

A preliminary comparison of cannabis use in subsyndromal gamblers: Select neurocognitive and behavioral differences based on use.

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ABSTRACT

Objectives: Cannabis and gambling are two common forms of impulsive behavior among young adults. Although both cannabis use and gambling have been associated with specific cognitive deficits on tasks related to decision making, no studies to date have examined the possible effects on neurocognition in those who simultaneously gamble and use cannabis.

Methods: To address this question, the present study analyzed 214 subsyndromal gamblers from a larger study on impulsivity. Of these subjects, 64 (29.9%) were current cannabis users (last use within the last three months), and 150 (70.1%) of whom had no history of cannabis use in the last three months, along with 163 healthy controls. Participants were assessed on various cognitive and clinical measures, including measures for gambling severity and impulsivity.

Results: Cannabis using subjects had higher rates of current alcohol use disorders and more frequent gambling behavior per week. Gamblers who used cannabis also exhibited significantly greater scores on one measure of attentional impulsivity. Both gambling groups differed from healthy controls on all clinical and select neurocognitive variables, consistent with previous research.

Conclusions: These results indicate that cannabis use in young adults who gamble is associated with nuanced behavioral differences, although causality could not be determined. Longitudinal research should examine cannabis use in subsyndromal gamblers over time to characterize whether these findings are causative.

Keywords: Cannabis; neurocognition; gambling; addiction

1. Introduction

Cannabis is one of the most commonly used illegal drugs in the United States, with one national survey noting that 18.7% of young adults from 18-26 had used cannabis in the past month, and 31.50% had used it in the past year (NIDA Report, 2012). This high rate of use has spurred numerous investigations on the possible detrimental health effects of cannabis, including increased risk for psychosis, respiratory disorders, and various psychosocial problems (Roth et al., 1998; Fergusson et al., 2002; Arsenal et al., 2004). Additionally, research has demonstrated that cannabis has negative effects on various cognitive measures, including psychomotor speed, planning/sequencing ability, and memory (Makela et al., 2006; Medina et al., 2007; McHale & Hunt, 2008; Indlekofer et al., 2009; Gonzalez et al., 2012; Grant et al., 2012). Studies have produced mixed results regarding the persistence of these cognitive differences following abstinence from cannabis.

Cannabis use has also been associated with a higher risk for other potentially addictive or impulsive behaviors, including alcohol use, illicit drug use, and problematic gambling behavior (Carvalho et al., 2005; Fergusson et al., 2006; Wanner et al., 2006). Cannabis use also predicts higher rates of both alcohol use and illicit substance use later in life, with weekly or more frequent consumption indicating up to a twofold elevation in risk of high-risk drinking later in life (Fergusson et al., 2006; Patton et al., 2007). Other studies examining alcohol use and gambling have shown cognitive differences between pathological gambling substance abusers and controls, with alcohol abuse and pathological gambling producing an additive effect on risky choices during card/deck selection tasks (Petry, 2001). Other research has noted similar cognitive deficits between

alcohol dependence and pathological gambling on tasks such as the Tower of London and Stop Signal Task (Goudriaan et al., 2006). These similarities and interactions between other addictive behaviors suggest that comparable interactions may exist between related behaviors, such as gambling and cannabis.

Knowledge regarding the effects of cannabis on gambling is been limited. The majority of research on cannabis and gambling has focused on rates of comorbidity between problem/pathological gamblers and cannabis use disorders, with one study finding that 37.9% of treatment-seeking individuals with cannabis use disorders qualified for problem gambling, and another finding a prevalence of 18% in an adolescent sample (Petry & Tawfik, 2001; Toneatto & Brennan, 2002). The rates found in these studies are appreciably higher than estimated prevalence rates for problem gambling (0.4%-4.7%) (Shaffer et al., 1999; Stucki & Rihs-Middel, 2007). These elevated rates of gambling disorder are also consistent with studies collapsing across various forms of substance addiction, including alcohol, cocaine, and cannabis (Carvalhoe al., 2005).

