Executive Functioning Outcomes Due to Various Cannabis Use Patterns in Adults

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October 16th, 2017

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Abstract

This study aimed to correlate cognitive functioning, specifically in the domains of memory and inhibition control, to number of days of cannabis use in adults (ages 20-40) and to examine whether gender, age, or average number of drinks per drinking day moderated these effects. Results from 79 participants were examined, 40 of whom had not ingested cannabis in the last 90 days (47.5% male) and 39 of whom had used cannabis in the past 90 days (48.72% male). Previous research showed conflicting results when looking between groups of adult cannabis users and non-users. Some studies showed an effect when the user group was heavy, chronic users. While other studies did not show an effect when assessing normal using adults (not clinical level chronic users). Research pertaining to adolescent cannabis use tended to have consistency when looking at cannabis use in unique ways that differed from a categorical analysis. Based on the previous research on cannabis use and executive functioning, this study looked at cannabis use as a continuous variable similar to the research on adolescents while assessing similar cognitive domains from both areas of research. A regression analysis was done in this study, controlling for age, gender and average number of drinks per drinking day, and did not show any significant associations between cannabis use frequency in the last 90 days and three different areas of executive functioning assessed. The current study was unable to associate increased levels of cannabis use to cognitive functioning, specifically in the domains of episodic memory, working memory and inhibition control. Future studies need to look at a sample of adult users specifically recruited for their cannabis use (as a continuous variable) in order to get an even distribution of cannabis use to examine how various levels of usage effects different domains of memory.

Executive Functioning Effects Due to Various Cannabis Use Patterns in Adults

Cannabis use has increased between 2003 to 2014 in the adult population in the U.S., from 2.95% to 9.8% (Salas-Wright et al., 2017). Usage remains high for adolescent users with 52.2% of 18-25-year old's reporting cannabis use in their lifetime (Becker et al., 2014). Therefore, cannabis use research in the United States is becoming more important. Assessing the impacts on various domains of cognitive functioning will give an in depth look at the impacts of the drug on developing and developed minds. In recent years more studies have focused on the association between cannabis use and cognitive functioning in adolescents, while fewer studies have explored this association in adults. Many studies aimed to determine which aspects of executive functioning are specifically effected and how that is impacted by different patterns of use in a categorical analysis (i.e., early onset use, late onset use, chronic use, sporadic use, acute intoxication and abstinence). Adolescent studies generally examine cannabis use as a continuous variable in terms of when use started, and/or comparing heavy chronic users to less frequent users and assess the impacts based on cannabis use as a continuous variable. This study aims to use the techniques displayed by previous research on adolescent cannabis, by looking at use as more than a binary variable, while using techniques familiar to both adult and adolescent research (i.e., inhibition control, working memory, memory sequencing and use of cognitive batteries).

Literature Review

Cannabis Use and Executive Functioning on Cognitive Batteries in Adolescents

Prior research has suggested that cannabis use is correlated with concurrent and lasting executive functioning impacts on youth who use cannabis. For example, adolescents who began using cannabis before the age of 16 showed a deficit in executive functioning (Dahlgren et al., 2016). This early onset of cannabis use may create long lasting impacts across a number of psychological measures regardless of frequency, amount consumed or alcohol use. They found inferior performance by adolescents who used cannabis before the age of 16 on the Stroop task and the Wisconsin Card Sort Task (WCST). The Stroop task measures one’s ability to inhibit a prepotent response to a stimulus (an automatic response to a visual stimuli) where participants had to make a quick response to a visual stimulus, such as saying the color a word is printed in, rather than the color the word spells. The WCST allows researchers to measure executive functioning because the task examines a participant’s ability to shift and maintain set (i.e., to change the rule of the task or continue following the current rule), form abstract concepts, and use feedback to help set-shifting (Dahlgren et al., 2016). The adolescent cannabis users performed worse on the Stroop task and WCST than control participants (adolescents who have never used cannabis). A trend emerged in which early onset users performed worse than late onset users. This research showed immediate impacts on executive functioning that could impact developing adolescents.

Comparable results were found among another group of young adults age 13-18 years old who commonly used cannabis and were abstinent from cannabis use 12 hours prior to the study, in order to avoid acute intoxication where the participant is still experiencing psychoactive effects of the drug. Spatial working memory and paired associate memory are both domains of executive functioning that were assessed to see if adolescent cannabis use impacted functioning. They found effects of cannabis use on cognitive performance beyond acute intoxication showing that there was in fact a deficit in executive functioning and working memory after use had ended (Harvey et al., 2007). These results were unexpected, given the relatively low cannabis use within their experimental group showing that adolescents incur an impact on executive functioning regardless of their degree of use.

Cannabis use was also independently associated with other domains of executive functioning than the previous studies examined. Poorer psychomotor speed and sequencing ability, sustained attention efficiency and cognitive inhibition was found to be negatively impacted in a dose-dependent manner (Lisdahl et al., 2012). This study not only examined cannabis use as a continuous variable but also looked at differences between male and female adolescent cannabis users. Male cannabis users showed a stronger negative relationship between cannabis use and psychomotor speed and sequencing ability. In other words, they showed a significantly slower ability to process and sequence information than female cannabis users on average. One interesting finding in this study that was also assessed in the aforementioned study was that cannabis users did not show a deficit in verbal memory (Harvey et al., 2007, Lisdahl et al, 2012). This means that both groups of adolescent cannabis users were able to retain and retrieve information provided to them verbally.

Cannabis use has been shown to impact executive functioning independently but it is uncommon for people to use just one substance. When looking at different substances used at the same time or separately in college age participants, scores on executive functioning batteries determined if participants had used cannabis recently (Meil et al., 2016). They were asked to be abstinent from all psychoactive substances for 7 days prior to the research session to avoid acute intoxication and to see if there were any lasting effects of the drugs that were detectable at that time. The FrSBe (Frontal Systems Behavior Scale) Disinhibition subscale predicted cannabis use frequency among participants. This scale looked at everyday behaviors associated with functions of the prefrontal cortex (the control center of executive functions). Similar to the previous study, inhibition control was impacted among cannabis users (Lisdahl et al., 2012, Meil et al., 2016). The participants who scored more poorly on the inhibition control portion of the FrSBe correlated with higher frequency cannabis use (another indication of cannabis use impacting executive functioning in a dose dependent manner).

Executive functioning was shown to be able to determine if someone was a current cannabis user, more recently this technique is being used to predict future cannabis use. Scores on executive functioning measures at age 12-14 (and have never used cannabis) can predict cannabis use at age 17-18 (Squegila et al., 2014). Executive functions such as, short-term memory, sustained attention, verbal learning and memory, visuospatial functioning, spatial planning and problem solving were assessed by way of the D-KEFS system. Inferior performance on inhibition tasks at a young age predicted substance use and is related to increased alcohol and cannabis use during late teenage years. Knowing what predicts substance use will allow researchers to better focus in on the extent to which specific executive functions lead to cannabis use and give them a way to predict when substance use first occurred as well as create better therapy based on the areas of cognitive functioning that lead to this behavior.

Some studies have had an inclination of lasting effects of cannabis use and furthermore, adolescents who have abstained from cannabis use for one month did show residual effects of cannabis use after the extended period of abstinence (Medina et al., 2007). In fact, complex attention, sequencing ability and verbal story memory were still impacted after a month of abstinence when using the D-KEFS system (Delis-Kaplan Executive Function System) to assess executive functioning. Alcohol use and depression, both of which have been demonstrated to independently correlate with impaired executive functioning, were controlled for due to the comorbidity of use and did not significantly contribute to the results. This means that adolescent cannabis users had lasting executive functioning deficits regardless of alcohol use or depression and that the results can more confidently be attributed to solely cannabis use.

