SUMMARY OF RESEARCH ARTICLES BY JOHNNY'S AMBASSADORS

Excerpted from johnnysambassadors.org/brain

IMPACTS OF MARIJUANA ON THE ADOLESCENT BRAIN



2023

SMOKE ALARM – As states relax their laws on cannabis, neuroscientist

Yasmin Hurd is warning about the drug's dangers for the developing brain.

The receptors, said Hurd, who heads an addiction research lab at the Icahn

School of Medicine at Mount Sinai, are "really critical for so many processes in the brain." And when a person uses cannabis—in any of its edible, dabbable, smokable forms—the drug overwhelms them and disrupts their ability to calibrate neuronal activity.

Long-Term Cannabis Use, Cognitive Decline, and the Hippocampus – March 2023. Psychology Today. New data shows the negative impact of long-term cannabis use on cognition and hippocampal volume at age 45. IQ declines by a mean of 5.5 points and hippocampal volume declines by 12 percent after decades of persistent cannabis use. Changes caused by long-term cannabis use resemble risk factors for dementia later in life.

2022

Aberrant hippocampal shape development in young adults with heavy cannabis use: Evidence from a longitudinal study — June 2022. Aberrant shape development pattern of the hippocampus was observed in young adults with HCU. There was no significant difference in hippocampal shape between the groups at BL, but young adults with HCU at FU exhibited significant shape atrophy of the right dorsal anterior hippocampus related to HCs. In addition, there was a significantly lower growth rate of the right hippocampal shape. Furthermore, there were significant associations of heavy cannabis use, as indicated by the age at onset first and frequent cannabis use, with the growth rate of hippocampal shape in young adults with HCU. The aberrant hippocampal shape development may reflect the effect of heavy cannabis use on young adults and it may be a potential target for heavy cannabis use treatment for young adults.

Long-Term Outcomes of Adolescent THC Exposure on Translational Cognitive Measures in Adulthood in an Animal Model and Computational Assessment of Human Data — Nov. 2022. Although perceived as relatively harmless and nonaddictive, adolescent cannabis use significantly increases the likelihood of developing cannabis use disorder in adulthood, especially for high-potency cannabis. Risky decision-making is associated with chronic cannabis use

2021

Annual Review of Developmental Psychology: The Effects of Cannabis Use on the Development of Adolescents and Young Adults — January 2021. The daily use of cannabis by adolescents and young adults poses risks to the successful completion of psychosocial development. The major acute risk of cannabis use is a car crash if a young person drives while intoxicated. Serious injuries can impair a young person's chances of living a full and productive life. The major risk of regular cannabis use in adolescence is cannabis dependence. This can be a problem if a young person spends much of their waking time in an intoxicated state and finds it difficult to cease using despite wishing to do so.

Association Between Friends Use of Nicotine and Cannabis and Intake of Both Substances among Adolescents – February 2021. We found that friends' use of nicotine and cannabis were independently associated with adolescents' use of each substance, and this was reflected in urinary biomarker levels. These findings underscore the important influence of friends' behavior in adolescent substance use and physiologic impact. Pediatricians should discuss friends' influence on behavior and physiology when counseling their adolescent patients on the smoking and vaping of both nicotine and cannabis products.

Association of Cannabis Use During Adolescence With Neurodevelopment – June 2021. To what extent is cannabis use associated with magnetic resonance imaging—measured cerebral cortical thickness development during adolescence? In this cohort study, linear mixed-effects model analysis using 1598 magnetic resonance images from 799 participants revealed that cannabis use was associated with accelerated age-related cortical thinning from 14 to 19 years of age in predominantly prefrontal regions. The spatial pattern of cannabis-related cortical thinning was significantly associated with a positron emission tomography—assessed map of cannabinoid 1 receptor availability. Results suggest that cannabis use during middle to late adolescence may be associated with altered cerebral cortical development, particularly in regions rich in cannabinoid 1 receptors.

Cannabis and synaptic reprogramming of the developing brain – May 2021. Recent years have been transformational in regard to the perception of the health risks and benefits of cannabis with increased acceptance of use. This has unintended neurodevelopmental implications given the increased use of cannabis and the potent levels of Δ^9 -tetrahydrocannabinol today being consumed by pregnant women, young mothers and teens. In this Review, we provide an overview of the neurobiological effects of cannabinoid exposure during prenatal/perinatal and adolescent periods, in which the endogenous cannabinoid system plays a fundamental role in neurodevelopmental processes. We highlight impaired synaptic plasticity as characteristic of developmental exposure.

