degree. They also had a much higher chance of developing dependence, using other drugs, and attempting suicide.[54] Several studies have also linked heavy marijuana use to lower income, greater welfare dependence, unemployment, criminal behavior, and lower life satisfaction.[55,56]

To what degree marijuana use is directly causal in these associations remains an open question requiring further research. It is possible that other factors independently predispose people to both marijuana use and various negative life outcomes such as school dropout.[57] That said, people report a perceived influence of their marijuana use on poor outcomes on a variety of life satisfaction and achievement measures. One study, for example, compared people involved with current and former long-term, heavy use of marijuana with a control group who reported smoking marijuana at least once in their lives but not more than 50 times.[58] All participants had similar education and income backgrounds, but significant differences were found in their educational attainment: Fewer of those who engaged in heavy cannabis use completed college, and more had yearly household incomes of less than $30,000. When asked how marijuana affected their cognitive abilities, career achievements, social lives, and physical and mental health, the majority of those who used heavily reported that marijuana had negative effects in all these areas of their lives.

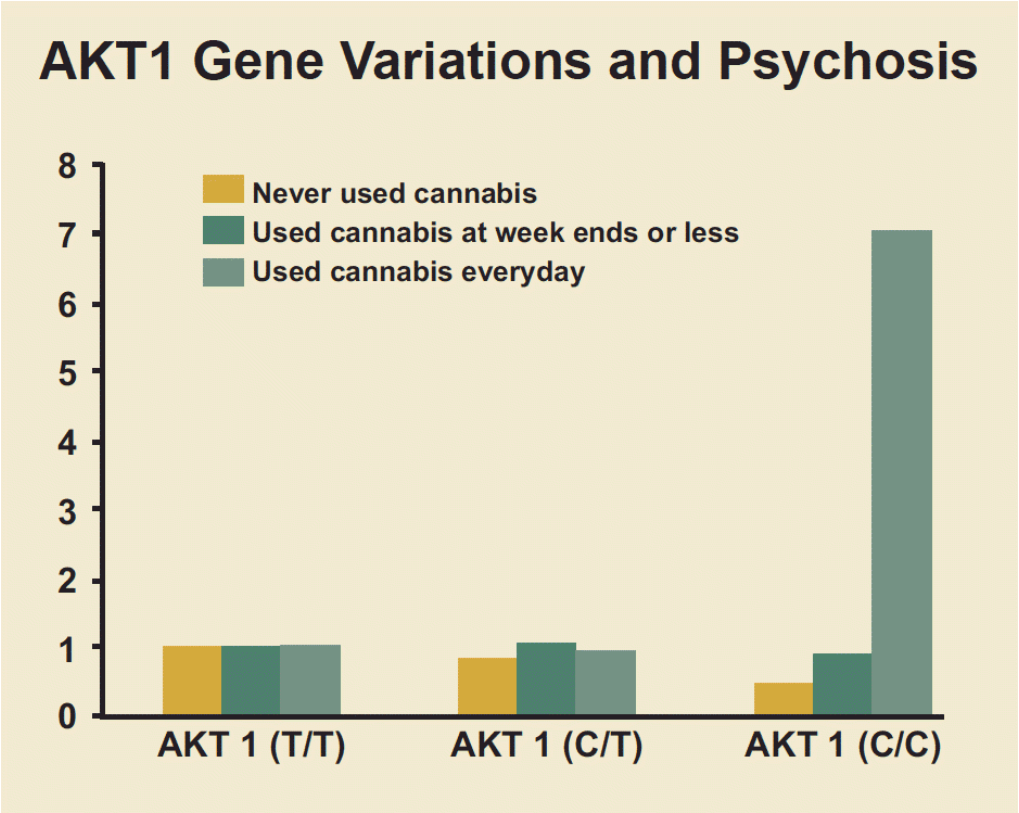
Studies have also suggested specific links between marijuana use and adverse consequences in the workplace, such as increased risk for injury or accidents.[59] One study among postal workers found that employees who tested positive for marijuana on a pre-employment urine drug test had 55% more industrial accidents, 85% more injuries, and 75% greater absenteeism compared with those who tested negative for marijuana use.[60]

Is there a link between marijuana use and psychiatric disorders?

Several studies have linked marijuana use to increased risk for psychiatric disorders, including psychosis (schizophrenia), depression, anxiety, and substance use disorders, but whether and to what extent it actually causes these conditions is not always easy to determine.[32] Recent research suggests that smoking high-potency marijuana every day could increase the chances of developing psychosis by nearly five times compared to people who have never used marijuana.[113] The amount of drug used, the age at first use, and genetic vulnerability have all been shown to influence this relationship. The strongest evidence to date concerns links between marijuana use and psychiatric disorders in those with a preexisting genetic or other vulnerability.[61]

Research using longitudinal data from the National Epidemiological Survey on Alcohol and Related Conditions examined associations between marijuana use, mood and anxiety disorders, and substance use disorders. After adjusting for various confounding factors, no association between marijuana use and mood and anxiety disorders was found. The only significant associations were increased risk of alcohol use disorders, nicotine dependence, marijuana use disorder, and other drug use disorders.[62]

Recent research (see "AKT1 Gene Variations and Psychosis") has found that people who use marijuana and carry a specific variant of the *AKT1* gene, which codes for an enzyme that affects dopamine signaling in the *striatum*, are at increased risk of developing psychosis. The striatum is an area of the brain that becomes activated and flooded with dopamine when certain stimuli are present. One study found that the risk of psychosis among those with this variant was seven times higher for those who used marijuana daily compared with those who used it infrequently or used none at all.[63]