Although no studies to date have directly assessed the cognitive effects of cannabis on individuals who gamble, certain cognitive deficits in cannabis users and in gamblers may be relevant to this possible interaction. Previous studies of cannabis use have shown deficits in decision-making in response to negative consequences, high-risk betting tendencies, and discounting of delayed rewards on tasks such as the Iowa Gamble Task (IGT) and deck/card selection task (Whitlow et al, 2004; Wesley et al., 2011). Similarly, previous research in individuals who gamble has noted the following deficits: proportion of points bet and decision making based on risk on the Cambridge Gamble Task (CGT) (Grant et al., 2011). Although no previous study to our knowledge has examined the

synergistic effects of cannabis use and gambling, related research on nicotine use found that it worsens gambling behaviors in those who smoke and gamble (Petry & Oncken, 2002; Grant & Potenza, 2005)

As both gambling and cannabis use are associated with cognitive deficits, recognizing the associations between cannabis use and current gambling symptomatology among individuals with subsyndromal gambling is important, as cannabis use may have implications for the clinical course of gambling. Based on these previous findings, we hypothesized that 1) cannabis use would be disproportionately common among individuals who gamble; 2) current cannabis use (past three months) would be associated with other substance use problems and worse gambling symptomatology; and 3) current cannabis use (past three months) would be associated with greater impulsivity and cognitive deficits in decision-making compared to subsyndromal gamblers who did not use cannabis as well as healthy controls.

2. Methods

2.1 Subjects

For this analysis, 214 non-treatment-seeking young adults and 163 controls (ages 18-29) were selected from ongoing study examining impulsivity. To participate in the overarching study, subjects needed to be between the ages of 18-29, and have gambled at least 5 times in the past year. Subjects included in this sub-sample are drawn from the pool provided by the larger study on impulsivity and gambling, which includes 548 total subjects. Thus our sample consisted of 377 (68.8%) subjects from the overall sample, with 171 subjects excluded from analysis because they did not meet the criterion for

inclusion in the healthy control group or either of the gambling groups (criterion described below). Subjects were each compensated with a \$50 gift card. Subsyndromal gambling was defined as having at least one but no more than 4 symptoms of pathological gambling based on the Structured Clinical Interview for Pathological Gambling (SCI-PG) (Grant et al., 2004). Healthy controls were defined as subjects with no cannabis use in the past 3 months, no current psychiatric diagnosis, and a score of zero on the SCI-PG. Subjects were excluded if they were unable to provide written informed consent.

The study procedures were carried out in accordance with the Declaration of Helsinki. The Institutional Review Board of the University of Chicago approved the study and the accompanying consent form. After all procedures were explained, subjects provided informed written consent.

2.2 Assessments

2.2.1 Psychiatric Assessments

Following consent procedures, all participants were screened using the Mini International Neuropsychiatric Inventory (MINI) (Sheehan et al., 1998) by trained raters. Additionally, all subjects completed general demographic information including age, race/ethnicity, education, and gender.

2.2.2 Measures of Gambling Severity

Structured Clinical Interview for Pathological Gambling (SCI-PG) (Grant et al., 2004): This diagnostic inventory assesses symptoms of pathological gambling. The criterion for inclusion in the gambling groups was a score of 1-4 on this scale (i.e. a subsyndromal gambler). Scores greater than four or less than one were excluded from analysis. The SCI-PG captures various clinical aspects of gambling behavior.

Pathological Gambling – Yale-Brown Obsessive-Compulsive Scale (PG-YBOCS)

(Pallanti et al., 2005): This clinician-administered instrument assesses thoughts, urges, and gambling behavior over the past seven days. This adaptation of the scale has been used to assess urges, thoughts, and overall severity specifically relating to gambling. The PG-YBOCS offers another assessment of gambling severity, providing a more specific account of obsessions and compulsions as they relate to gambling. (Pasche et al., 2013; Pallanti et al., 2005).

2.2.3 Impulsivity Self-Report

Barratt Impulsivity Scale, Version 11 (BIS-11) (Barratt, 1959; Patton et al., 1995): This is a valid, reliable, self-report inventory consisting of 30-items that measure distinct domains of impulsivity. The second order factors are defined as follows: motor impulsivity, attentional impulsivity, and non-planning impulsivity. This scale was included to assess self-reported levels of impulsivity, as cognitive impulsivity is a commonly cited factor in impulse control disorders, including gambling disorder, trichotillomania, and others. The self-report nature of the scale complements cognitive testing, as some studies have shown different levels of impulsivity between the two (Marazziti et al., 2014, Vonmoos et al., 2013). The three secondary measures were chosen to provide supplemental measures of impulsivity, thus further subdivisions of the categories were deemed unnecessary.

2.2.4 Neurocognitive Assessments

Selected tasks from the Cambridge Neuropsychological Test Automated Battery were used for this study: Cambridge Gamble Task (CGT), Stop-Signal Task (SST), and Intra/Extradimentional Set Shift (IED).