Frequency of use, abstinence from the substance and comorbidity of substance use have all shown to impact executive functioning among adolescent cannabis users (Harvey et al., 2007, Medina et al., 2007), but age of onset also has significant impacts in terms of cognitive functioning and development (Gruber et al., 2012). Similar to previous studies mentioned, performance on WCST, Stroop task, and the Trail making task (which measures attention and set shifting) correlated with cannabis use as a continuous variable and showed significant a group difference with participants who starting using cannabis before the age of 16 to perform worse (Gruber et al., 2012). Another fascinating finding from this study was that the younger cannabis users smoked twice as often and consumed about three times the amount of cannabis compared to the participants who started smoking after the age of 16. This could be due to a built-up tolerance within this specific population and thus they need more in order to experience the same psychoactive effects.

The impacts of age of onset of use and early initiation of use (before the age of 16) on executive functioning abilities were seen across a three-year period of time while controlling for alcohol use (Jacobus et al., 2015). It was hypothesized adolescent cannabis users would perform significantly worse on neurocognitive measures than controls at baseline, 1.5-year follow up, and 3-year follow up. The Delis-Kaplan Executive Functioning System (D-KEFS) was used to assesses visual scanning, trail making, number sequencing, letter sequencing and motor speed. Cannabis users who also used alcohol performed worse than controls across all the follow-up time periods on attention, memory, processing speed, and visuospatial functioning (Jacobus et al., 2015). They also found that at 19-year-olds, cannabis users used significantly more substances than control participants, but by age 20, cannabis users began using fewer substances, narrowing the gap between them and the control participants. This demonstrated that cannabis using adolescent's cognitive abilities remain lower than their non-using peers for the duration of use.

Not all studies show a negative correlation in executive functioning abilities and cannabis use. Cannabis users between 18 to 25 years of age had above average levels of general intellectual abilities (estimated from the administration of Vocabulary and Matrix Reasoning subtests of the Wechsler Abbreviated Scale of Intelligence), and performed well on the letter cancelation task and verbal fluency task (Becker et al., 2014). They did, however, find that cannabis users had deficits in different domains of memory tested, specifically in the areas of problem solving and motivated decision making and a slower ability to recall previously learned material. They also believed cannabis users' inferior performance could have been due to their relative deficits in memory, problem solving and motivated decision making (Becker et al., 2014). This study showed that while there are negative impacts of cannabis on adolescent users, not all domains of functioning are impaired.

Adolescent Cannabis Use Impacts on Executive Functioning and Structural Morphometry

As previously shown, a one-month period of abstinence is adequate to detect an effect of cannabis use on executive functioning. It was not however adequate to detect a size difference in terms of pre-frontal cortex (PFC) between cannabis users and non-users when using the D-KEFS system to analyze executive functioning in a group of adolescents (Medina et al., 2009). They were particularly interested in the morphometry related to cannabis use and executive functioning in 16-18-year-old participants. High resolution anatomical magnetic images were produced for each participant while they were performing executive functioning tasks. Controlling for alcohol use, gender and intercranial volume (ICV), cannabis users had similar PFC volumes compared to controls but there was a group specific gender difference. Female cannabis users had larger PFC's than male cannabis users. This could be due to decreased synaptic pruning in the PFC occurring from a disruption caused by cannabis use during development, but it was unclear as to why women would show less synaptic pruning than men (Medina et al., 2009).

It is clear that adolescent cannabis use impacts executive functioning but some researchers wanted to look at the structural changes in adolescent brains. Morphometry in the cerebellum in 16-18-year-old cannabis users, using the D-KEFS system again in order to assess executive functioning, showed that the inferior posterior vermis (a subdivision of the cerebellum) was larger in cannabis using adolescents (Medina et al., 2010). This result correlated with poorer executive functioning on the D-KEFS system. The cerebellum is important for executive functioning because it aids in attention, associative memory, and inhibition control. The same conclusions were drawn, that this increase in size for adolescent cannabis use is due to the lack of synaptic pruning occurring during development because of a disruption caused by the cannabis itself. These studies show that not only is executive functioning being impacted in adolescent users but the very structure of their brains have changed because of the substance use.

Inhibitory control was a major theme assessed and poorer performance in regards to inhibition control among adolescent cannabis users was a common result. Inhibition control is a crucial component of executive functioning and is beginning to be looked at through the lens of fMRI machines. The Go-No-Go task was used during an fMRI of cannabis using adolescents and had participants give a specific response to two different stimuli when presented back to back.

For example, if the participant sees an A, they press 1 and if they see a B following the A, they press 2 but if either of the letters are repeated (A then A or B then B) then they must inhibit their response and not press anything. Cannabis users had a higher correlation between parietal and cerebellar regions even though it was not correlated with task demand (how difficult the task is to complete), this may be due to brain synapses wiring differently due to cannabis use during development as the previous two studies mentioned (Behan et al., 2014). They found that using cannabis during the month prior to study participation was associated with the heightened brain activity between the aforementioned areas. They did not however find a difference in performance between cannabis users and control participants who never used cannabis. Cannabis users may show normal performance because their brain is compensating and overperforming (heightened connectivity during the fMRI) to complete a task.

Even without a display of inferior performance from cannabis using adolescents, brain structures and connections have been shown to be impacted due to the use. Increased connectivity was also found for boys age 13 to 19 who used cannabis during working memory tasks in the frontal lobes, but only during novel tasks (Jager et al., 2010). This was also attributed to the changes in synaptic pruning occurring during adolescents caused by cannabis use as aforementioned, it is suggested that the activation pattern returns to normal because the brain learns how to compensate the second time a task is performed.

Cannabis Use and Executive Functioning in Adults

Cannabis is widely known for its healing properties within popular culture. Adults who were diagnosed with anxiety or chronic pain (which are independently associated with decreased executive functioning) experienced an increase in executive functioning abilities when put on a cannabis treatment plan (Gruber et al., 2016). By alleviating the patients pain or anxiety it was purposed that their cognitive functioning would return to that of controls and that is exactly what was found. Cannabis use over a 6-month treatment course significantly improved cognitive performance on the Stroop task, the Wisconsin Card Sort Task, and other executive functioning tasks (Gruber et al., 2016). However, exciting as this finding may be, this was a novel result in the literature to show an increase in performance correlated with increased cannabis use.

Adolescent studies have shown that executive functioning impacts are noticeable up to a month after discontinuation of use but adult studies tell a different story. Adult participants ages 30 to 55 were assessed at various period of abstinence (Pope et al., 2001). This was a typical adult study assessing participants categorically, heavy users who reported at least 5000 episodes of cannabis use in their lifetime and control participants who had never used cannabis in their lifetime. They had a group of participants who abstained for 0 days, another group who abstained for 1 day, a third group who abstained for 7 days and a final group who abstained for 28 days. Poorer performance on executive functioning batteries were noticeable up to 7 days after abstaining from cannabis use across all domains of executive functioning tested (Pope et al., 2001). At 28 days of abstinence, no differences were observed between the former cannabis users and control participants. Furthermore, no significant relationships emerged between cumulative lifetime cannabis use and cognitive deterioration. This showed a much different result than the studies on adolescent users. Adult cannabis users returned to normal functioning somewhere between 7 days or abstinence and 28 days of abstinence where adolescent users performance remained inferior after one month of abstinence. The large difference regarding adult cannabis users functioning returning to normal could be due to age of onset of use or the technique used to assess participants (categorical vs. continuous).

