Influence of drug substances on adolescents

Adolescence is the most dramatic stage in development. Weed, alcohol, and marijuana are the most used. Adolescent substance users indicate abnormalities of brain functioning, connected to changes in neurocognition over time according to research. poor brain functioning and activation of cognitive tasks are most recognized abnormalities. adolescents who strongly use weed and marijuana show subtle anomalies too, which is definitely not the same percentage of divergence from randomly similar non-using adolescents. The use of drugs and alcohol mainly hit the neurocognition and brain function in adolescent substance users with an emphasis on the most commonly used substances, and of ongoing neuromaturational processes. treatment and special counseling are provided to those willing to leave drugs forever.

Substance use during adolescence has been associated with alterations in brain structure, function, and neurocognition. Research with adults have shown that chronic heavy drinking is associated with adverse consequences on the adult brain 1, this relationship has only recently been explored in the adolescent brain. Understanding the effects of alcohol and drug use on adolescent neurocognition is crucial, being that rates of use increase dramatically between ages 12 and 18. Epidemiological studies have shown that past month alcohol use increases 13 to 20% which is from 8th grade to12. 50% of adolescents have used alcohol and at least 46% have used other dangerous drugs which they think it could help them forget about all the problems they have and also do well in school. While the developing brain may be more affected by neurotoxic effects, exposure to alcohol and drugs during a period of brain development may interrupt the natural course of brain maturation and key processes of brain development. Adolescence may be a period of serious vulnerability for alcohol's effect on the brain 3-6. Cognitive facts that come from these alcohol and drug-related l insults have potentially harmful implications for subsequent academic, occupational, and social functioning extending into adulthood. Therefore, neurocognitive sequelae from heavy drinking and drug use are important to elucidate.

Youth's period of development between childhood and adulthood includes complex social, biological, and psychological changes. The relationship between these factors has considerable implications for adolescent development. Included in these are substantial changes in the efficiency and specialization of the adolescent brain, which is accomplished through synaptic refinement and myelination according to research in the new york times. Heavy drinking during adolescence does have a subtle, but significant, deleterious effects on adolescent neurocognitive functioning. Studies have found that adolescent heavy drinkers exhibit decrements in memory 24, attention and speeded information processing 25, 26, and executive functioning 27–29. findings are consistent with literature examining neurocognitive deficits in

young heavy drinkers, which found similar decreases on attention and information processing, along with deficits in language competence and academic achievement 26.

While it has often been assumed that marijuana use is not linked to long-term cognitive deficits, recent data suggest that even after four weeks of monitored abstinence, adolescents who regularly smoke marijuana performed poorer on performance tests of learning, cognitive flexibility, visual scanning, error commission, and working memory 30. Further, the number of lifetime marijuana use episodes was significantly related to overall poorer cognitive functioning, even after controlling for lifetime alcohol use. We 7 prospectively examined neuropsychological functioning in 26 youths with no histories of alcohol or drug problems and compared them to 47 youths with histories of heavy adolescent alcohol, marijuana, and stimulant use. Follow-up neuropsychological tests were given to the subjects seven different times across 8 years, on average between the ages of 16 to 24. While there were no significant differences between users and non-users on neurocognitive test scores at the first time point, heavy drinkers performed worse on cognitive tasks at age 24 than light drinkers. In particular, those who had a history of alcohol withdrawal symptoms (e.g., orthostatic hypotension, nausea, insomnia, or irritability) were the most likely to have decreased in performance scores, especially on tests of spatial functioning. Overall, heavy drinking during adolescence was linked to a reduction in keeping up with age expectations 7, 25, 31. In summary, adolescence is characterized by dramatic increases in rates of substance use concurrent with ongoing neuromaturation. While neuropsychological studies have shown that adolescent substance use is linked to poorer spatial, inhibitory, and learning and memory functioning, neuroimaging techniques may elucidate the neural mechanisms of these performance deficits.

Recent findings have suggested decrements in brain functioning associated with adolescent substance use. Functional magnetic resonance imaging (fMRI) investigates the neural activity of the brain by measuring changes in blood oxygen level dependent (BOLD) signal 50, which indicates areas of increased activation in response to a mental task or stimulus 51. This technique is noninvasive and does not require injections or radioactive materials, making it a safe and appropriate technique for examining adolescent brain functioning and affecting their memory as well.