The CGT assesses risk-taking and decision making behavior. During the task, ten boxes (a mix of red and blue) are shown on the screen. During each set, the subject selects a rectangle at the bottom of the screen indicating "red" or "blue". The subject's choice indicates that they think a yellow token is hidden under the color they select. During all of the trials, the yellow token has an equal likelihood of appearing under any given colored box on the screen. After selecting a color, the subjects select a total number of points to wager on successfully finding the yellow token. Bet options appear in a new box on the screen and advance from 5% of total points up to 95% of total points. The overall proportion of possible points bet during the task is summarized by the "Overall proportion of points bet" variable. The greater the number of points bet, the higher risk the wager. Risk adjustment describes a person's ability to adjust strategy in response to changes in the risk of a betting situation, and the likelihood that a given choice will be correct. Quality of decision making is related to the number of trials in which the subject chooses the color with the most total boxes on the screen, which is noted by the "Quality of decision making" variable. The "Delay aversion" variable accounts for individuals who are unable to wait for later options and select numbers earlier in both the ascending and descending sequences.

The SST examined the subject's ability to inhibit a prepotent motor response. During the task, subjects are given a button box with two buttons. During the task, arrows appear in a circle on the screen, facing either right or left. When the arrows face left, the subject presses the left button on the box, and when the arrow faces right, the right button on the box. After 16 initial trials, the task changes slightly, and some of the arrows are followed by a beep. When the beep occurs, the subject is instructed not to press the key for the arrow that immediately preceded the beep. Greater stop signal reaction time during this task suggests a higher level of motor impulsivity and is summarized by the "SST SSRT (last half)" variable.

The third task, the IED, assesses learning and cognitive flexibility. During the task, the subject views numerous sets of stimuli, with each set consisting of two blank boxes and two boxes with active stimuli. The computer has arbitrarily selected one stimulus as correct and the subject selects different stimuli in an attempt to learn the rule. On-screen feedback is provided after each choice, indicating if it was "correct" or "incorrect". Following six consecutive correct selections, the computer automatically selects a new rule. During this phase, the subject must determine the new rule. Doing so with fewer errors indicates a higher level of learning and flexibility. The test consists of nine stages, although not all subjects complete all nine stages. For this reason, the primary outcome measure for this test is the adjusted number of total error. This adjustment accounts for the decreased number of stages completed for individuals unable to successfully select the "correct" options in six consecutive sets.

The specific measures chosen for analysis were drawn from those specifically relating to impulsivity, gambling behavior, and quality of thinking. The descriptions provided here provide a brief summary of the different tasks and variables used in this study. Full task descriptions can be found at <u>www.camcog.com</u> along with previous validations.

2.2.5 Cannabis Use Assessment

Data on cannabis use was collected verbally through a series of free response questions. The questions used were phrased as follows:

- 1. Do you currently use cannabis/marijuana?
- 2. How often per week or per month do you use cannabis/marijuana?
- 3. When you use cannabis/marijuana, how much do you typically use?
- 4. When was the last time you used cannabis/marijuana?

If participants responded with "No" to the first question, they were not asked the remaining three. N values are limited for questions 3 and 4, as these questions were not added to the main study until later. The averages reported for the last two questions only include cannabis users who answered these questions during their first visit. Cannabis use was coded as frequency per week, for example, weekly use received a score of "1", bi-weekly use as a ".5", and daily use as a "7".

Nicotine use was identified with a question similar to #1.

2.3 Data Analysis

Subsyndromal gamblers were divided into two groups: "cannabis users" or "non-users". The "cannabis users" group was defined as having used cannabis at least once in the past 3 months, while the "non-users" group was defined by no cannabis use in the preceding 3 months. Healthy controls were kept separate as the third comparison group. The subjects included in this analysis were drawn from baseline results of an ongoing study on impulsivity, of which cannabis use was just one of the factors considered.

ANOVA tests were used to examine age, impulsivity scales, gambling measures, and neurocognitive measures. Chi-square (Pearson's) analyses were used for the remaining categorical variables. Further ANOVA and Chi-square analyses were conducted for significant results from the initial tests. As this was an exploratory study, significance was defined as p<.05, uncorrected.

3. Results

Of the 214 subsyndromal gamblers, 64 (30.0%) were current cannabis users. Both subsyndromal gambling groups differed significantly from controls in age (ANOVA: F=7.160, df=2; Cannabis: p<.05; No-cannabis: p=.001). The groups did not differ on any other demographic variables (Table 1).