Cannabis use in adults is also comorbid with alcohol use which both impact executive functioning. Participants, age 21-49, who used cocaine, cannabis and heroin all performed poorly on the Stroop task and an executive functioning battery even when controlling for alcohol use (Fernandez et al., 2010). When the effects of each of these drugs were added together, they found a marginally significant negative effect of the drugs on their performance. When they looked at each drug separately, there was no longer an effect. Duration of drug use also failed to predict the participant's performance due to any drug when assessed separately. This study failed to show that adult cannabis use independently had a negative impact on executive functioning even when controlling for alcohol use.

Cannabis use in relation to performance on the Stroop task and WCST task again showed no difference in performance between groups even when looking between schizophrenic and control participants (Scholes et al., 2010). They did however find an overall effect of poorer performance on the Stroop task due to participants who used cannabis and also were diagnosed with schizophrenia, but they found no difference from the control group with schizophrenia. When they looked at the control cannabis users compared to the control non-users they also found no significant difference in performance on the Stroop task. This is another study on adult participants to find no significant relationship between adult cannabis use and executive functioning deficits.

The research on adult cannabis use and executive functioning is full of mixed results. As aforementioned there are a few studies that found either a positive or no relationship between cannabis use and executive functioning. There are studies however that do show a negative relationship between chronic cannabis use and executive functioning. Scores on the Frontal Assessment Battery determined whether participants ages 18 to 55 years old had executive functioning deficits due to chronic cannabis use (Fontes et al., 2011). This battery assessed conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. A specific deficit was found in the domain of motor programing, which is the participants ability to mentally plan a physical movement and perform that movement accurately (Fontes et al., 2011). They attribute this specific deficit to cannabis users having difficulty with motor, planning and complex attentional processes.

Executive functioning deficits while under the influence of cannabis are effects that are much easier to see than after periods of abstinence in adults. Examining the effects of acute intoxication on cognitive performance during the first 6 hours after consuming a high dose of cannabis by using the tower of London task (participants must arrange three colored balls on three sticks to match the target configuration in as few moves as possible using all or some of the stick) to measures decision making and planning, two key components of executive functioning, and the Stroop task (participants had to make a quick response to a visual stimulus, such as pressing "1" when they see an "A" and "2" when they see an "B" and so on), which measures motor impulsivity and the inability to inhibit a propotent response (Rameakers et al., 2006). Performance on the Tower of London task was found to be negatively correlated with cannabis use. The closer to when the participant used the drug, the poorer their performance was, and performance remained significantly inferior to the control group even 6 hours after use. Cannabis use was also associated with longer reaction times on the Stroop task, meaning that participants took longer to respond and to inhibit an incorrect response. This study demonstrated a significant negative effect on executive functioning immediately after a participant had used cannabis.

The Stroop task is a common task used in adult participants to assess executive functioning. Similar to the aforementioned study, executive functioning in a non-clinical sample of adults who reported using cannabis recently or in the past showed impaired cognitive performance on the Stroop task (Thames et al., 2014). This study used the Color-Word condition for the Stroop task, meaning that participants had to say the color of the word, for example if the word is “RED” but is printed in blue the participant must inhibit the automatic response to say “red” and say the target word, “blue.” Participants who had used cannabis more recently had a poorer ability to inhibit a propotent response. Although this was the only difference between the groups, cannabis users in general had poorer performance compared to controls across most executive functioning domains.

Cannabis users tend to be motivated by immediate gains and unable to change their thinking to consider long term gains. In terms of finances cannabis users ages 18 to 45 were assessed using the gambling task to assess their executive functioning (Whitlo et al., 2004). This task asks participants to choose from four decks of cards and make 100 selections. Decks A and B have a net loss of $250 per 10 cards drawn, while decks C and D have net gain of $250 per 10 cards drawn but cards from the later decks yield $50 per card selection while the earlier mentioned decks yield $100 per card selection. Even though the first deck yields more in the beginning, there is greater net loss in the end. Cannabis users were found to favor larger, immediate gains and thus higher overall losses, indicating that they were looking for immediate rewards rather than overall long-term gains. Cannabis users tend to be more prone to poor or risky decision making because they are seeking immediate rewards (possibly why they use the drug in the first place). It is suggested that this may impact cannabis users drive to continue using cannabis despite the possibility of long term negative consequences (Whitlo et al., 2004). Control participants and cannabis users both preferred the first deck initially, but the controls realized the greater overall net loss of these decks and began choosing from the other two decks. The cannabis users however, perseverated and continued choosing the decks with the highest immediate gains despite the greater overall losses.

Cannabis Use and Real-World Executive Functioning in Adults

Studies on adult cannabis use have generated mixed results, which leads to research on how adults' executive functioning works while on the drug in the real world. Real-world memory (functioning in a work-like setting) and executive functioning (as measured by cognitive batteries) is an important outcome variable to assess in cannabis users. This can be measured by way of executive component processes, associative learning, everyday memory, prospective memory and cognitive failures (Fisk et al., 2008). Upon assessing participants ages 20 to 22 years old, they found that cannabis users did not differ significantly from non-users on any of the executive functioning tasks. They did, however, find a combined deficit in every day memory and cognitive failures in the cannabis user group when accounting for level of alcohol consumed. Real-world executive functioning was not completely disrupted in adult cannabis users, only certain domains.

A follow-up study was conducted to assess real world prospective memory and executive functioning in cannabis users. The JAAM (Jansari-Agnew-Akesson-Murphy) task was used to assess prospective memory and executive functioning in cannabis users aged 18-25 (Montgomery et al., 2012). The JAAM task is aimed at measuring real world executive functioning by way of a non-immersive virtual reality task in which the participants pretend to be an assistant in an office for the day. Participants are asked to do tasks that involve planning, prioritization, selection, creative thinking, adaptive thinking, action-based prospective memory, event-based prospective memory, and time-based prospective memory and found users to have impaired performance on the JAAM task in the domains specifically measuring executive functioning and prospective memory (Montgomery et al., 2012). They found cannabis users to perform significantly worse on time based prospective memory and event-based prospective memory than control participants. This study correlates with the aforementioned one because they both found a deficit in real-world memory (Montgomery et al., 2012, Fisk et al., 2008).

Cannabis Use Impacts on Electrophysiological Responses and Executive Functioning in Adult Participants

Electrophysiological responses made by the brain due to cannabis use is informative because it shows the impacts of the drug on how the brain is communicating with itself. In terms of chronic cannabis use and executive functioning, participants ages 18 to 55 were asked to abstain from cannabis use for 12 hours immediately before participating in the study, and found decreased accuracy in brain activity when completing the Stroop task (Battisti et al., 2010). This decrease in accuracy was seen specifically in the dorsolateral prefrontal cortex and the anterior cingulate cortex in relation to greater trial error. It is possible that cannabinoid 1 receptors, that are densely located in the prefrontal cortex, bind to the active ingredient in cannabis (THC) and therefore there is less accuracy in the activation of these regions (Battisti et al., 2010). They also found that age of onset of cannabis use was a predictor for performance on the Stroop task, such that users who began using cannabis earlier in life demonstrated poorer performance. This is a consistent finding to research on adolescent cannabis users where the younger a participant began use, the poorer they performed on executive functioning tasks. In addition to age of onset effecting task performance, they also found that chronic users showed different electrophysiological responses than all other types of users, suggesting that not only does age of onset effect the brains responses but duration of use has a significant impact as well (Batisti et al., 2010).