Correlates of patterns of cannabis use, abuse and dependence: evidence from two national surveys in Ireland – February 2021. Males, adolescents/young adults and individuals with lower educational levels are more likely to be current users of cannabis and are at a greater risk of having a Cannabis Use Disorder. The results from this study suggest that a high percentage of current cannabis users are at risk of cannabis abuse or dependence. Key findings indicate that males, adolescents/young adults and individuals with lower educational levels are more likely to be current users of cannabis and are at a greater risk of having a CUD. Given the potential public health implications of cannabis legalization, it is imperative that valid and reliable information on cannabis use, CUD and cannabis-related harm is collected in Ireland and other countries to ensure that the impact of any changes arising from cannabis legalization can be accurately measured.

Intelligence quotient decline following frequent or dependent cannabis use in youth: a systematic review and meta-analysis of longitudinal studies – January 2021. This is the first longitudinal quantitative synthesis to our knowledge examining the association between frequent or dependent cannabis use during adolescence and IQ change over time. We found that young people who use cannabis frequently or dependently by age 18 have declined in IQ at follow up and this may be due to a decline in verbal IQ. All studies showed point estimates of IQ decline. Our inclusion criteria were broad and the cannabis-using cohort represents a spectrum of intensity of use. Findings from our exploratory analysis indicate that there were no differences between pre-cannabis exposure IQ of cannabis users compared to control subjects, however, this was a heterogeneous finding.

The Effects of Marihuana on Adolescents and Young Adults – Kolansky & Moore, 1971 – February 2021. The large amount of marihuana smoking (12 million to 20 million people) in this country was reviewed, as well as some of the literature concerning adverse effects. Thirty-eight individuals from age 13 to 24 years, all of whom smoked marihuana two or more times weekly, were seen by us between 1965 and 1970, and all showed adverse psychological effects. Some also showed neurologic signs and symptoms. Of the 20 male and 18 female individuals seen, there were eight with psychoses; four of these attempted suicide. Included in these cases are 13 unmarried female patients who became sexually promiscuous while using marihuana; seven of these became pregnant.

Young adult compared to adolescent onset of regular cannabis use: A 20-year prospective cohort study of later consequences – January 2021. Cannabis users who began regular use in their teens had poorer later life outcomes than non-using peers. The larger group who began regular cannabis use after leaving high school accounted for most cannabis-related harms in adulthood. Given the legalisation of cannabis use in an increasing number of jurisdictions, we should increasingly expect harms from cannabis use to lie in those commencing use in young adulthood.

2020

Adolescent Brain Cognitive Development (ABCD) Study — ongoing. Adolescence is a period of dramatic brain development in which children are exposed to all sorts of experiences. Yet, our understanding of precisely how these experiences interact with each other and a child's biology to affect brain development and, ultimately, social, behavioral, health, and other outcomes, is still incomplete. As the only study of its kind, the ABCD Study will yield critical insights into the foundational aspects of adolescence that shape a person's future.

Adolescent Δ 9-Tetrahydrocannabinol Exposure Selectively Impairs Working Memory – Nov. 2020. As the frequency of cannabis use by 14-16-year-olds increases, it becomes increasingly important to understand the effect of cannabis on the developing central nervous system. Using mice as a model system, we treated adolescent (28 day old) C57BL6/J mice of both sexes for 3 weeks with 3 mg/kg tetrahydrocannabinol (THC). Starting a week after the last treatment, several cognitive behaviors were analyzed. Mice treated with THC as adolescents acquired proficiency in a working memory task more slowly than vehicle-treated mice. Working memory recall in both sexes of THC-treated mice was also deficient during increasing cognitive load compared to vehicle-treated mice. Our adolescent THC treatment did not strongly affect social preference, anxiety behaviors, or decision-making behaviors on the elevated T maze task. In summary, under the conditions of this study, adolescent THC treatment of mice markedly affected the establishment, and persistence of working memory, while having little effect on decision-making, social preference or anxiety behaviors.