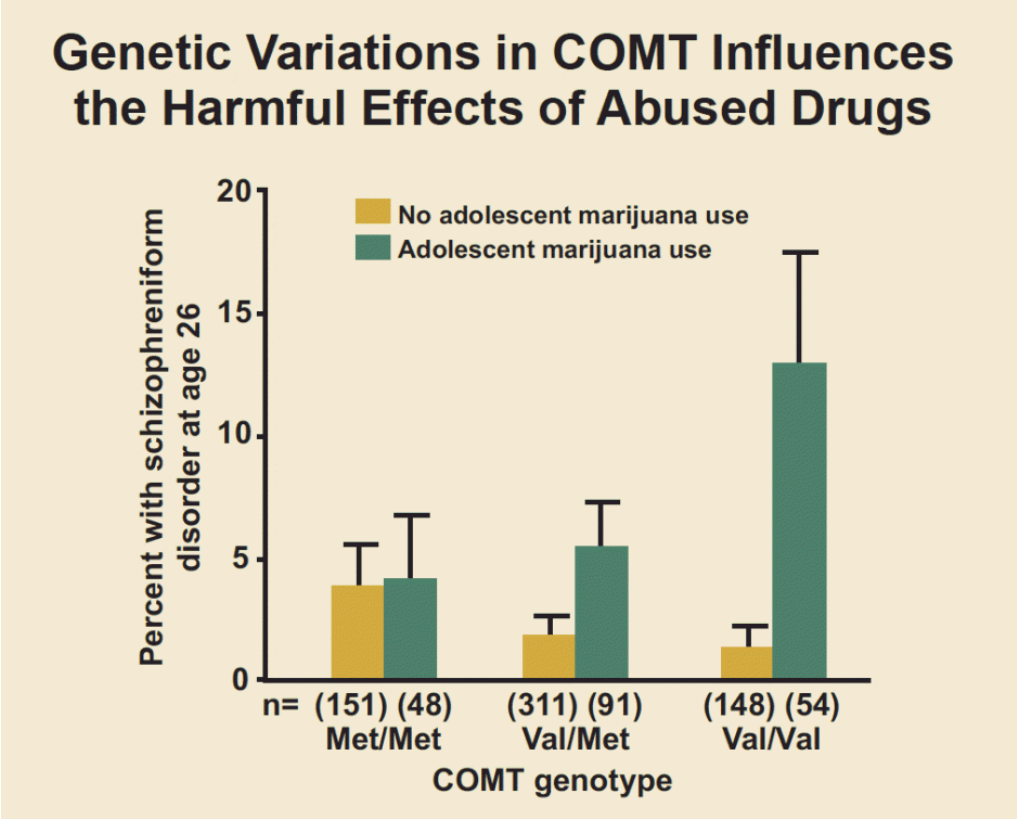


Source: Di Forti et al. Biol Psychiatry. 2012.

Whether adolescent marijuana use can contribute to developing psychosis later in adulthood appears to depend on whether a person already has a genetically based vulnerability to the disorder. The AKT1 gene governs an enzyme that affects brain signaling involving the neurotransmitter dopamine. Altered dopamine signaling is known to be involved in schizophrenia. AKT1 can take one of three forms in a specific region of the gene implicated in susceptibility to schizophrenia: T/T, C/T, and C/C. Those who use marijuana daily (green bars) with the C/C variant have a seven times higher risk of developing psychosis than those who use it infrequently or use none at all. The risk for psychosis among those with the T/T variant was unaffected by whether they used marijuana.

Another study found an increased risk of psychosis among adults who had used marijuana in adolescence and also carried a specific variant of the gene for *catechol-O-methyltransferase* (COMT), an enzyme that degrades neurotransmitters such as dopamine and norepinephrine[64] (see "Genetic Variations in COMT Influences the Harmful Effects of Abused Drugs"). Marijuana use has also been shown to worsen the course of illness in patients who already have schizophrenia. As mentioned

previously, marijuana can produce an acute psychotic reaction in non-schizophrenic people who use marijuana, especially at high doses, although this fades as the drug wears off.



Source: Di Forti et al. Biol Psychiatry. 2012.

The influence of adolescent marijuana use on adult psychosis is affected by genetic variables. This figure shows that variations in a gene can affect the likelihood of developing psychosis in adulthood following exposure to cannabis in adolescence. The COMT gene governs an enzyme that breaks down dopamine, a brain chemical involved in schizophrenia. It comes in two forms: "Met" and "Val." Individuals with one or two copies of the Val variant have a higher risk of developing schizophrenic-type disorders if they used cannabis during adolescence (dark bars). Those with only the Met variant were unaffected by cannabis use.

Inconsistent and modest associations have been reported between marijuana use and suicidal thoughts and attempted suicide among teens.[65,66] Marijuana has also been associated with an

amotivational syndrome, defined as a diminished or absent drive to engage in typically rewarding activities. Because of the role of the endocannabinoid system in regulating mood and reward, it has been hypothesized that brain changes resulting from early use of marijuana may underlie these associations, but more research is needed to verify that such links exist and better understand them.

Adverse Consequences of Marijuana Use

Acute (present during intoxication)

- Impaired short-term memory
- Impaired attention, judgment, and other cognitive functions
- Impaired coordination and balance
- Increased heart rate
- Anxiety, paranoia
- Psychosis (uncommon)

Photo by ©getttyimages.com/Fuse

Persistent (lasting longer than intoxication, but may not be permanent)

- Impaired learning and coordination
- Sleep problems

Long-term (cumulative effects of repeated use)

- Potential for marijuana addiction
- Impairments in learning and memory with potential loss of IQ*
- Increased risk of chronic cough, bronchitis
- Increased risk of other drug and alcohol use disorders
- Increased risk of schizophrenia in people with genetic vulnerability**

*Loss of IQ among individuals with persistent marijuana use disorder who began using heavily during adolescence

**These are often reported co-occurring symptoms/disorders with chronic marijuana use. However, research has not yet determined whether marijuana is causal or just associated with these mental problems.

What are marijuana's effects on lung health?

Like tobacco smoke, marijuana smoke is an irritant to the throat and lungs and can cause a heavy cough during use. It also contains levels of volatile chemicals and tar that are similar to tobacco smoke, raising concerns about risk for cancer and lung disease.[67]

Marijuana smoking is associated with large airway inflammation, increased airway resistance, and lung hyperinflation, and those who smoke marijuana regularly report more symptoms of chronic bronchitis than those who do not smoke.[67,68] One study found that people who frequently smoke marijuana had more outpatient medical visits for respiratory problems than those who do not smoke.[69] Some case studies have suggested that, because of THC's immune-suppressing effects, smoking marijuana might increase susceptibility to lung infections, such as pneumonia, in people with immune deficiencies; however, a large AIDS cohort study did not confirm such an association.[67] Smoking marijuana may also reduce the respiratory system's immune response, increasing the likelihood of the person acquiring respiratory infections, including pneumonia.[68] Animal and human studies have not found that marijuana increases risk for emphysema.[67]

Reports of Deaths Related to Vaping Marijuana

The Food and Drug Administration has alerted the public to hundreds of reports of serious lung illnesses associated with vaping, including several deaths. They are working with the Centers for Disease Control and Prevention (CDC) to investigate the cause of these illnesses. Many of the

> suspect products tested by the states or federal health officials have been identified as vaping products containing THC, the main psychotropic ingredient in marijuana. Some of the patients reported a mixture of THC and nicotine; and some reported vaping nicotine alone. No one substance has been identified in all of the samples tested, and it is unclear if the illnesses are related to one single compound. Until more details are known, FDA officials have warned people not to use any vaping products bought on the street, and they warn against modifying any products purchased in stores. They are also asking people and health professionals to report any adverse effects. The CDC has posted an information page for consumers.

Whether smoking marijuana causes lung cancer, as cigarette smoking does, remains an open question.[67,70] Marijuana smoke contains carcinogenic combustion products, including about 50% more benzoprene and 75% more benzanthracene (and more phenols, vinyl chlorides, nitrosamines, reactive oxygen species) than cigarette smoke.[67] Because of how it is typically smoked (deeper inhale, held for longer), marijuana smoking leads to four times the deposition of tar compared to cigarette smoking.[71] However, while a few small, uncontrolled studies have suggested that heavy, regular marijuana smoking could increase risk for respiratory cancers, well-designed population studies have failed to find an increased risk of lung cancer associated with marijuana use.[67]

One complexity in comparing the lung-health risks of marijuana and tobacco concerns the very different ways the two substances are used. While people who smoke marijuana often inhale more deeply and hold the smoke in their lungs for a longer duration than is typical with cigarettes, marijuana's effects last longer, so people who use marijuana may smoke less frequently than those who smoke cigarettes.