Functional Magnetic Resonance Imaging is a unique technique that locates specific regions within the brain that are activated during executive functioning tasks and predict whether someone will become a cannabis user 6 months later. Participants ages 18 to 25 were asked to complete an N-back task in order to assess working-memory (Cousjin et al., 2014). A stronger working-memory network response was expected in participants who used cannabis chronically, specifically in the ventral-lateral pre-frontal cortex, dorsolateral prefrontal cortex and the bilateral frontal pole. The N-back test they used had three levels, 0-back, 1-back, and 2-back. 0-back occurs as a participant sees a stream of 15 letters and must indicate when the target letter appears on the screen. A 1-back occurs when a participant sees a stream of 15 letters and must decide if the letter on the screen is identical to the one they just saw. In a 2-back task, participants are presented with a stream of 15 letters and must determine if the letter they are seeing was identical to the one they saw two trials previously. It was thought that baseline scores could predict whether a participant would be using cannabis 6 months later (Cousjin et al., 2014). Upon analysis of the baseline data, the network strength did not show a statistical difference from cannabis users compared to non-users during the preliminary trial. But they did find a significant effect on behavioral performance and working memory network functioning during the N-back task on cannabis use at baseline and at the 6 month follow up (Cousjin et al., 2014). Therefore, more cannabis use at baseline correlated with stronger working memory when compared to control participants and the specific strength was able to predict cannabis use at the 6 month follow up. This means that the brain regions controlling working memory showed greater activation during the N-Back task than control participants and that this difference was also correlated with future use. This is a similar finding to aforementioned research where the bran is compensating by overworking in order to complete a task at the same level of control participants.

Summary of Adolescent Research and Adult Research

Among adolescent substance users, similar deficits have been demonstrated across studies. The Stroop task and WCST showed impaired performance by cannabis users even when abstaining from use for 12 hours before being tested (Dahlgren et al., 2016, Gruber et al., 2012). Spatial working memory deficits and paired associate memory deficits were also found for adolescents who used cannabis (Harvey et al., 2007). Impairments in inhibition, an important aspect of executive functioning, was apparent in adolescent cannabis users (Meil et al., 2016, Squegila et al., 2014). When looking past group differences, psychomotor speed and sequencing, sustained attention and cognitive inhibition were found to be impaired in a dose dependent relationship among adolescent cannabis users (Lisdahl et al., 2012). Further, adolescents who abstained from cannabis for longer periods of time also showed deficits in performance on the D-KEFS system which assesses a range of executive functions (Medina et al., 2007, Jacubus et al., 2015). Structural differences in the brains of cannabis users were found in regards to the PFC and Cerebellum. Specifically, they found larger PFC volume’s in female cannabis users compared to male cannabis users and larger Cerebellums for all cannabis using participants (Medina et al., 2009, Medina et al., 2010). They explained this could be due to the disruption during the synaptic pruning process during development (i.e., connections are lost in the brain in order to streamline and increase efficiency). Expanding on this research, the parietal lobe and cerebellar connections were assessed in adolescent cannabis users and were found to have more active connections in cannabis users when performing executive functioning tasks (Behan et al., 2014). Increased activity in the working memory systems of adolescent cannabis users was also found when taking a functional approach to executive functioning (Jager et al., 2010). These findings show immediate impairment as well as long term impairment for adolescent cannabis users in many domains of executive functioning.

Research examining the relationship between adult cannabis use and executive functioning has generated mixed results. Adult participants who were acutely intoxicated at the time of the Stroop task and the Tower of London task showed greater levels of impairment closer to the time they used cannabis (Ramaekers et al., 2006). This finding displays an immediate effect of cannabis on executive functioning. In terms of long term effects of cannabis on executive functioning it was found that these effects are detectable 7 days after abstinence but at 28 days of abstinence from cannabis there was no significant difference in executive functioning for chronic cannabis users and controls (Pope et al., 2012). It is possible that adult participants who began using cannabis after adolescence can return to normal levels of functioning after one month of abstinence. However, there is research that directly opposes this finding. When looking at the Stroop task and WCST task, again there was no significant relationship between cannabis use and performance on either of the tasks (Scholes et al., 2010). When accounting for other drugs and alcohol used in conjunction with cannabis, it was found that there was no effect of cannabis on executive functioning (Fernandez et al., 2006). A deficit on the Stroop task was found however for chronic cannabis users (Thames et al., 2014). This finding supports a previous study that looked at executive functioning in chronic cannabis users, more specifically it was found that motor programing was significantly worse among chronic cannabis users (Fontes et al., 2011). Chronic cannabis users were also found to have an impairment in real world executive functioning after a 12-hour period of abstinence (Montgomery et al., 2012, Fisk et al., 2008).

Participants who were chronic cannabis users were also found to be more concerned with immediate gain and were not cognizant of the overall losses during a gambling task (Whitlo et al., 2004).

My hypothesis in the present study is that cannabis use in adult participants will be negatively correlated with executive functioning in a dose dependent manner. Many studies on adult cannabis use assess use in a categorical manner, either they are users or they are not users. This study will examine cannabis use as a continuous variable as seen in some of the adolescent research on cannabis use. Specifically, the study will use number of days of self-reported cannabis use over a 90-day period as an independent variable and scores on executive functioning batteries as the dependent variable. Some studies looked at cannabis use in a dose dependent manner for adolescents and found significant differences in executive functioning directly related to the amount of cannabis used (Lisdahl et al. 2012). The study will use a regression analysis to control for sex, alcohol use and age because these factors have the possibility of influencing executive functioning. Generally, the overarching hypothesis is that I expect the more days a participant has previously used cannabis (in a 90-day time line followback), the worse their performance will be on all cognitive measures.

Methods

Participants

In this study, 79 participants (38 are male, refer to graph 1 for a sex breakdown between groups) age 24 to 40 (average age was 29, see graph 2 for an age breakdown between groups) were recruited from the community through posters and online advertisement. Participants were screened out during a preliminary phone call to determine if they were daily cigarette smokers

(I.e., they were excluded if they reported smoking more than three times per week) and had to have no history of or current psychiatric or bipolar disorders, and could not be currently taking psychiatric medications. Participants were specifically recruited for heavy drinking, meaning they had to binge with at least five drinks per day five times per month for men and woman had to binge 4 drinks per day at least five times per month. Light drinkers were also recruited and constituted as drinking alcoholic beverages no more than two drinks per day two days per month and were used as the control group for the larger study being conducted. Measures were administered to all participants who made it through the screening process. They were also required to remain abstinent from any drug or alcohol use 24 hours prior to the study and were given a breathalyzer test upon entering the testing facility.

All participants gave written informed consent to participate in a research study that has been reviewed by the Instructional Review Board (IRB) and is being paid for by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), a division of the National Institutes for Health (NIH). Participants were informed of the risks, benefits, procedures and purpose of being involved with this study. Once they agreed to the terms they went through the procedures of the study and were compensated $50.00 for completing all aspects of the study.

Procedures

79 participants were assessed on their working memory, inhibition control and episodic memory. They were first taken for a blood draw, to be used in the larger study. Their cognitive functioning was then measured using an iPad that presented the following tests to each participant. The NIH Toolbox Inhibitory Control and Attention Test (National Institutes of Health and Northwestern University, 2006) was used to assess participants ability to maintain

attention. This test asked participants to look at a screen with 5 arrows on it pointing either left or right. They must indicate which direction the middle arrow is pointing after a brief pause. The NIH Toolbox List Sorting Working Memory Test asks participants to look at individual photos of food or animals and repeat back to the analyst what they saw in size order from smallest to largest assessing the participants ability to use their working memory to manipulate information previously seen. NIH Toolbox Picture Sequence Memory Test assessed episodic memory. This task showed each participant different objects and activities in a specific order and the participant had to reassemble the pictures in the order previously seen once the pictures have been scrambled. Participants completed a 90-day time-line follow back of all their substance use. The participants were asked to determine the amount of each substance they used during each instance of use.