Cannabis and the Adolescent Brain – Jan. 2020. Ultimately, most researchers stress that, despite increasingly relaxed societal views toward the drug, cannabis use—especially in adolescence—is not benign. Many say that public health messaging should encourage teens to abstain from cannabis use as long as possible. A host of unanswered questions remain: What specific harms can individual users expect if they start using in adolescence? Are only certain people susceptible to potential ill effects? Is there a threshold age, or degree of cannabis use, that is safe or safer? Is cannabis-related damage reversible over time? We still don't have a handle on how THC affects the adolescent brain. There's a lot of evidence pointing toward negative outcomes, but more research needs to be done.

Can neuroimaging connect specific brain structures and functions with suicidal thoughts and behaviors? Apr. 2020. Many of the studies indicated that changes in the ventral (lower) regions of the prefrontal cortex (VPFC) could explain both thoughts and behaviors commonly associated with risk for suicidal thoughts and behaviors. This region plays a role in how one views themselves and assesses emotion. There's reason to believe this is where the increase of negative thoughts, the blunting or flattening of positive emotions, and the resistance to inherently good events and situations comes from. The other area of the brain with major associations to suicidal ideation and behavior is the dorsal (upper) region of the prefrontal cortex (DPFC). Research revealed that the DPFC may play a part in enabling suicide attempts through its role in the control of behavior, mental flexibility, and complex decision-making.

<u>College students using more pot in legal states; binge drinking less</u> – Jan. 2020. College students in states with recreational marijuana laws are 18 percent more likely to have used cannabis within the past 30 days compared to students in states where it remains illegal. Across the country, rates of overall usage rates for marijuana had a modest increase of 3 percent growing from 14 to 17 percent. In states with legalized recreational marijuana there was a marked decline in rates of binge drinking.

Familial factors may not explain the effect of moderate-to-heavy cannabis use on cognitive functioning in adolescents: a sibling-comparison study — Sept. 2020. The current study used a quasi-experimental, family-controlled design to examine the effects of cannabis use in a high-risk sample of adolescent sibling pairs. In contrast to previous co-twin-controlled designs, findings suggest that an earlier onset of regular use and persistent use may adversely affect cognitive functioning. Thus, recruiting high-risk genotyped samples for family-controlled studies may be a critical step forward for understanding the potential effects of drug use.

Is the Adolescent Brain at Greater Vulnerability to the Effects of Cannabis? A Narrative Review of the Evidence – Aug. 2020. This is a particular concern as specific cannabinoids (such as cannabidiol) with therapeutic potential are often conflated with cannabis/medicinal cannabis in the public discourse leading to potential trivialization of possible harm from cannabis use in adolescent users and reinforcement of the narrative that cannabis use is a harmless recreational activity in young people. Collectively, despite the obvious limitations outlined above, current evidence indicates that adolescence is a sensitive period during which cannabis use may result in adverse neurocognitive effects that appear to show a level of permanency into adulthood.

<u>National Institute on Drug Abuse for Teens</u> – Updated Jul. 2020. Mental and emotional wellbeing is critical to overall health. By supporting teens in developing healthy coping skills, you can set them up for success in dealing with stress and challenging circumstances in the future. This website is full

of articles, games and activities and helps to promote mindfulness by teaching teens how to practice health-enhancing behaviors, which can support better management of stress and reduce the chances of exploring substance use as an alternative.

Pediatric Chest Radiographic and CT Findings of Electronic Cigarette or Vaping Product Use—associated Lung Injury — Mar. 2020. Chest imaging findings of electronic cigarette or vaping product use—associated lung injury (EVALI) in pediatric patients were bilateral symmetric ground-glass opacities with subpleural sparing, consolidation, and lower lobe predominance. Electronic cigarette or vaping product use—associated lung injury (EVALI) is a serious public health concern with substantial morbidity and mortality, particularly in young individuals. In pediatric patients, electronic cigarette or vaping product use—associated lung injury is characterized by bilateral symmetric ground-glass opacities, consolidation, and a lower lobe predominance at CT.

2019

<u>A Deep Dive into Adolescent Development</u> – June 2019. With its breadth, depth and flexible experimental design, the ABCD Study will serve as a model for other large-scale, long-term projects, investigators say. It also serves to showcase just how much psychology can do. This is 'team science,' led in large part by psychologists. It speaks to the strength of our science, and the opportunity for psychologists to play a leading role in interdisciplinary research.