The 64 cannabis-using subsyndromal gamblers reported using cannabis an average of 2.76 (\pm 2.67) days per week. Of the 64 cannabis users, 20 reported their average amount consumed, with an average of .82g (\pm .77). Additionally, 27 cannabis users reported a specific last day of use, with an average of 6.17 (\pm 11.92) days elapsed since last use. Data for quantity used and day of last used have lower N values because these measures were not added until later in the overarching study of impulsivity.

In terms of co-occurring psychiatric disorders, the gamblers who also used cannabis were significantly more likely to have an alcohol use disorder ($\chi^2 = 21.829$, df=1; p<.001). In general, the cannabis group was also significantly more likely to have any co-occurring psychiatric disorder ($\chi^2 = 39.844$, df=1; p<.001) (Table 2). All three groups differed

significantly on current nicotine use, with the cannabis group reporting the highest overall percentage current nicotine users, followed by the non-cannabis gamblers (χ^2 =22.099, df=2; p=.001).

On measures of gambling severity, gamblers who used cannabis gambled significantly more times per week than other gamblers (F=4.628, df=1; p<.05), who in turn gambled more frequently than healthy controls (F=7.911; df=1; p<.05). The same pattern was found on the BIS measure of attentional impulsivity, with gamblers who used cannabis reporting higher levels than other gamblers (F=5.505, df=1; p<.05), and the non-cannabis using gamblers reporting higher levels than healthy controls. The gambling groups did not differ on any other gambling or impulsivity measures, but both differed significantly from healthy controls on all other clinical variables (summarized in Table 2).

Both gambling groups differed significantly from healthy controls on measures of stopsignal reaction time, proportion of points bet, quality of decision making, and risk adjustment (summarized in Table 3). The cannabis using gamblers did not differ significantly from the non-using gamblers on any of the cognitive tasks.

4. Discussion

This study examined the possible effects of cannabis use on gambling behavior and cognition in young adult subsyndromal gamblers relative to healthy controls. Consistent with our first hypothesis that rates of past-year cannabis use would be high among gamblers, we found that almost one-third of young adult gamblers were current cannabis users. This rate reflects a 60% increase in current cannabis use relative to the general

population of young adults age 18-25 (18.7%), and a 410% increase over all Americans over ages 12 and above (7.30%) (NIDA, 2012).

Consistent with our second hypothesis, gamblers who used cannabis were significantly more likely to have an alcohol use disorder, other psychiatric diagnosis, and to be current nicotine users relative to subsyndromal gamblers who do not use cannabis. Results regarding the increased incidence of alcohol use disorders in cannabis users versus non-users are consistent with previous research on cannabis use (Fergusson et al., 2006; Patton et al., 2007). These results suggest that several addictive behaviors seem to co-occur. Even on the subsyndromal level of gambling behavior we see aggregation with other externalizing disorders such as alcohol dependence. Whether this reflects a shared pathophysiology, common genetic underpinning or environmental influences is not yet fully understood (Blanco et al., 2012; Grant et al., 2009; Slutske et al., 2000).

Partly consistent with our second hypothesis was the finding that gamblers who used cannabis had worse gambling symptomatology on at least one measure - frequency of gambling per week. Cannabis was not associated with a stronger urge to gamble (reflected in no differences on the PG-YBOCS), which has been seen in gamblers who use nicotine (Grant & Potenza, 2005). These findings suggest one area in which cannabis may influence gambling behavior. For example, differences in gambling behavior but not thoughts or urges suggest that impairments in behavioral control might be related to the co-occurrence of cannabis use and gambling.

As noted previously, nicotine use has previously been associated with higher urge scores on the PG-YBOCS scale, a relationship that was not found in this study, despite a

significantly higher rate of coexisting cannabis and nicotine use. This difference could suggest that cannabis moderates the effects that other substances have on gambling, such as nicotine's cognitive implications. This interpretation would suggest that treatments emphasizing behavioral control might be particularly helpful for individuals with coexisting gambling and cannabis use. The increased incidence of multiple externalizing disorders may indicate a third variable contributing to cannabis use, gambling, as well as other types of substance use.