Data Analysis

Multiple regression was used to assess if number of days of cannabis use has a significant impact on the different cognitive measures (NIH Toolbox Inhibitory Control and Attention Test, NIH Toolbox List Sorting Working Memory Test, NIH Toolbox Picture Sequencing Memory Test (National Institutes of Health and Northwestern University, 2006), while controlling for other independent explanatory variables (gender, age, and number of drinks per drinking day) for each cognitive test.

Results

This study found no significant effects of cannabis use on executive functioning. This means that participants who used cannabis in the past 90 days did not score differently than control participants nor did number of days of use impact scores. First, I regressed NIH Toolbox

Inhibitory Control and Attention Test on age, gender, number of drinks per drinking day and number of days of cannabis use. The overall regression model accounted for 3.8% of the variance in performance on the NIH Toolbox Inhibitory Control and Attention Test f(4, 77)=0.295, p=0.88. The effect of cannabis use frequency was not significant, b=-0.05 t(-.118)=-0.905, P=0.37 (refer to figure 7). I then regressed NIH Toolbox List Sorting Working Memory test on gender, age, number of drinks per drinking day and number of days of cannabis use. The overall model accounted for -4.2% of the variance in performance on the NIH Toolbox List Sorting Working Memory Test f(4, 77)=0.227, p=0.922 with cannabis' effect on this test as b=-0.019, t(-0.053)=-0.043, p=0.688 revealing no significant main effect (refer to figure 8). Finally, I regressed NIH Toolbox Picture Sequencing Memory Test on gender, age, number of drinks per drinking day and number of days of cannabis use. The overall model accounted for .5% of the variance in performance on the NIH Toolbox Picture Sequencing Memory Test f(4, 78)=1.01, p=0.363 with cannabis' main effect on the test as b=0.094 t(0.184)=1.472, p=0.158 suggesting no significant main effects (refer to figure 9).

In addition, the study assessed if cannabis users performed poorer as a group when compared to a control group (people who did not smoke cannabis at all in the past 90 days) by using a t-test to assess if there are differences of the means between groups. There was no statistical difference on the NIH Toolbox Inhibition Control and Attention Test between cannabis user and control participant conditions; t(75)= 0.575, p= 0.567 (see figure 4). There was also no significant difference on the NIH Toolbox List Sort Working Memory Test between cannabis user and control participant conditions; t(74)= -0.0342, p= 0.973 (see figure 5). Finally, there was no significant difference on the NIH Toolbox Picture Sequence Memory Test between cannabis user and control participant conditions; t(76)= -0.5127, p= 0.6097 (see figure 6).

Discussion

Previous research has demonstrated chronic, heavy cannabis users have shown decreases in executive functioning. However, among the present group of adults reporting a wide range of patterns of use, cannabis had no relationship with executive functioning. My hypothesis was that cannabis use in adults would be negatively correlated with scores from executive functioning batteries. When NIH Toolbox Picture Sequence Memory test, NIH Toolbox List Sort Working Memory test, NIH Toolbox Inhibitory Control and Attention test, were each regressed separately on age, gender, sex, number of drinks per drinking day and number of days of cannabis use, no significant results emerged. In other words, cannabis use in adults did not negatively correlate with scores across all executive functioning batteries. Thus, these data did not support my hypothesis.

One explanation for these unexpected findings is that half of the sample had not smoked cannabis in the last 90 days. Thus, a between-group analysis would be appropriate and consistent with the analyses of past research on marijuana and executive functioning. Consistent with my regression findings, the t-test analysis between the cannabis user participants and control participants also showed no significant results. Cannabis users in the present study did not score lower on average than control participants on any of the NIH Toolbox executive functioning batteries. The only significant result appeared when comparing alcohol use between groups. Cannabis users on average drank more alcohol per drinking day than control participants. This result however, did not impact performance on the executive functioning batteries.

The results of this study are different from the research on adolescent cannabis users and executive functioning. For example, Dahlgren et al. (2016) and Gruber et al. (2012) found inferior performance by cannabis users on the Stroop Task and WCST. Lisdahl et al. (2012) found an inhibition deficit among adolescent cannabis users. These tasks are similar to the inhibitory control battery in the NIH Toolbox. Both are looking at participants' ability to inhibit a proponent response in order to deliver a less frequent target response. This study did not find the same effect on adults when using the NIH Toolbox battery assessing inhibition control and attention. We found no effect of cannabis on participants' performance on executive functioning tests. Conversely, Medina et al. (2007) and Jacubus et al. (2015) used the D-KEFS system to assess executive functioning and found a poorer performance among cannabis using adolescents. This system assesses a wide array of executive functioning skills in participants. They found a deficit across all of the functions assessed in cannabis users which is inconsistent with the findings of this research.

Notably, the present study differed from the aforementioned adolescent studies, likely due to the difference in subject pools. The present study examined adults 25 to 40 years old while previous studies primarily focused on adolescents under the age of 18. They looked at the impacts of cannabis on the developing brain. It is possible that cannabis effects executive functioning differently through development (e.g., adolescence and young adult hood). The results of this study suggest that there is likely a difference in cannabis' impact on executive functioning between adolescents and adults who use the drug. Research on adolescents overwhelmingly show results of poorer performance on executive functioning tasks while use of cannabis among adult participants did not show a difference in performance in this study. Future studies should further examine these differences in executive functioning specifically between adolescent users and adult users to attempt to determine how development may impact the relationship between cannabis use and cognitive functioning.

In terms of research on adult cannabis users, Pope et al. (2012) was a highly cited article on cannabis use and executive functioning. They found cannabis users had impaired executive functioning up to 7 days after abstinence. Ramaekers et al. (2006) also found that participants who were acutely intoxicated performed poorer on executive functioning tasks. In this study, we asked participants to abstain for 12 hours before the study took place. Even after such a brief period of abstinence there were no significant differences among cannabis users. Fontes et al. (2011) Thames et al. (2014), Montgomery et al. (2012) and Whitlo et al. (2004) all found executive functioning deficits among chronic adult users. This study did not recruit specifically for chronic cannabis users, instead we looked at the use naturally occurring (participants were not recruited for specific levels of cannabis use, instead they were recruited for alcohol use for the larger study and we assessed if and how much cannabis was used in this group) in a sample of participants recruited for alcohol use due to the needs of the larger study.

The studies that found significantly worse performance on cognitive batteries for participants who used cannabis recruited participants specifically based on their cannabis use. For example, Pope et al. (2001) recruited participants who had reported at least 5000 episodes of cannabis use in their lifetime. Whitlo et al. (2004) recruited participants who had a history of long-term heavy cannabis use. Montgomery et al. (2012) recruited participants from a college campus who had used cannabis at least 4 times in the past month. These participants are considerably different from the participants included in the present study in that they report much heavier cannabis use on average. The present study recruited participants who were not necessarily in college and did not need to have a history of cannabis use, or even report any current cannabis use.