Additionally, the fact that many people use both marijuana and tobacco makes determining marijuana's precise contribution to lung cancer risk, if any, difficult to establish. Cell culture and animal studies have also suggested THC and CBD may have antitumor effects, and this has been proposed as one reason why stronger expected associations are not seen between marijuana use and lung cancer, but more research is needed on this question.[67]

What are marijuana's effects on other aspects of physical health?

Within a few minutes after inhaling marijuana smoke, a person's heart rate speeds up, the breathing passages relax and become enlarged, and blood vessels in the eyes expand, making the eyes look bloodshot. The heart rate—normally 70 to 80 beats per minute—may increase by 20 to 50 beats per minute or may even double in some cases. Taking other drugs with marijuana can amplify this effect.

Limited evidence suggests that a person's risk of heart attack during the first hour after smoking marijuana is nearly five times his or her usual risk.[72] This observation could be partly explained by marijuana raising blood pressure (in some cases) and heart rate and reducing the blood's capacity to carry oxygen.[73] Marijuana may also cause *orthostatic hypotension* (head rush or dizziness on standing up), possibly raising danger from fainting and falls. Tolerance to some cardiovascular effects often develops with repeated exposure.[74] These health effects need to be examined more closely, particularly given the increasing use of "medical marijuana" by people with health issues and older adults who may have increased baseline vulnerability due to age-related cardiovascular risk factors (see "Is marijuana safe and effective as medicine?").

A few studies have shown a clear link between marijuana use in adolescence and increased risk for an aggressive form of testicular cancer (nonseminomatous testicular germ cell tumor) that predominantly strikes young adult males.[75,76] The early onset of testicular cancers compared to lung and most other cancers indicates that, whatever the nature of marijuana's contribution, it may accumulate over just a few years of use.

Studies have shown that in rare cases, chronic use of marijuana can lead to Cannabinoid Hyperemesis Syndrome—a condition marked by recurrent bouts of severe nausea, vomiting, and dehydration. This syndrome has been found to occur in persons under 50 years of age and with a long history of marijuana use. Cannabinoid Hyperemesis Syndrome can lead sufferers to make frequent trips to the emergency room, but may be resolved when a person stops using marijuana.[77]

Is marijuana safe and effective as medicine?

The potential medicinal properties of marijuana and its components have been the subject of research and heated debate for decades. THC itself has proven medical benefits in particular formulations. The U.S. Food and Drug Administration (FDA) has approved THC-based medications, dronabinol (Marinol®) and nabilone (Cesamet®), prescribed in pill form for the treatment of nausea in patients undergoing cancer chemotherapy and to stimulate appetite in patients with wasting syndrome due to AIDS.

In addition, several other marijuana-based medications have been approved or are undergoing clinical trials. Nabiximols (Sativex®), a mouth spray that is currently available in the United Kingdom, Canada, and several European countries for treating the spasticity and neuropathic pain that may accompany multiple sclerosis, combines THC with another chemical found in marijuana called cannabidiol (CBD).

The FDA also approved a CBD-based liquid medication called Epidiolex® for the treatment of two forms of severe childhood epilepsy, Dravet syndrome and Lennox-Gastaut syndrome. It’s being delivered to patients in a reliable dosage form and through a reproducible route of delivery to ensure that patients derive the anticipated benefits. CBD does not have the rewarding properties of THC.

Researchers generally consider medications like these, which use purified chemicals derived from or based on those in the marijuana plant, to be more promising therapeutically than use of the whole marijuana plant or its crude extracts. Development of drugs from botanicals such as the marijuana plant poses numerous challenges. Botanicals may contain hundreds of unknown, active chemicals, and it can be difficult to develop a product with accurate and consistent doses of these chemicals. Use of marijuana as medicine also poses other problems such as the adverse health effects of smoking and THC-induced cognitive impairment. Nevertheless, a growing number of states have legalized dispensing of marijuana or its extracts to people with a range of medical conditions.

An additional concern with "medical marijuana" is that little is known about the long-term impact of its use by people with health- and/or age-related vulnerabilities—such as older adults or people with cancer, AIDS, cardiovascular disease, multiple sclerosis, or other neurodegenerative diseases. Further research will be needed to determine whether people whose health has been compromised by disease or its treatment (e.g., chemotherapy) are at greater risk for adverse health outcomes from marijuana use.

Medical Marijuana Laws and Prescription Opioid Use Outcomes

A new study underscores the need for additional research on the effect of medical marijuana laws on opioid overdose deaths and cautions against drawing a causal connection between the two. Early research suggested that there may be a relationship between the availability of medical marijuana and opioid analgesic overdose mortality. In particular, a NIDA-funded study published in 2014 found that from 1999 to 2010, states with medical cannabis laws experienced slower rates of increase in opioid analgesic overdose death rates compared to states without such laws.[78]

A 2019 analysis, also funded by NIDA, re-examined this relationship using data through 2017. Similar to the findings reported previously, this research team found that opioid overdose mortality rates between 1999-2010 in states allowing medical marijuana use were 21% lower than expected. When the analysis was extended through 2017, however, they found that the trend reversed, such that states with medical cannabis laws experienced an overdose death rate 22.7% higher than expected.[79] The investigators uncovered no evidence that either broader cannabis laws (those allowing recreational use) or more restrictive laws (those only permitting the use of marijuana with low tetrahydrocannabinol concentrations) were associated with changes in opioid overdose mortality rates.

These data, therefore, do not support the interpretation that access to cannabis reduces opioid overdose. Indeed, the authors note that neither study provides evidence of a causal relationship between marijuana access and opioid overdose deaths. Rather, they suggest that the associations are likely due to factors the researchers did not measure, and they caution against drawing conclusions on an individual level from ecological (population-level) data. Research is still needed on the potential medical benefits of cannabis or cannabinoids.

What are the effects of secondhand exposure to marijuana smoke?

People often ask about the possible psychoactive effect of exposure to secondhand marijuana smoke and whether a person who has inhaled secondhand marijuana smoke could fail a drug test.

Researchers measured the amount of THC in the blood of people who do not smoke marijuana and had spent 3 hours in a well-ventilated space with people casually smoking marijuana; THC was present in the blood of the nonsmoking participants, but the amount was well below the level needed to fail a drug test. Another study that varied the levels of ventilation and the potency of the marijuana found that some nonsmoking participants exposed for an hour to high-THC marijuana (11.3% THC concentration) in an unventilated room showed positive urine assays in the hours directly following exposure[80]; a follow-up study showed that nonsmoking people in a confined space with people smoking high-THC marijuana reported mild subjective effects of the drug—a "contact high"—and displayed mild impairments on performance in motor tasks.[81]

The known health risks of secondhand exposure to cigarette smoke—to the heart or lungs, for instance—raise questions about whether secondhand exposure to marijuana smoke poses similar health risks. At this point, very little research on this question has been conducted. A 2016 study in rats found that secondhand exposure to marijuana smoke affected a measure of blood vessel function as much as secondhand tobacco smoke, and the effects lasted longer.[82] One minute of exposure to secondhand marijuana smoke impaired flow-mediated dilation (the extent to which arteries enlarge in response to increased blood flow) of the femoral artery that lasted for at least 90 minutes; impairment from 1 minute of secondhand tobacco exposure was recovered within 30 minutes. The effects of marijuana smoke were independent of THC concentration; i.e., when THC was removed, the impairment was still present. This research has not yet been conducted with human subjects, but the toxins and tar levels known to be present in marijuana smoke (see “What are marijuana’s effects on lung health?”) raise concerns about exposure among vulnerable populations, such as children and people with asthma.