A Population-Based Analysis of the Relationship Between Substance Use and Adolescent Cognitive Development – Feb. 2019. Common vulnerability effects were detected for cannabis and alcohol on all domains. Cannabis use, but not alcohol consumption, showed lagged (neurotoxic) effects on inhibitory control and working memory and concurrent effects on delayed memory recall and perceptual reasoning (with some evidence of developmental sensitivity). Cannabis effects were independent of any alcohol effects. Conclusions: Beyond the role of cognition in vulnerability to substance use, the concurrent and lasting effects of adolescent cannabis use can be observed on important cognitive functions and appear to be more pronounced than those observed for alcohol.

Age-related differences in the impact of cannabis use on the brain and cognition: a systematic review — January 2019. In humans, general executive functioning seems to be more impaired in adolescent, frequent cannabis users compared to adult, frequent cannabis users. Also, in humans, age-effects may be most prominent among very heavy and dependent users, which may suggest CUD-specific effects. Craving and inhibitory control may not decrease as much after cannabis intoxication in adolescents compared to adults. Lastly, in rodents, the age-effects of cannabis on learning appear to be reversible if followed by sustained abstinence. If these hypotheses prove correct, it could lead to important developments in targeted prevention strategies.

Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood – Feb. 2019. Although individual-level risk remains moderate to low and results from this study should be confirmed in future adequately powered prospective studies, the high prevalence of adolescents consuming cannabis generates a large number of young people who could develop depression and suicidality attributable to cannabis. This is an important public health problem and concern, which should be properly addressed by health care policy.

Grey Matter Volume Differences Associated with Extremely Low Levels of Cannabis Use in Adolescence – March 2019. Almost 35% of American 10th graders have reported using cannabis and existing research suggests that initiation of cannabis use in adolescence is associated with long-term neurocognitive effects. We understand very little about the earliest effects of cannabis use, however, because most research is conducted in adults with a heavy pattern of lifetime use. This study presents evidence suggesting structural brain and cognitive effects of just one or two instances of cannabis use in adolescence. Converging evidence suggests a role for the endocannabinoid system in these effects. This research is particularly timely as the legal status of cannabis is changing in many jurisdictions and the perceived risk by youth associated with smoking cannabis has declined in recent years.

Early, heavy, and chronic cannabis use does have substantive negative effects on the brain – Oct. 2019. We studied a unique population for whom cannabis use is central and necessary to their way of life. They are forbidden from using other substances, including tobacco and alcohol. Their use of cannabis is heavy, chronic, and begins early. The cases were compared with matched controls who did not use cannabis, alcohol, or drugs. The controls were from the same location and shared similar beliefs and lifestyle, except for cannabis use. Attenuated psychosis-relevant phenomena were assessed with the Schizotypal Personality Questionnaire (SPQ) and cognitive functioning with a culture-neutral computerized cognitive battery. This study showed that heavy, chronic, and early cannabis use that is not confounded by other drug use is associated with psychosis-relevant phenomena and cognitive deficits. The findings are relevant to the evolving attitudes and laws about cannabis.

For Your Consideration: Brain Pro Dr. Amen on Cannabis + The Developing Brain — Oct. 2019. In his book *Change Your Brain, Change Your Grades*, Dr. Amen unpacks the reasons why students need to avoid addictive substances like cannabis. They change your brain in ways that make it harder for you to learn new things, memorize class material and maintain good study habits. They are likely to change your grades but in the wrong direction.

Growing up high: Understanding the impacts of adolescent cannabis use on mental health and brain development – Aug. 2019. This study involved a unique population for whom cannabis use is central and necessary to their way of life. They are forbidden from using other substances, including tobacco and alcohol. Their use of cannabis is heavy, chronic, and begins early. The cases were compared with matched controls who did not use cannabis, alcohol, or drugs. The controls were from the same location and shared similar beliefs and lifestyle, except for cannabis use. The result was found to be that heavy, chronic, and early cannabis use that is not confounded by other drug use is associated with psychosis-relevant phenomena and cognitive deficits. The findings are relevant to the evolving attitudes and laws about cannabis.