We did, however, find results consistent with some of the past research. For example, one study found that after accounting for other drug use there was no significant effect for cannabis use on executive functioning (Fernandez et al., 2006). This study used a regression analysis to account for alcohol use among the participants. This study also did not find a difference in performance between cannabis users and control participants. The Stroop Test and WCST on adult participants and found no difference between cannabis users and control participants (Scholes et al., 2010). The Stroop Test assesses inhibition control and attention which is what the NIH Toolbox Inhibitory Control and Attention test assesses as well. Both studies did not find a significant result when looking at batteries assessing the same cognitive process.

Some limitations of this study are that we did not assess for psychopathology, such as depression or anxiety symptoms, which are known to be significantly associated with certain aspects of executive functioning. Notably, we did collect non-diagnostic data on depression and anxiety by administering the Beck Depression Inventory and the Beck Anxiety Inventory, but too few participants completed these inventories and thus the data was too low powered to give a meaningful result. Participants were, however, screened out for having a psychotic spectrum disorder or bipolar disorder or a serious mental illness. Another limitation is that we asked participants to abstain from all substance use for 12 hours prior to the study. It is possible that in rare cases, this could still allow for acute alcohol intoxication during the time of the study. We tried to account for this by making each participant take a breathalyzer at the beginning of the study session. Another limitation was that we did not have a measure of IQ, which can also contribute to performance on executive functioning tests. A final limitation is that all subjects were recruited from areas in and around Boulder, Colorado a very distinct city in Colorado known for their fitness and health habits. Emerging studies have demonstrated an association between aerobic exercise and cognitive functioning, thus future research should examine these variables and how they impact executive functioning in relation to cannabis use. Future research should also investigate how cannabis use in adults impacts executive functioning across a broad spectrum of cannabis use patterns (i.e., occasional users, every day users, heavy chronic users, etc.), in order to be able to generalize the results to the population more accurately. It could be helpful to recruit participants with different levels of substance use over the past 90 days to be able to conduct a regression analysis with a continuous cannabis use variable to see if dose or frequency of use effects executive functioning. It is also possible that the measures used in the present study were not sensitive enough to detect the effect of cannabis on executive functioning. There are a few measures that have increased sensitivity such as, the Iowa Gambling task is a measure that is more sensitive to the effects of substances on executive functioning specifically in the domain of risky-decision making (Whitlo et al., 2004), the Stroop task is particularly sensitive to differences in a person's ability to inhibit a pre-potent response (Karoly, Weiland, Sabbineni, & Hutchison, 2014), and the Trail-Making test is sensitive to attention and set switching (Day, Celio, Lisman, Johansen, & Spear, 2013). It is possible that using any one or all three of the aforementioned measures would result in a significant finding.

Previously, it has been suggested that cannabis has immediate and lasting deleterious impacts on cognitive functioning, and specifically on executive functioning. For this reason, cannabis is currently considered a Schedule I drug in the United States of America. Past research has shown that there is reason to be concerned in regard to adolescent use during their development. With mixed results on the impacts for adult use, this is an area in need of research.

This study enriches the area of cannabis use in adults by using the NIH Toolbox executive functioning batteries to assess cannabis users by way of a regression analysis and a between groups t-test and neither showed a significant difference in performance. Upon graphing the means of each cognitive test produced by the t-test, performance was near identical. With an average number of days of cannabis use being 47 out of 90, they were not light users, and still no significant effect was found. Further research is needed in order to find consistency across studies of different age groups, and to gain a deeper understanding of the impact of cannabis use on executive functioning.

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	Cannabis Users means	Control Group means	df	P value
Age	M=29.32	M=29.48	(df)=76	P=0.864
Sex distribution	Male M=20 Female M=18	Male M=21 Female M=18	(df)=77	P=0.4872
Number of drinks per drinking day	M=4.068	M=2.589	(df)=77	P=0.0045
NIH Inhibitory Control and Attention Test	M=93.35	M=95.40	(df)=75	P=0.567
NIH List Sort Working Memory Test	M=101.722	M=101.625	(df)=74	P=0.9728
NIH Picture Sequence Memory Test	M=108.553	M=106.475	(df)=76	P=0.6097

Table 1: Descriptive statistics looking at the mean differences between the cannabis user group and the control group in terms of age, sex, number of drinks per drinking day, Inhibitory Control and Attention test, NIH List Sort Working Memory Test, and the NIH Picture Sequence Memory test and showing the level of significance (P value) between the groups