Adolescent response to alcohol advertising is of concern, as they are exposed to alcohol-related ads on a daily basis in many countries 60. We 61 have observed that heavy drinking youth show greater brain activation while viewing alcohol advertisements than they do to non-alcohol beverage ads. This substantially greater brain activation to alcoholic beverage pictures was observed throughout the brain, particularly in the prefrontal area, nucleus accumbens, hypothalamus, posterior cingulate, and temporal lobe, and was prominent in the left hemisphere, limbic, and visual cortices. This suggests that reward, visual attention limbic, appetitive, and episodic memory systems were preferentially invoked in response to alcohol ads

relative to non-alcohol ads in heavy drinking teens.

Only the inferior frontal gyrus showed more activation in light drinkers during the task, potentially indicating a negative valence to these alcohol stimuli in non-drinking teens. Overall, light drinkers showed more response to non-alcoholic beverage pictures. These findings extend previous studies in adults and link alcohol advertisement exposure in youth to activation in reward, desire, positive emotion, and episodic recall brain areas 62. Predicting RelapseRelapse is a common clinical problem in individuals with substance dependence. Previous studies have implicated a multifactorial process underlying relapse; however, the contribution of specific neural substrates had yet to be examined. We 63 looked at whether results from functional imaging shortly after drug cessation could predict relapse in stimulant-dependent individuals. The goals were to evaluate the neurobiology of decision-making dysfunction in stimulant-dependent subjects and to determine if functional imaging could be used as a tool to predict relapse. Participants included treatment-seeking methamphetamine-dependent adult males (N=46). All individuals underwent fMRI three to four weeks after cessation of substance use. Of the 40 subjects who have followed a median of 370 days, 18 relapsed and 22 did not. The main outcome measure was BOLD activation during a simple two-choice prediction task. During the prediction task, a house was presented, flanked by a person on its left and right. The participant decided on which side of the house a car would appear. Each trial was self-paced to maximize self-determined action, thus the subject determined the number of trials by the latency to select a response. Immediately following the subject's response, the car was presented for 300 ms on the far left or right side. The screen provided the feedback whether the prediction was correct. Unbeknownst to the participant, the computer determined the response based on the participant's selection. Three error rate block types included a high chance level (20% of responses were "correct"), a 50% chance-level, and a low (80% of responses were "correct") chance level. The task captures the key elements of decision-making: the probability of an outcome associated with an option, the positive or negative consequence, and the magnitude of the consequence 64. The fMRI activation patterns in right insular, posterior cingulate, and temporal cortex correctly predicted 20 out of 22 subjects who did not relapse, and 17 out of 18 subjects who did. A Cox regression analysis revealed that the combination of the right middle frontal gyrus, middle temporal gyrus, and posterior cingulate activation best predicted the time to relapse. In total, this is the first investigation to show that fMRI can be used to predict relapse in substance dependent individuals. It is likely that relapse corresponds with less activation in structures that are critical for decision-making, and thus poor decision-making sets the stage for relapse. The insular cortex may act through the interoceptive system to influence the ability to differentiate between good versus poor choices, while the inferior parietal lobule may play a role in the poor assessment of decision-making situations and subsequent reliance on habitual behavior.

Overall, substance dependent adults show brain patterns that can be used to predict whether

and when relapse may occur. Future studies are needed to determine if this is true for adolescents and whether brain activation patterns can be used to evaluate an individuals' readiness for treatment completion or treatment response.

Overall, changes in brain functioning in adolescents differ by substance use pattern. Research has shown that heavy drinking during adolescence can lead to a decreased performance on cognitive tasks of memory, attention, spatial skills, and executive functioning. These behavioral ramifications of heavy alcohol use may emerge as a consequence of the reduced volume of important brain structures (e.g., hippocampus), compromised quality of white matter, and abnormalities in activation during cognitive tasks. Studies have also shown that marijuana use during adolescence can result in decreases in cognitive functioning, particularly learning and sequencing scores. In integrating and interpreting the results of adolescent marijuana studies from our laboratory, it is important to note that the groups are generally equivalent on task performance, and therefore the underlying brain responses in controls and users can be largely assumed to represent activity to the same mental action. Corresponding marijuana-related changes in cognition may be related to increases in gray matter tissue volume, decreases in white matter microstructural integrity, and increases in neuronal activation during cognitive tasks. In sum, we can reasonably rule out recent use as accounting for the observed differences between substance groups, given that participants in some studies have been abstinent one month or greater. Substance-using adolescents have been found to differ from non-users on neuropsychological performance, brain tissue volume, white matter integrity, and functional brain response. Longitudinal studies are essential to fully understand how alcohol and marijuana use affect adolescent neurodevelopment.