Growing Up High PDF – Jun. 2019. Moving forward, advancing our understanding of cannabis-related neurodevelopmental risk factors must include ongoing identification of specific biomarkers that may render specific individuals more or less susceptible to cannabis-related neurodevelopmental risks. To date, only a small handful of genetic susceptibility markers have been identified which seem be related to a person's increased likelihood of suffering from cannabis-related psychiatric disorders. No doubt, complex psychiatric conditions such as depression, anxiety, schizophrenia and addiction are linked to a multitude of genetic susceptibility markers and it is therefore critical to round out our understanding of these specific genetic loci and the downstream molecular and neurochemical pathways they control. Beyond genetics, basic neuroscience research continues to characterize the

specific effects of adolescent cannabinoid exposure on neurotransmitter pathways and neural circuits that are fundamentally altered by adolescent cannabinoid exposure.

Impact of neuroimmune activation induced by alcohol or drug abuse on adolescent brain development – Oct. 2019. Evidence demonstrates that alcohol or drug abuse in adolescence can alter normal physiological processes, which leads to long-lasting cognitive and behavioral dysfunction, including predisposition to substance use disorders. Recent studies support a role of the innate immune response and TLRs in glial cells in many actions of alcohol and drug abuse in the brain, including neural damage cognitive dysfunctions and alterations to neurocircuitry that contribute to drug addiction-related behaviors. Targeting the immune response, such as using anti-inflammatory compounds, exercise, or inhibiting microglial activation, are a potential therapeutic strategy to treat the neuroinflammation and alcohol drinking associated with alcohol and drug abuse in adolescence.

Is the Adolescent Brain at Greater Vulnerability to the Effects of Cannabis? A Narrative Review of the Evidence — August 2020. There is a need for caution when considering the therapeutic potential of cannabis for adolescence and particularly in public discourse leading to potential trivialization of possible harm from cannabis use in adolescence. Current evidence indicates that adolescence is a sensitive period during which cannabis use may result in adverse neurocognitive effects that appear to show a level of permanency into adulthood.

Longitudinal Alterations in Prefrontal Resting Brain Connectivity in Non-Treatment-Seeking Young Adults with Cannabis Use Disorder – July 2019. Intrinsic functional organization of the brain continues to change in early adulthood. The current study provides evidence that these changes may be altered in the context of chronic cannabis use. There are relatively few studies that have assessed intrinsic functional connectivity in the context of heavy cannabis use. We observed disruption in the circuitry of the anterior cingulate cortex that underlies sensorimotor and cognitive control in young adults with CUD, which could not be attributed to comorbid nicotine and alcohol use and which may have longer-range impacts on behavior.

Marijuana use among adolescents is associated with deleterious alterations in mature BDNF – Jan. 2019. This is the first study demonstrating brain derived neurotropic-factor (BDNF) alterations were not a precondition. Rather, BDNF alteration was secondary to marijuana use, serving as cautionary evidence of marijuana's deleterious effects. Findings suggest that when marijuana use escalates, the BDNF pathway becomes more deregulated. Analyses confirm that age of marijuana use onset influences the magnitude of these changes.

National Institute on Drug Abuse – What are marijuana's long-term effects on the brain? – December 2019. 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.

2018

Adolescent neurocognitive development and impacts of substance use: Overview of the adolescent brain cognitive development (ABCD) baseline neurocognition battery — August 2018. Based on the ABCD study data collected to date, each task appears to show appropriate sensitivity to individual variations in performance that may later prove to index risk-taking vulnerabilities. Because ABCD includes a wealth of additional information on participant demographics, mental health, substance use, pubertal status and genetic predispositions (as presented elsewhere in this issue), a wide range of hypotheses regarding neurocognitive development can be tested.

Connectome Project – Oct. 2018. The present findings provide evidence for significant links between recent cannabis use and specific visuospatial neurocognitive abilities, and an association between CUD and overall fluid intelligence, but not other areas. No links to age of first use were apparent. Although the effect sizes were of small magnitude and most domains were unaffected, this study nonetheless documents potential risks of recent cannabis use to people in professions that rely on optimum cognitive performance.