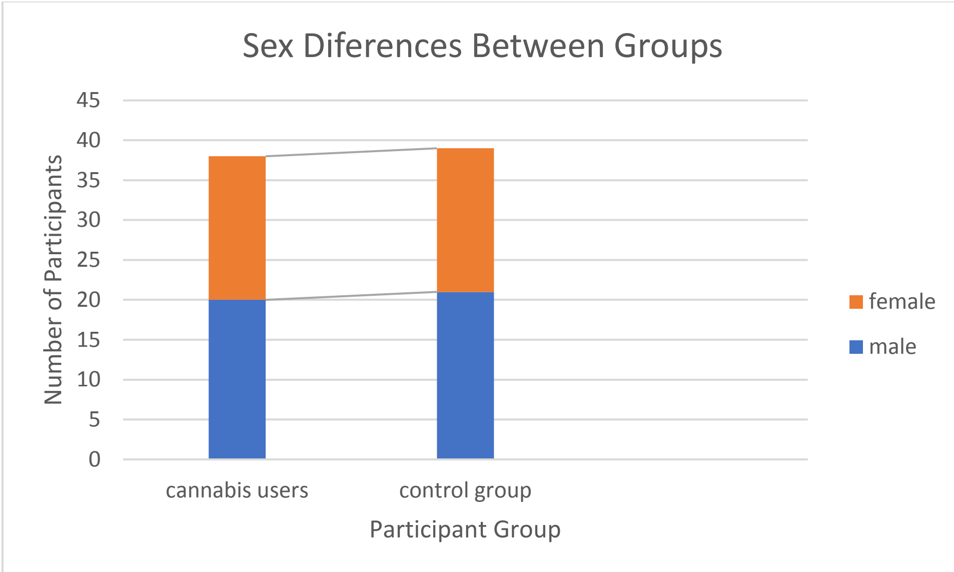

Figure 1: Shows the distribution of male and female participants between groups

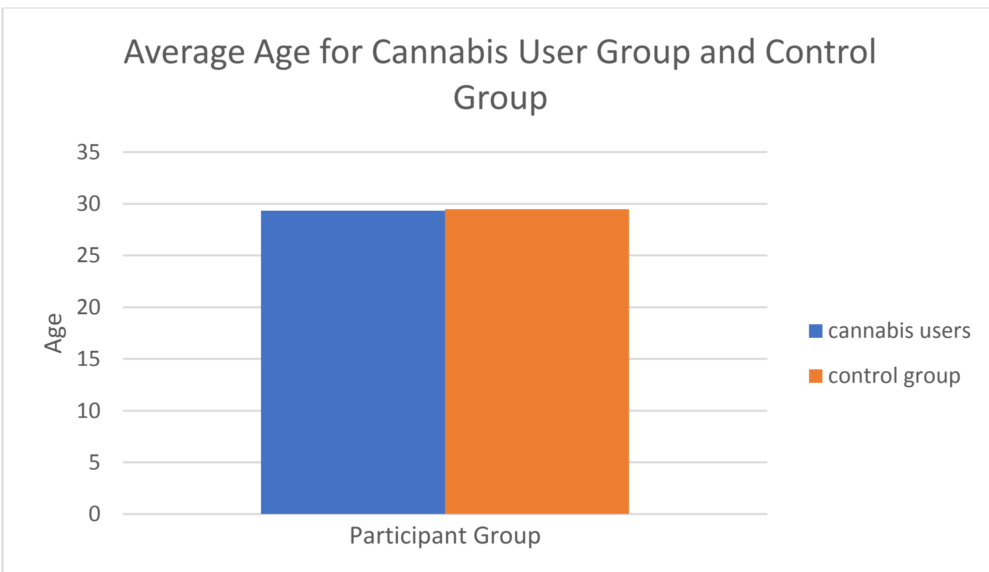

Figure 2: Shows the average age of the participants in each group

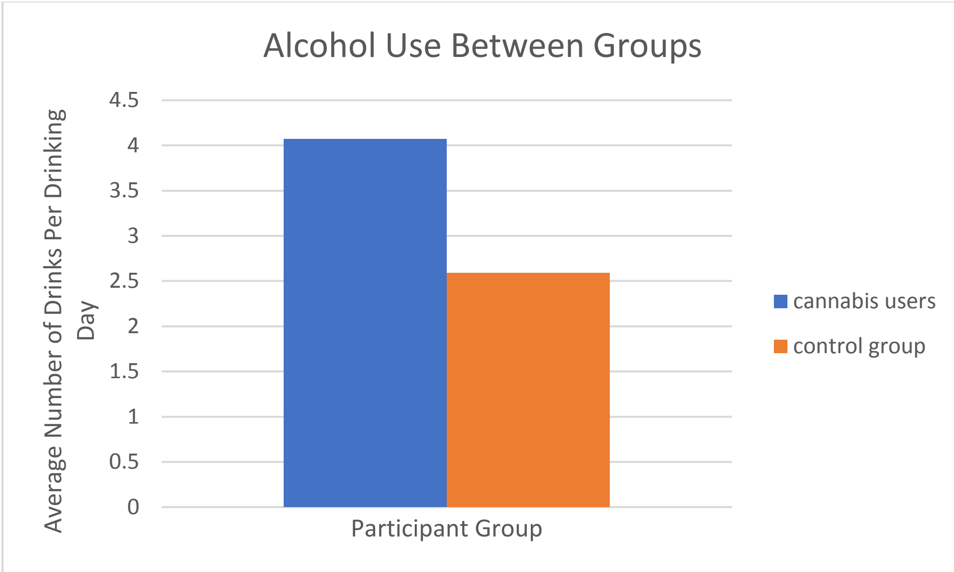

Figure 3: Shows the average alcohol used per drinking day between study groups

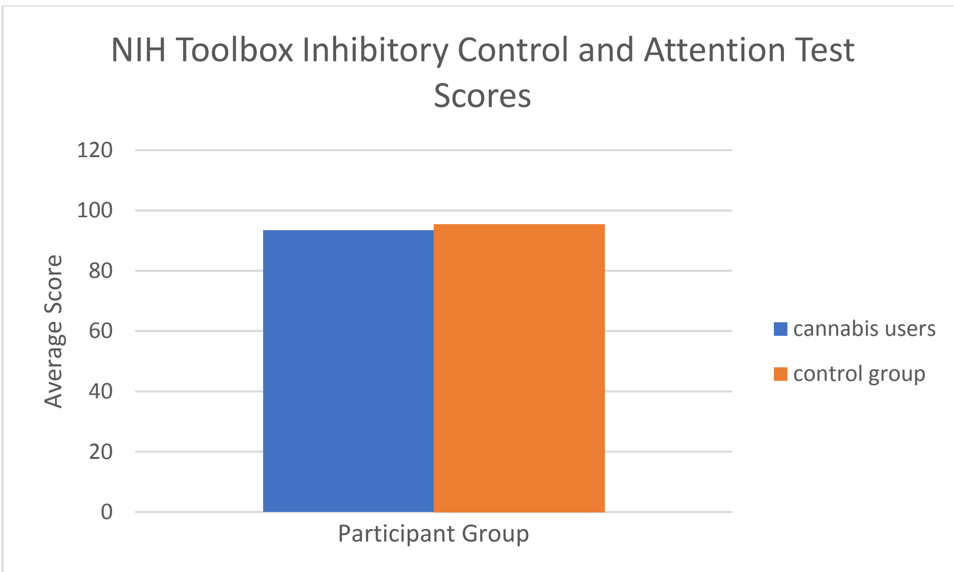

Figure 4: Shows the average score on NIH Toolbox Inhibitory Control and Attention Test between groups

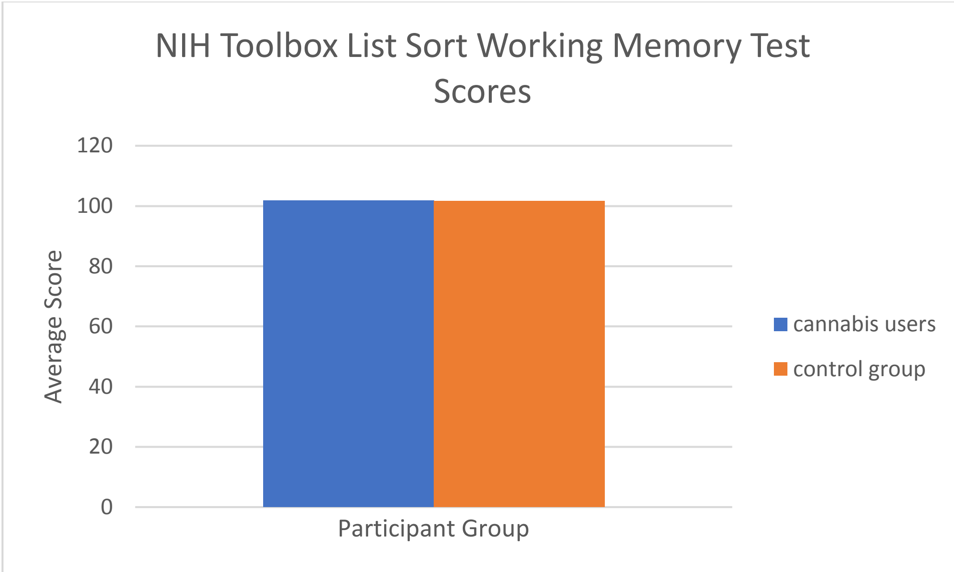

Figure 5: Shows the average scores on NIH Toolbox List Sort Working Memory test between groups

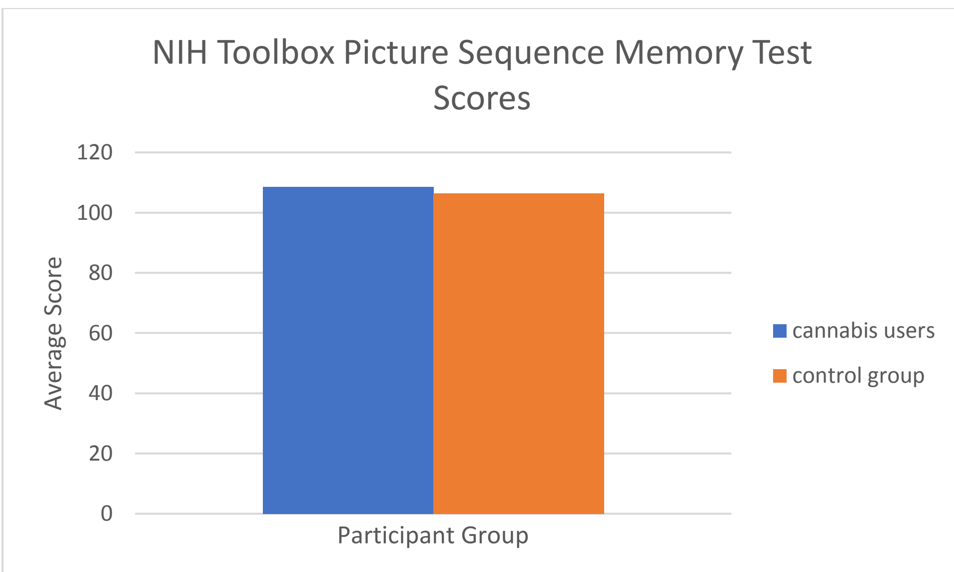

Figure 6: Shows the average scores on NIH Toolbox Picture Sequence Memory test between groups