The cross-sectional nature of the majority of studies examining adolescent neurocognitive functioning makes it difficult to determine the influence of alcohol and drug use on adolescent neurocognition. Therefore, ongoing longitudinal neuroimaging studies are essential to ascertain the degree to which substance intake is linked temporally to adverse changes on indices of brain integrity, or whether neural abnormalities reflect pre-existing patterns. In cross-sectional or longitudinal work, several methodological features are critical to evaluating the potential influence of adolescent substance use on neurocognition. These issues pertain to ensuring participant compliance, accurately assessing potential confounds, and maximizing participant follow-up. Adolescent compliance as a research participant can be maximized by attending to rapport, building trust, and ensuring the privacy of self-report data to the extent that is ethical and feasible to the setting. For behavioral tasks within or outside of imaging, it is critical to ensure participants comprehend task instructions, are fully trained on fMRI tasks, and then are given reminders just prior to task administration. Motion during scan acquisition is detrimental to the quality of imaging data and is often worse in younger adolescents than older teens or adults. Adolescent head motion can be minimized by the following steps: discuss the importance and rationale for keeping the head still multiple times before and at the scan appointment; model

and practice how to say “yes” and “no” when communicating with the research subject from the scanner; model and practice techniques for relaxing and ensuring subjects are in a position suitable for long-term comfort (e.g., legs are not crossed) before scanning begins; maximize participant comfort by using soft cushions around the head and under the knees; and many studies, especially those with younger participants, find practicing scanning in a less expensive mock scanner results in improved participant comfort and more reliable data during data acquisition. Accurately measuring and accounting for confounds frequently present in adolescent substance-using populations is essential for elucidating the true effect of substance use on adolescent neurocognitive functioning.

Common confounds in this population include head injury, depression, ADHD, conduct disorder, prenatal exposure to neurotoxins, family history-related effects, and polysubstance involvement. Conversely, excluding subjects for the aforementioned confounds may impede the generalizability of results. The tradeoff between minimizing confounds and having meaningful, ecologically valid results is an important study design decision, especially given the high cost of fMRI sessions. Accurately measuring abstinence is another important consideration in substance-related research protocols. If abstinence is required for participation (and compensation) in a study, the dynamics of self-report could change. While biological data may help confirm self-report, these measures are imperfect and do not pinpoint the quantity of specific timing of substance intake 65, 66. Regarding abstinence from cannabis, obtaining serial quantitative THC metabolite levels, normalized to creatinine, is the best approach for guarding against new use episodes 67. Tracking participants over time is a critical part of many clinical issues when interested in the degree to which a variable (e.g., alcohol or marijuana use) might result in neural changes.

Although some statistical approaches can help manage attrition, effective tracking procedures are more desirable to ensure study integrity. To maximize participant follow-up, frequent contact with participants must be maintained 68. Having a well-trained, friendly staff experienced with the population also helps retain participants and parents, and ensures that all participants fully understand the tasks and expectations during the study. Collecting comprehensive contact information can help track adolescents over time in case they should relocate. Additionally, follow-up measures and procedures should be as similar as possible to baseline, except to mitigate learning and practice effects 69. For imaging studies, field map unwarping of EPIs (e.g., fMRI and DTI) should also be considered, as this technique appears to produce more consistent localization of activations 70. Finally, as technical problems are common, back up plans for each piece of equipment used in the neuroimaging session should be in place.

Current research suggests that substance use in adolescence leads to abnormalities in brain functioning, including poorer neurocognitive performance, white matter quality, changes in brain volume, and abnormal neuronal activation patterns. fMRI studies have illuminated enhanced

cue response in adolescent drinkers, and have shown the potential to predict treatment outcomes in stimulant-dependent adults. A few questions still remain, such as whether heavy substance use during adolescence causes cognitive impairments and changes in neurodevelopment, if and when are critical periods of heightened vulnerability to such effects, and if observed abnormalities remit with reduced use. We have the capability to design studies in which we restrict or control for nicotine and most other drug use, but few adolescent drug users do not also use alcohol. It is also important to understand if results generalize to youth with psychiatric problems, other substance use histories, and low socioeconomic status, and to further explore implications for changes in brain activation for learning and behavioral control, along with mood and psychiatric illness. Harder parametric tasks that include conditions on which behavior does differ between groups would help us better understand the cognitive domains we have observed differences on. Lastly, we need to better understand the biochemical changes that may mediate macrostructural, microstructural, and functional neuronal changes in response to substance use, such as cannabinoid receptor activity changes. Multimodal approaches to neuroimaging may help us disentangle such questions (e.g., PET, spectroscopy).