How Marijuana May Damage Teenage Brains in Study Using Genetically Vulnerable Mice – Dec. 2018. In a study of adolescent mice with a version of a gene linked to serious human mental illnesses, Johns Hopkins Medicine researchers say they have uncovered a possible explanation for how marijuana may damage the brains of some human teens. In a report that will be published in a 2019 print issue of the journal Biological Psychiatry, the researchers say they showed that pot exposure increases inflammation in a specific type of brain cell in adolescent mice that carries a rare genetic mutation linked to schizophrenia, bipolar disorder and other major psychiatric disorders.

One Month of Abstinence from Cannabis Improves Memory in Adolescents, Young Adults – Science Daily Oct. 2018. A Massachusetts General Hospital (MGH) study finds that one month of abstaining from cannabis use resulted in measurable improvement in memory functions important for learning among adolescents and young adults who are regular cannabis users. The study published in the *Journal of Clinical Psychiatry* is one of the first to prospectively track over time changes in cognitive function associated with halting cannabis use.

Synthetic Cannabinoids: Spice, K2 and similar marijuana-like substances – Dec. 2018. The effects of synthetic THC on the brain are more pronounced than the effects of natural THC since the THC found in synthetic marijuana is more potent than natural marijuana. The affinity of synthetic THC for cannabinoid receptors is 5 times greater than that of THC. There have been no scientific studies of the effects of synthetic cannabinoids on the human brain, but it is known that the synthetic cannabinoid compounds act on the same receptors as THC. Normal brain functions, like memory and decision-making, rely on neurons communicating with each other. When cannabinoids attach to the receptors, normal regulation of communication in the brain is disrupted. Teens that chronically use marijuana have reduced problem-solving skills and exhibit "cognitive inflexibility."

What are the effects of increasing cannabis potency on adolescent health? – Lancet 2018. Given the growing body of research finding on cannabis potency and cannabis related harms, there is now a pressing need to understand how different types of cannabis products impact on adolescent health. Furthermore, a better understanding of the impact of cannabis use potency on adolescent

neurocognition and mental health could inform future prevention programs, policy decisions and clinical practice.

2017 and later

Adolescent Brain Development and Drug Abuse — June 2008. There is a need for age-appropriate curriculum to educate youth about their developing brain. The sciences of the neurobiology of addiction and of brain development are providing new insights about how drugs affect the brain and how teenagers make critical and life influencing decisions, including their decisions about drug use. Resources are needed to educate youth about this critical new knowledge in brain development. This information can be harnessed to reframe and strengthen current drug prevention approaches by encouraging youth to capitalize on the assets of the developing brain, avail themselves of alternatives to potentially health-compromising risk-taking, and to promote personal growth and healthy lifestyles.

Adolescent Cannabis Use and Psychosis: Epidemiology and Neurodevelopmental Models – 2010. Epidemiological evidence suggests that cannabis use is a risk factor for schizophrenia, while cannabis use in individuals with a predisposition for schizophrenia results in an exacerbation of symptoms and worsening of the schizophrenic prognosis. The neurodevelopmental characteristic of adolescence probably creates a more vulnerable circumstance for cannabis to produce psychotic-like symptoms and possibly cause schizophrenia. In the past few years there has been an increase in evidence of the important role of the endocannabinoid system in moderating adolescent neurodevelopmental processes such as synaptic pruning. We can speculate that adolescent exposure to cannabinoids might tamper with the normal developmental neuronal processes occurring in the still developing adolescent brain, thus leading to a predisposition to develop schizophrenia, possibly involving GABAergic and dopaminergic dysfunction.

Adverse Effects of Cannabis on Adolescent Brain Development: A Longitudinal Study – March 2017. The current study provides important longitudinal evidence of detrimental effects of cannabis use during adolescence on brain resting functional connectivity, intelligence, and executive function. Two patterns of dynamic changes of caudal ACC resting functional connectivity in individuals with cannabis use disorder (CUD) are reported: (1) decrease of resting functional connectivity with dorsolateral prefrontal and orbitofrontal cortices and (2) lack of increase of resting functional connectivity with SFG across time. Importantly, we identified a potential neural marker of relapse vulnerability in adolescents with CUD at treatment entrance characterized by lower resting functional connectivity between caudal ACC and orbitofrontal cortex.