The possible association between cannabis use and gambling could also be mediated in multiple, non-mutually exclusive manners. For example, cannabis use may influence gambling through experiences of reward or pleasure that influence behavioral decisionmaking. Alternatively, specific individuals (e.g., those who are more impulsive) may be predisposed to engage in both cannabis use and gambling. Due to the high incidence rate of alcohol use disorders, nicotine use, and comorbid MINI diagnoses, it was not possible to control for each of these significant differences. There are likely to be many overlapping vulnerability factors implicated in the etiology of both substance use and gambling. This study examined potential commonalities and differences between gamblers with and without cannabis use, and healthy controls. Differences between cannabis users and non-users could be accounted for by factors other than cannabis use (for example, higher alcohol use disorder in the cannabis using group). To tease apart causality, larger scale studies would be needed, ideally incorporating a longitudinal design. We did not subdivide groups based on potential confounds because we wished to examine the ecological clinical and cognitive profiles of these groups as they presented.

Our third hypothesis was only partially supported by these data, and the findings are of note. First, cannabis users reported significantly higher levels of attentional impulsivity relative to both other gamblers and healthy controls. Previous research using the attentional impulsivity subscale has shown significantly higher levels of various impulsive and addictive behaviors, including pathological gambling, alcohol abuse, and illegal drug abuse (Kjome et al., 2010; Knezevic & Ledgerwood, 2012; Nielson et al., 2012; Blackwell & Burke, 2013). From these results, we expected to find higher rates of attentional impulsivity in cannabis users, which was confirmed in this study. A higher level of attentional impulsivity in subsyndromal gamblers who use cannabis denotes a self-reported deficit in ability to focus on tasks and maintain attention for an extended period of time. As with other results, this is tempered by the high incidence of alcohol use disorders, but remains a significant point of consideration for clinicians working with comorbid cannabis use and gambling.

In terms of neurocognitive findings, gamblers who used cannabis did not differ significantly from gamblers who did not use cannabis. Both groups did, however, perform significantly worse than healthy controls on measures of reaction time, quality of decision making, and risk adjustment. The similarities between the two gambling groups on neurocognitive tests does not generally support our hypothesis that cannabis use in subsyndromal gamblers would be associated with cognitive deficits. One measure of note was the proportion of points bet during the CGT. One explanation for the lack of significant differences between the gambling groups is that gambling is associated with such extreme cognitive deficits (Grant et al., 2011) that the addition of cannabis use does not appreciably worsen these deficits. As expected, a score of 1-4 on the SCI-PG scale

predicted a number of cognitive differences, and confirmed previous findings in gamblers compared with healthy controls (Grant et al., 2011). Further research is necessary to explore the relationship between gambling, cannabis use, and cognition, including the extent to which each behavior may contribute to the other's development and maintenance.

These results highlight the idea that the potential interaction between cannabis and gambling is likely not a straight forward relationship. Rather, the absence of pervasive changes in neurocognitive factors suggests that the interaction between cannabis and subsyndromal gambling may produce more limited changes in neurocognition. Additionally, with increases in gambling severity isolated to frequency per week, it appears that cannabis may not have as drastic effect on gambling severity as was predicted.

There are several limitations to this study that should be noted when interpreting its results. One possible limitation was that cannabis use was only considered over the preceding three months. Thus, we were unable to control for individuals with a history of cannabis use beyond the prior three months. Additionally, quantity of cannabis used at a time was not assessed for all subjects, as measures differed significantly between subjects, with no consistent measurement method. The relationship between potency and quantity is a common problem in research on cannabis and requires more precise measures. As a result of the self-report nature of the overarching study from which the subjects were drawn, it was not possible to determine cannabis potency or accurate quantity. In future studies, it would be advantageous to include standardized measures of quantity used in order to provide a better control of extraneous factors, with similar

consideration given to potency of the strains of cannabis (THC concentration). In selfreport studies, it is not possible to assess potency, thus future research hoping to control for quantity of the drug consumed would need to standardize both potency and quantity to sufficiently control for both.

Similarly, the cross-sectional nature of this study inherently limited the conclusions that could be drawn from these results. Although this study provides a snapshot of this sample, it cannot differentiate between factors that were preexisting and those that may have been caused by cannabis use. A final consideration for the present study was the high degree of nicotine use and alcohol use disorders in the cannabis use group. Due to the prevalence of these disorders in the cannabis users, it was not feasible to selectively include individuals with no history of these problems. Future studies will likely benefit from controlling for these factors and limiting inclusion to individuals with no other substance abuse.

5. Conclusions

Ultimately, this study emphasizes the complex interaction between cannabis use and gambling behavior. Future studies will likely need to examine the roles that frequency of use, potency of the drug, and longitudinal factors play in this issue. Although the present study raises numerous questions, it offers some evidence that cannabis and gambling have a more subtle relationship than might be expected, meriting further investigation

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