Can marijuana use during and after pregnancy harm the baby?

More research is needed on how marijuana use during pregnancy could impact the health and development of infants, given changing policies about access to marijuana, as well as significant increases over the last decade in the number of pregnant women seeking substance use disorder treatment for marijuana use.[83] One study found that about 20% of pregnant women 24-years-old and younger screened positive for marijuana. However, this study also found that women were about twice as likely to screen positive for marijuana use via a drug test than they state in self-reported measures. This suggests that self-reported rates of marijuana use in pregnant females may not be an accurate measure of marijuana use.[84] Additionally, in one study of dispensaries, nonmedical personnel at marijuana dispensaries were recommending marijuana to pregnant women for nausea, but medical experts warn against it.

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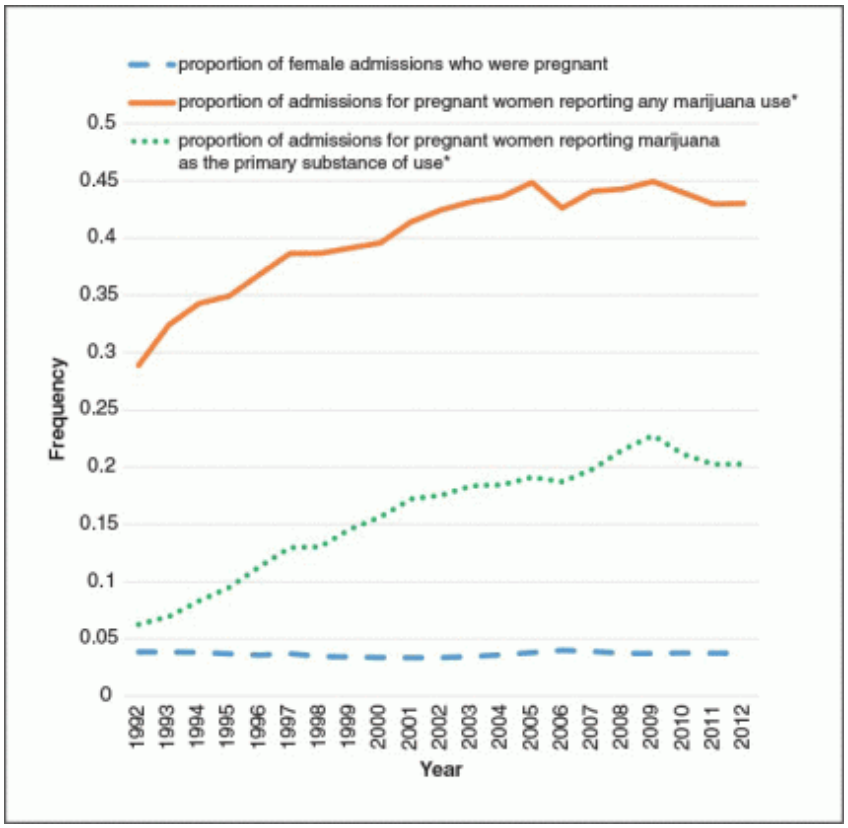
There is no human research connecting marijuana use to the chance of miscarriage,[85,86] although animal studies indicate that the risk for miscarriage increases if marijuana is used early in pregnancy.[87] Some associations have been found between marijuana use during pregnancy and future developmental and hyperactivity disorders in children.[88–91] Evidence is mixed as to whether marijuana use by pregnant women is associated with low birth weight[92–96] or premature birth,[95] although long-term use may elevate these risks.[94] Research has shown that pregnant women who use marijuana have a 2.3 times greater risk of stillbirth.[97] Given the potential of marijuana to negatively impact the developing brain, the American College of Obstetricians and Gynecologists recommends that obstetrician-gynecologists counsel women against using marijuana while trying to get pregnant, during pregnancy, and while they are breastfeeding.[98] It is important to note that despite the growing popularity of using marijuana in vaping devices, the Food and Drug Administration recommends that pregnant women should not use any vaping product, regardless of the substance.



Source: Martin et al., 2015

Recent Trends in Treatment Admissions for Marijuana Use During Pregnancy

Some women report using marijuana to treat severe nausea associated with their pregnancy;[99,100] however, there is no research confirming that this is a safe practice, and it is generally not recommended. Women considering using medical marijuana while pregnant should not do so without checking with their health care providers. Animal studies have shown that moderate concentrations of THC, when administered to mothers while pregnant or nursing, could have long-lasting effects on the child, including increasing stress responsivity and abnormal patterns of social interactions.[101] Animal studies also show learning deficits in prenatally exposed individuals.[33,102]

Human research has shown that some babies born to women who used marijuana during their pregnancies display altered responses to visual stimuli, increased trembling, and a high-pitched cry,[103] which could indicate problems with neurological development.[104] In school, marijuana-exposed children are more likely to show gaps in problem-solving skills, memory,[105] and the ability to remain

attentive.[106] More research is needed, however, to disentangle marijuana-specific effects from those of other environmental factors that could be associated with a mother's marijuana use, such as an impoverished home environment or the mother's use of other drugs.[96] Prenatal marijuana exposure is also associated with an increased likelihood of a person using marijuana as a young adult, even when other factors that influence drug use are considered.[107] More information on marijuana use during pregnancy can be found in the NIDA's *Substance Use in Women Research Report*.

Very little is known about marijuana use and breastfeeding. One study suggests that moderate amounts of THC find their way into breast milk when a nursing mother uses marijuana.[108] Some evidence shows that exposure to THC through breast milk in the first month of life could result in decreased motor development at 1 year of age.[109] There have been no studies to determine if exposure to THC during nursing is linked to effects later in the child's life. With regular use, THC can accumulate in human breast milk to high concentrations.[92] Because a baby's brain is still forming, THC consumed in breast milk could affect brain development. Given all these uncertainties, nursing mothers are discouraged from using marijuana.[98,110] New mothers using medical marijuana should be vigilant about coordinating care between the doctor recommending their marijuana use and the pediatrician caring for their baby.