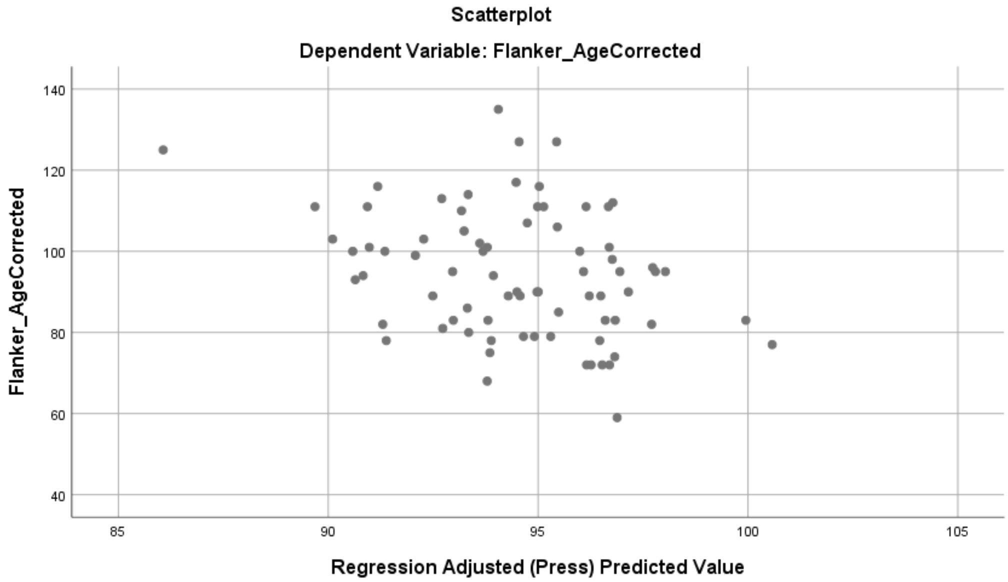

Figure 7: Scatter plot representing how sex, age, number of drinks per drinking day, and number of days of cannabis use (Regression Adjusted(press) Predicted Value) impacts scores on the Flanker inhibition and attention test (Flanker_AgeCorrected). No relationship emerged from this regression.

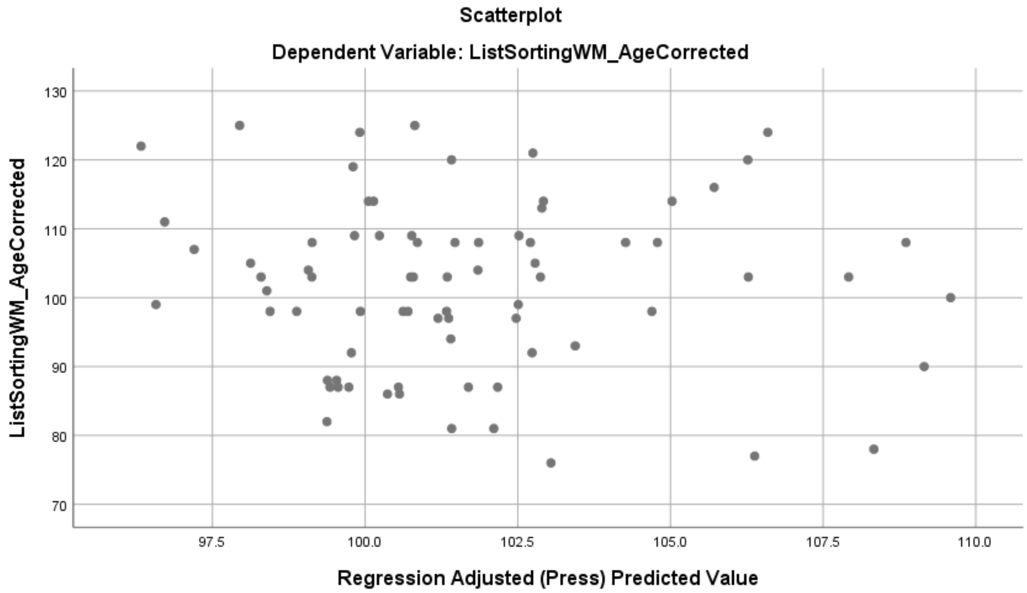

Figure 8: Scatter plot representing how sex, age, number of drinks per drinking day, and number of days of cannabis use (Regression Adjusted(press) Predicted Value) impacts scores on the List Sorting Working Memory test (ListSortWM_AgeCorrected). No relationship emerged from this regression.

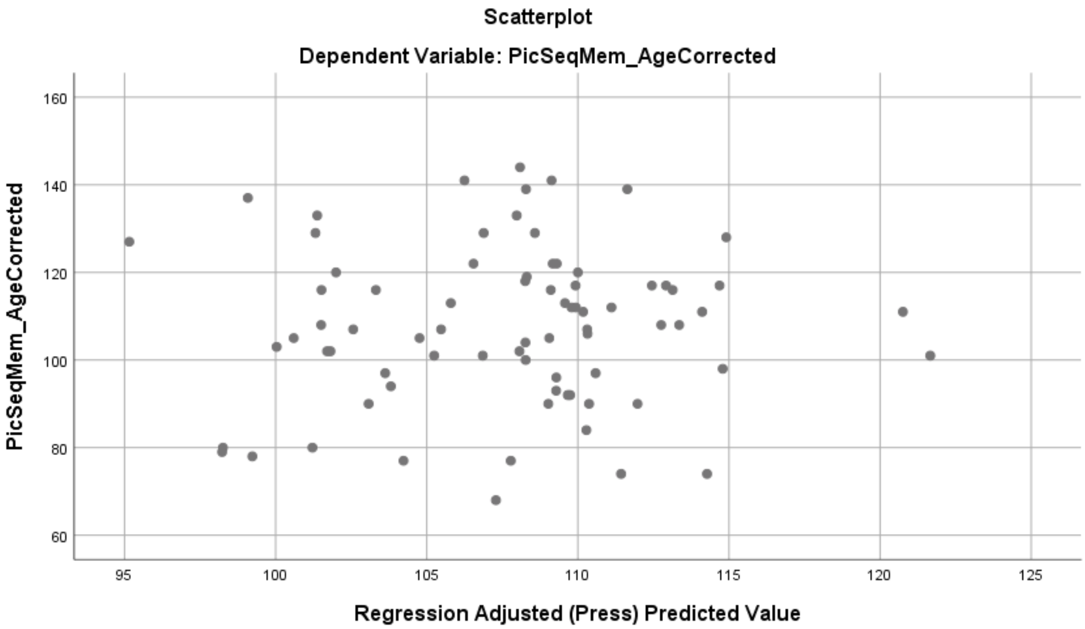

Figure 9: Scatter plot representing how sex, age, number of drinks per drinking day, and number of days of cannabis use (Regression Adjusted(press) Predicted Value) impacts scores on the Picture Sequence Memory test (PicSeqMem_AgeCorrected). No relationship emerged from this regression.