Biology of Addiction: Drugs and Alcohol Can Hijack Your Brain — Oct. 2015. NIH-funded scientists are working to learn more about the biology of addiction. They've shown that addiction is a long-lasting and complex brain disease, and that current treatments can help people control their addictions. The biological basis of addiction helps to explain why people need much more than good intentions or willpower to break their addictions. The brain actually changes with addiction, and it takes a good deal of work to get it back to its normal state. The more drugs or alcohol you've taken, the more disruptive it is to the brain.

<u>Cannabis and Adolescent Brain Development</u> – 2015. While epidemiological and clinical studies have consistently linked cannabis use with psychiatric illness and cognitive impairment, the mechanisms

that underlie these associations are still not well understood. Research from both the animal and human literature appears to support the notion that adolescence is a period of particular risk, with exposure during this stage of development potentially resulting in more severe and persistent adverse effects than exposure during adulthood. Given the importance of the endocannabinoid system in human brain development, it is plausible that prolonged use during adolescence results in a disruption in the normative neuro-maturational processes that occur during this period. In turn, this could result in long-lasting changes to brain structure and function that underlie many of the adverse cognitive and emotional outcomes associated with heavy use.

Cannabis Exposure May Lead to Psychosis – Jan. 2015. As clinicians, it is important for us to educate our young patients about the risks of psychosis associated with early, heavy cannabis use. Epidemiologic data indicates that young people who are daily users of cannabis before the age of 15 have a greater risk of developing schizophrenia than their peers who either abstain from cannabis or wait until adulthood to begin using the drug. This risk is further increased by the use of cannabis that is high in THC (9-delta tetrahydrocannabinol), the psychoactive ingredient in cannabis, as many contemporary strains are grown for high levels of this compound. This relationship between psychosis and cannabis use appears to be dose dependent, which further underscores the harm reduction message that while no use is best, any reduction or forestalling of use is better.

<u>Cannabis Use and Later Life Outcomes</u> – Jun. 2008. The results of the present study suggest that increasing cannabis use in late adolescence and early adulthood is associated with a range of adverse outcomes in later life. High levels of cannabis use are related to poorer educational outcomes, lower income, greater welfare dependence and unemployment and lower relationship and life satisfaction. The findings add to a growing body of knowledge regarding the adverse consequences of heavy cannabis use.

Insights into Human Behavior from Lesions to the Prefrontal Cortex – Sept. 2014. The prefrontal cortex (PFC), a cortical region that was once thought to be functionally insignificant, is now known to play an essential role in the organization and control of goal-directed thought and behavior. Neuroimaging, neurophysiological, and modeling techniques have led to tremendous advances in our understanding of PFC functions over the last few decades. It should be noted, however, that neurological, neuropathological, and neuropsychological studies have contributed some of the most essential, historical, and often prescient conclusions regarding the functions of this region. Importantly, examination of patients with brain damage allows one to draw conclusions about whether a brain area is necessary for a particular function. Here, we provide a broad overview of PFC functions based on behavioral and neural changes resulting from damage to PFC in both human patients and nonhuman primates.

Longitudinal Development of Human Brain Wiring Continues from Childhood into Adulthood – July 2011. Childhood and adolescence are periods of significant change, with behavioral, emotional, hormonal, and cognitive processes undergoing maturation. Development does not end there, as young adulthood also provides new challenges and experiences that may continue to impact brain development. Function is inherently linked with brain structure, so a detailed knowledge of healthy brain development is crucial for better understanding cognitive and behavioral changes that occur as one ages. Four landmark studies approximately a decade ago (two cross-sectional, two longitudinal) demonstrated significant brain maturation during adolescence and early adulthood using sophisticated image processing of conventional MRI scans.

Longitudinal Changes in White Matter Microstructure After Heavy Cannabis Use – May 2015. Cannabis users displayed reduced longitudinal growth in fractional anisotropy in the central and parietal regions of the right and left superior longitudinal fasciculus, in white matter adjacent to the left superior frontal gyrus, in the left corticospinal tract, and in the right anterior thalamic radiation lateral to the genu of the corpus callosum, along with less longitudinal reduction of radial diffusion in the right central/posterior superior longitudinal fasciculus, corticospinal tract, and posterior cingulum. Greater amounts of cannabis use were correlated with reduced longitudinal growth in FA as was relatively impaired performance on a measure of verbal learning. These findings suggest that continued heavy cannabis use during adolescence and young adulthood alters ongoing development of white matter microstructure, contributing to functional impairment.