Available Treatments for Marijuana Use Disorders

Marijuana use disorders appear to be very similar to other substance use disorders, although the long-term clinical outcomes may be less severe. On average, adults seeking treatment for marijuana use disorders have used marijuana nearly every day for more than 10 years and have attempted to quit more than six times.[111] People with marijuana use disorders, especially adolescents, often also suffer from other psychiatric disorders (*comorbidity*).[112] They may also use or be addicted to other substances, such as cocaine or alcohol. Available studies indicate that effectively treating the mental health disorder with standard treatments involving medications and behavioral therapies may help reduce marijuana use, particularly among those involved with heavy use and those with more chronic mental disorders. The following behavioral treatments have shown promise:

- **Cognitive-behavioral therapy**: A form of psychotherapy that teaches people strategies to identify and correct problematic behaviors in order to enhance self-control, stop drug use, and address a

range of other problems that often co-occur with them.

- **Contingency management**: A therapeutic management approach based on frequent monitoring of the target behavior and the provision (or removal) of tangible, positive rewards when the target behavior occurs (or does not).
- **Motivational enhancement therapy**: A systematic form of intervention designed to produce rapid, internally motivated change; the therapy does not attempt to treat the person, but rather mobilize his or her own internal resources for change and engagement in treatment.

Currently, the FDA has not approved any medications for the treatment of marijuana use disorder, but research is active in this area. Because sleep problems feature prominently in marijuana withdrawal, some studies are examining the effectiveness of medications that aid in sleep. Medications that have shown promise in early studies or small clinical trials include the sleep aid zolpidem (Ambien®), an anti-anxiety/anti-stress medication called buspirone (BuSpar®), and an anti-epileptic drug called gabapentin (Horizant®, Neurontin®) that may improve sleep and, possibly, executive function. Other agents being studied include the nutritional supplement N-acetylcysteine and chemicals called FAAH inhibitors, which may reduce withdrawal by inhibiting the breakdown of the body's own cannabinoids. Future directions include the study of substances called *allosteric modulators* that interact with cannabinoid receptors to inhibit THC's rewarding effects.

Where can I get further information about marijuana?

The NIDA website includes:

- information about drugs and related health consequences
- NIDA publications, news, and events
- resources for health care professionals
- funding information (including program announcements and deadlines)
- international activities
- links to related websites (access to websites of many other organizations in the field)
- information in Spanish (en español)

NIDA webpages

- nida.nih.gov/drugs-abuse/marijuana
- nida.nih.gov/related-topics/hivaids
- researchstudies.drugabuse.gov
- irp.drugabuse.gov

For physician information

- NIDAMED: nida.nih.gov/nidamed

Other websites

Information about marijuana is also available through the following websites:

- Substance Abuse and Mental Health Services Administration (SAMHSA)
- Drug Enforcement Administration (DEA)
- Monitoring the Future
- Partnership for Drug-Free Kids

References

1. Timberlake DS. A comparison of drug use and dependence between blunt smokers and other cannabis users. *Subst Use Misuse*. 2009;44(3):401-415. doi:10.1080/10826080802347651
2. Mehmedic Z, Chandra S, Slade D, et al. Potency trends of ?9-THC and other cannabinoids in confiscated cannabis preparations from 1993 to 2008. *J Forensic Sci*. 2010;55(5):1209-1217. doi:10.1111/j.1556-4029.2010.01441.x

3. Substance Abuse Center for Behavioral Health Statistics and Quality. Results from the 2018 National Survey on Drug Use and Health: Detailed Tables, SAMHSA. https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables. Accessed December 2019.
4. Carliner H, Mauro PM, Brown QL, et al. The widening gender gap in marijuana use prevalence in the U.S. during a period of economic change, 2002-2014. *Drug Alcohol Depend*. 2016;170:51-58. doi:10.1016/j.drugalcdep.2016.10.042
5. Johnston L, O'Malley P, Miech R, Bachman J, Schulenberg J. *Monitoring the Future National Survey Results on Drug Use: 1975-2018: Overview: Key Findings on Adolescent Drug Use.* Ann Arbor, MI: Institute for Social Research, The University of Michigan; 2018.
6. Center for Behavioral Health Statistics and Quality (CBHSQ). *Drug Abuse Warning Network: 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.
7. Lenné MG, Dietze PM, Triggs TJ, Walmsley S, Murphy B, Redman JR. The effects of cannabis and alcohol on simulated arterial driving: Influences of driving experience and task demand. *Accid Anal Prev*. 2010;42(3):859-866. doi:10.1016/j.aap.2009.04.021
8. Hartman RL, Huestis MA. Cannabis effects on driving skills. *Clin Chem*. 2013;59(3):478-492. doi:10.1373/clinchem.2012.194381
9. Hartman RL, Brown TL, Milavetz G, et al. Cannabis effects on driving lateral control with and without alcohol. *Drug Alcohol Depend*. 2015;154:25-37. doi:10.1016/j.drugalcdep.2015.06.015
10. Brady JE, Li G. Trends in Alcohol and Other Drugs Detected in Fatally Injured Drivers in the United States, 1999–2010. *Am J Epidemiol*. January 2014:kwt327. doi:10.1093/aje/kwt327
11. Biecheler M-B, Peytavin J-F, Sam Group, Facy F, Martineau H. SAM survey on "drugs and fatal accidents": search of substances consumed and comparison between drivers involved under the influence of alcohol or cannabis. *Traffic Inj Prev*. 2008;9(1):11-21. doi:10.1080/15389580701737561
12. *DRUID Final Report: Work Performed, Main Results and Recommendations.* EU DRUID Programme; 2012. http://www.roadsafetyobservatory.com/Evidence/Details/10940.
13. Elvik R. Risk of road accident associated with the use of drugs: a systematic review and meta-analysis of evidence from epidemiological studies. *Accid Anal Prev*. 2013;60:254-267. doi:10.1016/j.aap.2012.06.017
14. Ramaekers JG, Berghaus G, van Laar M, Drummer OH. Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend*. 2004;73(2):109-119.

15. Li M-C, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, Li G. Marijuana Use and Motor Vehicle Crashes. *Epidemiol Rev*. 2012;34(1):65-72. doi:10.1093/epirev/mxr017

16. Asbridge M, Hayden JA, Cartwright JL. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. *BMJ*. 2012;344:e536. doi:10.1136/bmj.e536

17. Compton RP, Berning A. *Drug and Alcohol Crash Risk*. Washington, DC: National Highway Traffic Safety Administration; 2015. DOT HA 812 117.

18. Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of Marijuana Use Disorders in the United States Between 2001-2002 and 2012-2013. *JAMA Psychiatry*. 2015;72(12):1235-1242. doi:10.1001/jamapsychiatry.2015.1858

19. Winters KC, Lee C-YS. Likelihood of developing an alcohol and cannabis use disorder during youth: Association with recent use and age. *Drug Alcohol Depend*. 2008;92(1-3):239-247. doi:10.1016/j.drugalcdep.2007.08.005

20. Budney AJ, Hughes JR. The cannabis withdrawal syndrome. *Curr Opin Psychiatry*. 2006;19(3):233-238. doi:10.1097/01.yco.0000218592.00689.e5

21. Gorelick DA, Levin KH, Copersino ML, et al. Diagnostic Criteria for Cannabis Withdrawal Syndrome. *Drug Alcohol Depend*. 2012;123(1-3):141-147. doi:10.1016/j.drugalcdep.2011.11.007

22. Rotter A, Bayerlein K, Hansbauer M, et al. CB1 and CB2 receptor expression and promoter methylation in patients with cannabis dependence. *Eur Addict Res*. 2013;19(1):13-20. doi:10.1159/000338642

23. Morgan CJA, Page E, Schaefer C, et al. Cerebrospinal fluid anandamide levels, cannabis use and psychotic-like symptoms. *Br J Psychiatry J Ment Sci*. 2013;202(5):381-382. doi:10.1192/bjp.bp.112.121178

24. Anthony JC, Warner LA, Kessler RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey. *Exp Clin Psychopharmacol*. 1994;2(3):244-268. doi:10.1037/1064-1297.2.3.244

25. Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend*. 2011;115(1-2):120-130. doi:10.1016/j.drugalcdep.2010.11.004

26. Anthony JC. The epidemiology of cannabis dependence. In: Roffman RA, Stephens RS, eds. *Cannabis Dependence: Its Nature, Consequences and Treatment.* Cambridge, UK: Cambridge

University Press; 2006:58-105.

27. Hall WD, Pacula RL. *Cannabis Use and Dependence: Public Health and Public Policy*. Cambridge, UK: Cambridge University Press; 2003.

28. Center for Behavioral Health Statistics and Quality (CBHSQ). *Treatment Episode Data Set (TEDS): 2003-2013. National Admissions to Substance Abuse Treatment Services.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2015. BHSIS Series S-75, HHS Publication No. (SMA) 15-4934.

29. *Office of National Drug Control Policy, National Drug Control Strategy Data Supplement 2020, Feb. 2020, p. 95, Table #77* https://www.whitehouse.gov/wp-content/uploads/2020/02/2020-NDCS-Data-Supplement.pdf

30. Freeman TP, Morgan CJA, Hindocha C, Schafer G, Das RK, Curran HV. Just say “know”: how do cannabinoid concentrations influence users’ estimates of cannabis potency and the amount they roll in joints? *Addict Abingdon Engl*. 2014;109(10):1686-1694. doi:10.1111/add.12634

31. Van der Pol P, Liebregts N, Brunt T, et al. Cross-sectional and prospective relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: an ecological study. *Addict Abingdon Engl*. 2014;109(7):1101-1109. doi:10.1111/add.12508

32. Campolongo P, Trezza V, Cassano T, et al. Perinatal exposure to delta-9-tetrahydrocannabinol causes enduring cognitive deficits associated with alteration of cortical gene expression and neurotransmission in rats. *Addict Biol*. 2007;12(3-4):485-495. doi:10.1111/j.1369-1600.2007.00074.x

33. Antonelli T, Tomasini MC, Tattoli M, et al. Prenatal exposure to the CB1 receptor agonist WIN 55,212-2 causes learning disruption associated with impaired cortical NMDA receptor function and emotional reactivity changes in rat offspring. *Cereb Cortex N Y N 1991*. 2005;15(12):2013-2020. doi:10.1093/cercor/bhi076

34. Verrico CD, Gu H, Peterson ML, Sampson AR, Lewis DA. Repeated ?9-tetrahydrocannabinol exposure in adolescent monkeys: persistent effects selective for spatial working memory. *Am J Psychiatry*. 2014;171(4):416-425. doi:10.1176/appi.ajp.2013.13030335

35. Rubino T, Realini N, Braida D, et al. Changes in hippocampal morphology and neuroplasticity induced by adolescent THC treatment are associated with cognitive impairment in adulthood. *Hippocampus*. 2009;19(8):763-772. doi:10.1002/hipo.20554

36. Gleason KA, Birnbaum SG, Shukla A, Ghose S. Susceptibility of the adolescent brain to cannabinoids: long-term hippocampal effects and relevance to schizophrenia. *Transl Psychiatry*. 2012;2:e199. doi:10.1038/tp.2012.122

37. Quinn HR, Matsumoto I, Callaghan PD, et al. Adolescent rats find repeated Delta(9)-THC less aversive than adult rats but display greater residual cognitive deficits and changes in hippocampal protein expression following exposure. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol*. 2008;33(5):1113-1126. doi:10.1038/sj.npp.1301475

38. Batalla A, Bhattacharyya S, Yücel M, et al. Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings. *PloS One*. 2013;8(2):e55821. doi:10.1371/journal.pone.0055821

39. Filbey FM, Aslan S, Calhoun VD, et al. Long-term effects of marijuana use on the brain. *Proc Natl Acad Sci U S A*. 2014;111(47):16913-16918. doi:10.1073/pnas.1415297111

40. Pagliaccio D, Barch DM, Bogdan R, et al. Shared predisposition in the association between cannabis use and subcortical brain structure. *JAMA Psychiatry*. 2015;72(10):994-1001. doi:10.1001/jamapsychiatry.2015.1054

41. Volkow ND, Swanson JM, Evins AE, et al. Effects of cannabis use on human behavior, including cognition, motivation, and psychosis: a review. *JAMA Psychiatry*. 2016;73(3):292-297. doi:10.1001/jamapsychiatry.2015.3278

42. Auer R, Vittinghoff E, Yaffe K, et al. Association between lifetime marijuana use and cognitive function in middle age: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *JAMA Intern Med*. February 2016. doi:10.1001/jamainternmed.2015.7841

43. Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A*. 2012;109(40):E2657-E2664. doi:10.1073/pnas.1206820109

44. Jackson NJ, Isen JD, Khoddam R, et al. Impact of adolescent marijuana use on intelligence: Results from two longitudinal twin studies. *Proc Natl Acad Sci U S A*. 2016;113(5):E500-E508. doi:10.1073/pnas.1516648113

45. Secades-Villa R, Garcia-Rodríguez O, Jin CJ, Wang S, Blanco C. Probability and predictors of the cannabis gateway effect: a national study. *Int J Drug Policy*. 2015;26(2):135-142. doi:10.1016/j.drugpo.2014.07.011

46. Weinberger AH, Platt J, Goodwin RD. Is cannabis use associated with an increased risk of onset and persistence of alcohol use disorders? A three-year prospective study among adults in the United States. *Drug Alcohol Depend*. February 2016. doi:10.1016/j.drugalcdep.2016.01.014

47. Pistis M, Perra S, Pillolla G, Melis M, Muntoni AL, Gessa GL. Adolescent exposure to cannabinoids induces long-lasting changes in the response to drugs of abuse of rat midbrain dopamine neurons. *Biol Psychiatry*. 2004;56(2):86-94. doi:10.1016/j.biopsych.2004.05.006

48. Agrawal A, Neale MC, Prescott CA, Kendler KS. A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. *Psychol Med*. 2004;34(7):1227-1237.

49. Panlilio LV, Zanettini C, Barnes C, Solinas M, Goldberg SR. Prior exposure to THC increases the addictive effects of nicotine in rats. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol*. 2013;38(7):1198-1208. doi:10.1038/npp.2013.16

50. Cadoni C, Pisanu A, Solinas M, Acquas E, Di Chiara G. Behavioural sensitization after repeated exposure to Delta 9-tetrahydrocannabinol and cross-sensitization with morphine. *Psychopharmacology (Berl)*. 2001;158(3):259-266. doi:10.1007/s002130100875

51. Levine A, Huang Y, Drisaldi B, et al. Molecular mechanism for a gateway drug: epigenetic changes initiated by nicotine prime gene expression by cocaine. *Sci Transl Med*. 2011;3(107):107ra109. doi:10.1126/scitranslmed.3003062

52. Schweinsburg AD, Brown SA, Tapert SF. The influence of marijuana use on neurocognitive functioning in adolescents. *Curr Drug Abuse Rev*. 2008;1(1):99-111.

53. Macleod J, Oakes R, Copello A, et al. Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. *Lancet Lond Engl*. 2004;363(9421):1579-1588. doi:10.1016/S0140-6736(04)16200-4

54. Silins E, Horwood LJ, Patton GC, et al. Young adult sequelae of adolescent cannabis use: an integrative analysis. *Lancet Psychiatry*. 2014;1(4):286-293. doi:10.1016/S2215-0366(14)70307-4

55. Fergusson DM, Boden JM. Cannabis use and later life outcomes. *Addict Abingdon Engl*. 2008;103(6):969-976; discussion 977-978. doi:10.1111/j.1360-0443.2008.02221.x

56. Brook JS, Lee JY, Finch SJ, Seltzer N, Brook DW. Adult work commitment, financial stability, and social environment as related to trajectories of marijuana use beginning in adolescence. *Subst Abuse*. 2013;34(3):298-305. doi:10.1080/08897077.2013.775092

57. McCaffrey DF, Pacula RL, Han B, Ellickson P. Marijuana Use and High School Dropout: The Influence of Unobservables. *Health Econ*. 2010;19(11):1281-1299. doi:10.1002/hec.1561

58. Gruber AJ, Pope HG, Hudson JI, Yurgelun-Todd D. Attributes of long-term heavy cannabis users: a case-control study. *Psychol Med*. 2003;33(8):1415-1422.

59. Macdonald S, Hall W, Roman P, Stockwell T, Coghlan M, Nesvaag S. Testing for cannabis in the work-place: a review of the evidence. *Addict Abingdon Engl*. 2010;105(3):408-416. doi:10.1111/j.1360-0443.2009.02808.x

60. Zwerling C, Ryan J, Orav EJ. The efficacy of preemployment drug screening for marijuana and cocaine in predicting employment outcome. *JAMA*. 1990;264(20):2639-2643.

61. Radhakrishnan R, Wilkinson ST, D'Souza DC. Gone to Pot - A Review of the Association between Cannabis and Psychosis. *Front Psychiatry*. 2014;5:54. doi:10.3389/fpsyt.2014.00054

62. Blanco C, Hasin DS, Wall MM, et al. Cannabis Use and Risk of Psychiatric Disorders: Prospective Evidence From a US National Longitudinal Study. *JAMA Psychiatry*. February 2016. doi:10.1001/jamapsychiatry.2015.3229

63. Di Forti M, Iyegbe C, Sallis H, et al. Confirmation that the AKT1 (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biol Psychiatry*. 2012;72(10):811-816. doi:10.1016/j.biopsych.2012.06.020

64. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. *Biol Psychiatry*. 2005;57(10):1117-1127. doi:10.1016/j.biopsych.2005.01.026

65. Delforterie MJ, Lynskey MT, Huizink AC, et al. The relationship between cannabis involvement and suicidal thoughts and behaviors. *Drug Alcohol Depend*. 2015;150:98-104. doi:10.1016/j.drugalcdep.2015.02.019

66. Borges G, Bagge CL, Orozco R. A literature review and meta-analyses of cannabis use and suicidality. *J Affect Disord*. 2016;195:63-74. doi:10.1016/j.jad.2016.02.007

67. Tashkin DP. Effects of marijuana smoking on the lung. *Ann Am Thorac Soc*. 2013;10(3):239-247. doi:10.1513/AnnalsATS.201212-127FR

68. Owen KP, Sutter ME, Albertson TE. Marijuana: respiratory tract effects. *Clin Rev Allergy Immunol*. 2014;46(1):65-81. doi:10.1007/s12016-013-8374-y

69. Polen MR, Sidney S, Tekawa IS, Sadler M, Friedman GD. Health care use by frequent marijuana smokers who do not smoke tobacco. *West J Med*. 1993;158(6):596-601.

70. Hashibe M, Morgenstern H, Cui Y, et al. Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study. *Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol*. 2006;15(10):1829-1834. doi:10.1158/1055-9965.EPI-06-0330

71. Hancox RJ, Poulton R, Ely M, et al. Effects of cannabis on lung function: a population-based cohort study. *Eur Respir J*. 2010;35(1):42-47. doi:10.1183/09031936.00065009

72. Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering Myocardial Infarction by Marijuana. *Circulation*. 2001;103(23):2805-2809. doi:10.1161/01.CIR.103.23.2805

73. Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. *Am J Cardiol*. 2014;113(1):187-190. doi:10.1016/j.amjcard.2013.09.042

74. Jones RT. Cardiovascular system effects of marijuana. *J Clin Pharmacol*. 2002;42(11 Suppl):58S - 63S.

75. Lacson JCA, Carroll JD, Tuazon E, Castelao EJ, Bernstein L, Cortessis VK. Population-based case-control study of recreational drug use and testis cancer risk confirms an association between marijuana use and nonseminoma risk. *Cancer*. 2012;118(21):5374-5383. doi:10.1002/cncr.27554

76. Daling JR, Doody DR, Sun X, et al. Association of marijuana use and the incidence of testicular germ cell tumors. *Cancer*. 2009;115(6):1215-1223. doi:10.1002/cncr.24159

77. Galli JA, Sawaya RA, Friedenberg FK. Cannabinoid Hyperemesis Syndrome. *Curr Drug Abuse Rev* . 2011;4(4):241-249.

78. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. JAMA Intern Med. 2014;174(10):1668-1673. doi:10.1001/jamainternmed.2014.4005

79. Chelsea L. Shover, Corey S. Davis, Sanford C. Gordon, and Keith Humphreys, Association between medical cannabis laws and opioid overdose mortality has reversed over time, PNAS June 25, 2019 116 (26) 12624-12626.

80. Röhrich J, Schimmel I, Zörntlein S, et al. Concentrations of delta9-tetrahydrocannabinol and 11-nor-9-carboxytetrahydrocannabinol in blood and urine after passive exposure to Cannabis smoke in a coffee shop. *J Anal Toxicol*. 2010;34(4):196-203.