Marijuana and the developing brain – Nov. 2015. Marijuana producers have a strong incentive to hook young users. While about 9 percent of adults who use cannabis become addicted, the rate is 17 percent for people who start smoking in their teens, according to NIDA figures. And as the tobacco and alcohol industries have demonstrated, she says, such companies make the majority of their profits on a relatively small proportion of chronic users. When there is a profit motive, companies tend to make a product more addictive. Legalization is moving ahead prematurely without considering the lessons we've learned from nicotine and alcohol prevention policy research.

Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife – July 2012. Persistent cannabis use was associated with neuropsychological decline broadly across domains of functioning, even after controlling for years of education. Informants also reported noticing more cognitive problems for persistent cannabis users. Impairment was concentrated among adolescent-onset cannabis users, with more persistent use associated with greater decline. Further, cessation of cannabis use did not fully restore neuropsychological functioning among adolescent-onset cannabis users. Findings are suggestive of a neurotoxic effect of cannabis on the adolescent brain and highlight the importance of prevention and policy efforts targeting adolescents.

Recreational marijuana use impacts white matter integrity and subcortical (but not cortical) morphometry – Jun. 2016. Our results indicate that the earlier the age of onset of marijuana use, the lower was white matter coherence. Age of onset also affected the shape of the accumbens, while the number of total uses in a lifetime impacted the shape of the amygdala and hippocampus. Marijuana use had no effect on cortical volumes. These findings suggest subtle but significant effects of recreational marijuana use on brain structure.

Teens who smoke pot at risk for later schizophrenia, psychosis – Mar. 2011. Evidence is mounting that regular marijuana use increases the chance that a teenager will develop psychosis, a pattern of unusual thoughts or perceptions, such as believing the television is transmitting secret messages. It also increases the risk of developing schizophrenia, a disabling brain disorder that not only causes psychosis, but also problems concentrating and loss of emotional expression. In one recent study that followed nearly 2,000 teenagers as they became young adults, young people who smoked marijuana at least five times were twice as likely to have developed psychosis over the next 10 years as those who didn't smoke pot.

<u>The Addictive Brain: All Roads Lead to Dopamine</u> – April 2012. Scientists across the globe have suggested that dopamine agonist therapy would reduce cravings and prevent relapse and drug-

seeking behavior. The bottleneck to date is that typical pharmaceutical agents that have dopaminergic activation qualities are too powerful and as such have profound side effects. Studies are beginning to support the idea that the dopaminergic system can be stimulated with a patented natural, nonaddictive D2 agonist KB220 neuro-adaptogen.

The effects of Δ9-tetrahydrocannabinol on the dopamine system – May 2017. Δ 9

-tetrahydrocannabinol (THC), the main psychoactive ingredient in cannabis, is a pressing concern to global mental health. Patterns of use are changing drastically due to legalisation, availability of synthetic analogues ('spice'), canna-vaping and aggrandizements in the purported therapeutic effects of cannabis. Many of THC's reinforcing effects are mediated by the dopamine system. Due to complex cannabinoid-dopamine interactions there is conflicting evidence from human and animal research fields. Acute THC causes increased dopamine release and neuron activity, whilst long-term use is associated with blunting of the dopamine system.

Why Teens Are Impulsive, Addiction-Prone and Should Protect Their Brains – Jan. 2015. Addiction is actually a form of learning. ... What happens in addiction is there's also repeated exposure, except it's to a substance and it's not in the part of the brain we use for learning — it's in the reward-seeking area of your brain. ... It's happening in the same way that learning stimulates and enhances a synapse. Substances do the same thing. They build a reward circuit around that substance to a much stronger, harder, longer addiction.

Youth and marijuana: Youth are at special risk for harm – Jun. 2016. Examined from multiple perspectives including white matter integrity, subcortical shape, and brain volume, our parametric analyses suggest that an early onset of marijuana use may be associated with subtle changes in brain regions implicated as being altered in substance abuse. These findings provide for the possibility that marijuana use during adolescence, which is a time of rapid brain development, might, at least in some individuals, have long-lasting effects, independent of the genetic effects suggested by a recent analysis of cortical volume on a somewhat overlapping sample.