81. Cone EJ, Bigelow GE, Herrmann ES, et al. Non-smoker exposure to secondhand cannabis smoke. I. Urine screening and confirmation results. *J Anal Toxicol*. 2015;39(1):1-12. doi:10.1093/jat/bku116

82. Wang X, Derakhshandeh R, Liu J, et al. One Minute of Marijuana Secondhand Smoke Exposure Substantially Impairs Vascular Endothelial Function. *J Am Heart Assoc*. 2016;5(8). doi:10.1161/JAHA.116.003858

83. Martin CE, Longinaker N, Mark K, Chisolm MS, Terplan M. Recent trends in treatment admissions for marijuana use during pregnancy. *J Addict Med*. 2015;9(2):99-104. doi:10.1097/ADM.0000000000000095

84. Young-Wolff KC, Tucker L-Y, Alexeeff S, et al. Trends in Self-reported and Biochemically Tested Marijuana Use Among Pregnant Females in California From 2009-2016. *JAMA*. 2017;318(24):2490. doi:10.1001/jama.2017.17225

85. Kline J, Hutzler M, Levin B, Stein Z, Susser M, Warburton D. Marijuana and spontaneous abortion of known karyotype. *Paediatr Perinat Epidemiol*. 1991;5(3):320-332.

86. Wilcox AJ, Weinberg CR, Baird DD. Risk factors for early pregnancy loss. *Epidemiol Camb Mass*. 1990;1(5):382-385.

87. Asch RH, Smith CG. Effects of delta 9-THC, the principal psychoactive component of marijuana, during pregnancy in the rhesus monkey. *J Reprod Med*. 1986;31(12):1071-1081.

88. Campolongo P, Trezza V, Ratano P, Palmery M, Cuomo V. Developmental consequences of perinatal cannabis exposure: behavioral and neuroendocrine effects in adult rodents. *Psychopharmacology (Berl)*. 2011;214(1):5-15. doi:10.1007/s00213-010-1892-x

89. Fried PA, Watkinson B, Gray R. A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes, and alcohol. *Neurotoxicol Teratol*. 1992;14(5):299-311.

90. Goldschmidt L, Day NL, Richardson GA. Effects of prenatal marijuana exposure on child behavior problems at age 10. *Neurotoxicol Teratol*. 2000;22(3):325-336.

91. Fried PA, Smith AM. A literature review of the consequences of prenatal marihuana exposure. An emerging theme of a deficiency in aspects of executive function. *Neurotoxicol Teratol*. 2001;23(1):1-11.

92. Janisse JJ, Bailey BA, Ager J, Sokol RJ. Alcohol, tobacco, cocaine, and marijuana use: relative contributions to preterm delivery and fetal growth restriction. *Subst Abuse*. 2014;35(1):60-67. doi:10.1080/08897077.2013.804483

93. Hayatbakhsh MR, Flenady VJ, Gibbons KS, et al. Birth outcomes associated with cannabis use before and during pregnancy. *Pediatr Res*. 2012;71(2):215-219. doi:10.1038/pr.2011.25

94. Shiono PH, Klebanoff MA, Nugent RP, et al. The impact of cocaine and marijuana use on low birth weight and preterm birth: a multicenter study. *Am J Obstet Gynecol*. 1995;172(1 Pt 1):19-27.

95. Mark K, Desai A, Terplan M. Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes. *Arch Womens Ment Health*. 2016;19(1):105-111. doi:10.1007/s00737-015-0529-9

96. Schempf AH, Strobino DM. Illicit Drug Use and Adverse Birth Outcomes: Is It Drugs or Context? *J Urban Health Bull N Y Acad Med*. 2008;85(6):858-873. doi:10.1007/s11524-008-9315-6

97. Tobacco, drug use in pregnancy can double risk of stillbirth. https://www.nichd.nih.gov/news/releases/Pages/121113-stillbirth-drug-use.aspx. Accessed December 16, 2016.

98. Marijuana Use During Pregnancy and Lactation - ACOG. ACOG. http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Marijuana-Use-During-Pregnancy-and-Lactation. Published July 2015. Accessed October 12, 2016.

99. Roberson EK, Patrick WK, Hurwitz EL. Marijuana use and maternal experiences of severe nausea during pregnancy in Hawai'i. *Hawaii J Med Public Health J Asia Pac Med Public Health*. 2014;73(9):283-287.

100. Westfall RE, Janssen PA, Lucas P, Capler R. Survey of medicinal cannabis use among childbearing women: patterns of its use in pregnancy and retroactive self-assessment of its efficacy against "morning sickness." *Complement Ther Clin Pract*. 2006;12(1):27-33. doi:10.1016/j.ctcp.2005.09.006

101. Trezza V, Campolongo P, Cassano T, et al. Effects of perinatal exposure to delta-9-tetrahydrocannabinol on the emotional reactivity of the offspring: a longitudinal behavioral study in Wistar rats. *Psychopharmacology (Berl)*. 2008;198(4):529-537. doi:10.1007/s00213-008-1162-3

102. Mereu G, Fà M, Ferraro L, et al. Prenatal exposure to a cannabinoid agonist produces memory deficits linked to dysfunction in hippocampal long-term potentiation and glutamate release. *Proc Natl Acad Sci U S A*. 2003;100(8):4915-4920. doi:10.1073/pnas.0537849100

103. Fried PA, Makin JE. Neonatal behavioural correlates of prenatal exposure to marihuana, cigarettes and alcohol in a low risk population. *Neurotoxicol Teratol*. 1987;9(1):1-7.

104. De Moraes Barros MC, Guinsburg R, Mitsuhiro S, Chalem E, Laranjeira RR. Neurobehavioral profile of healthy full-term newborn infants of adolescent mothers. *Early Hum Dev*. 2008;84(5):281-287. doi:10.1016/j.earlhumdev.2007.07.001

105. Richardson GA, Ryan C, Willford J, Day NL, Goldschmidt L. Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years. *Neurotoxicol Teratol*. 2002;24(3):309-320.

106. Goldschmidt L, Day NL, Richardson GA. Effects of prenatal marijuana exposure on child behavior problems at age 10. *Neurotoxicol Teratol*. 2000;22(3):325-336.

107. Sonon KE, Richardson GA, Cornelius JR, Kim KH, Day NL. Prenatal marijuana exposure predicts marijuana use in young adulthood. *Neurotoxicol Teratol*. 2015;47:10-15. doi:10.1016/j.ntt.2014.11.003

108. Perez-Reyes M, Wall ME. Presence of delta9-tetrahydrocannabinol in human milk. *N Engl J Med*. 1982;307(13):819-820. doi:10.1056/NEJM198209233071311

109. Astley SJ, Little RE. Maternal marijuana use during lactation and infant development at one year. *Neurotoxicol Teratol*. 1990;12(2):161-168.

110. Djulus J, Moretti M, Koren G. Marijuana use and breastfeeding. *Can Fam Physician Médecin Fam Can*. 2005;51:349-350.

111. Budney AJ, Roffman R, Stephens RS, Walker D. Marijuana Dependence and Its Treatment. *Addict Sci Clin Pract*. 2007;4(1):4-16.

112. Diamond G, Panichelli-Mindel SM, Shera D, Dennis M, Tims F, Ungemack J. Psychiatric Syndromes in Adolescents with Marijuana Abuse and Dependency in Outpatient Treatment. *J Child Adolesc Subst Abuse*. 2006;15(4):37-54. doi:10.1300/J029v15n04_02

113. Di Forti M, Quattrone D, Freeman TP, et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *The Lancet* 2019;6(5);427-436 doi. 10.1016/S2215-0366(19)30048-3