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## Behavioral Inhibition and Reward Processing in College Binge Drinkers with and without Marijuana Use

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## Abstract

**Aim:** Binge drinking is common during college, and studies have shown that many college students drink in quantities that far exceed the standard binge drinking threshold. Previous research has noted personality differences in individuals who engage in binge drinking, but few studies have examined neurobiological differences in both standard bingers (4/5 drinks in two hours for females/males; sBinge) and extreme binge drinkers (8+/10+ drinks in two hours for females/males; eBinge).

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**Method:** The current study of 221 college students used functional magnetic resonance imaging (fMRI) to study neural activation on a stop signal task (SST) to assess behavioral inhibition and a monetary incentive delay (MID) task to assess activation to rewards and losses. Non-bingeing controls, sBinge, and eBinge freshmen and sophomores were recruited. In addition, because binge/ extreme binge drinking is often associated with marijuana (MJ) use, MJ+sBinge and MJ+eBinge groups were also included.

**Results:** All five groups showed strong activation in expected key cortical and striatal regions on both the SST and the MID. However, there were no significant differences between groups either at the whole-brain level or in specific regions of interest. Behavioral performance on the fMRI tasks also did not differ between groups.

**Conclusions:** These results suggest that our sample of individuals who engage in binge or extreme binge drinking with or without MJ co-use do not differ in brain activity on reward and inhibitory tasks. Neural differences may be present on other cognitive tasks or may emerge later after more sustained use of alcohol, MJ, and other drugs.

## Keywords

binge drinking; combined substance use; brain imaging; marijuana; inhibition; reward

## 1. Introduction

College students engage in greater alcohol use than high school students and similarly aged individuals who are not in college (Substance Abuse and Mental Health Services Administration, 2017). Many college students engage in "binge drinking" (consuming 4+/5+ drinks within a two-hour period for females/males). Binge drinking is problematic because it is associated with negative consequences such as blackouts, hangovers, accidents, and alcohol poisoning (Hermens and Lagopoulos, 2018; Kanny et al., 2015; Labhart et al., 2018; O'Leary et al., 2019) and is a leading cause of alcohol-attributable deaths (Stahre et al., 2014).

Personality and behavioral measures of behavioral disinhibition have been linked to binge drinking (Banca et al., 2016; Carbia et al., 2018; Carlson et al., 2010; Kazemi et al., 2011; Lees et al., 2019; Sanchez-Roige et al., 2014). Binge drinkers also show higher sensation seeking (O'Leary et al., 2019), a construct linked to reward sensitivity (Castellanos-Ryan et al., 2011). Consequently, there is significant interest in identifying neural correlates of inhibition and reward processing in binge drinkers.

To date, few consistent findings have emerged from functional magnetic resonance imaging (fMRI) tasks measuring behavioral inhibition. For instance, despite both assessing successful inhibition among young adult bingers, Ahmadi and colleagues (2013) reported decreased activation in fronto-parietal regions (supplementary motor area - SMA, anterior cingulate - ACC, superior parietal, precuneus), and subcortical regions (thalamus, putamen, hippocampus), whereas Ames and colleagues (2014) reported the reverse pattern, albeit in slightly different loci (dorsolateral prefrontal cortex, ACC, and insula). Whelan and colleagues (2014) also reported hyperactivation (left and right precuneus) during successful

inhibition to be an important feature for classifying adolescent binge drinkers from nonbingers.

Studies assessing reward processing and reward-related decision-making are also inconsistent. For instance, Whelan and colleagues (2014) reported reduced activity (putamen and hippocampus) in adolescent binge drinkers on a monetary incentive delay (MID) task. Cservenka and colleagues also report decreased activation on a Wheel of Fortune task, although the regions showing reduced activation included the cerebellum (Cservenka et al., 2015) and portions of the fronto-parietal cortex (Jones et al., 2016). On the other hand, Crane and colleagues (2017) reported increased nucleus accumbens activation to reward (the Doors task) in young adult bingers, and Xiao and colleagues reported higher activity in amygdala and insula on the Iowa Gambling Task in adolescent binge drinkers (Xiao et al., 2013).

One possible factor contributing to these inconsistent findings is variable levels of binge drinking. Many adolescents and young adults commonly drink well beyond the standard bingeing threshold, meeting the extreme bingeing threshold of 8+/10+ drinks in two hours for females/males (Hingson and White, 2013; Naimi et al., 2010; Patrick et al., 2013; White et al., 2006). Compared to standard binge drinking, extreme binge drinking is particularly problematic, as it is linked to a greater number of alcohol-related consequences and greater risk for developing alcohol use disorder (Hingson and White, 2013; Linden-Carmichael et al., 2017; Read et al., 2008). While contextual factors such as sporting events, holidays, and 21<sup>st</sup> birthdays contribute to extreme bingeing (Neighbors et al., 2011; Rutledge et al., 2008), individual differences factors may also be important (O'Leary et al., 2019). Indeed, researchers have emphasized the need for differentiating between standard and extreme bingeing both in terms of their consequences, as well as their predictors, such as drinking motives, at-risk traits, and sociodemographic variables (O'Leary et al., 2019; Patrick, 2016; Patrick et al., 2013; White et al., 2016).

Furthermore, individuals who engage in binge drinking are also more likely to use other substances (Jones et al., 2001), especially marijuana (MJ; Jones et al., 2018; Pampati et al., 2018; Subbaraman and Kerr, 2015), highlighting the importance of studying binge drinking and combined substance use (CSU). CSU refers to either simultaneous use (consuming more than one substance at the same time/in close temporal proximity) or concurrent use (consuming more than one substance over a specific period of time (e.g., past 6 months), but not at the same time; Martin et al., 1992). Compared to using alcohol alone, CSU significantly increases the risk for binge drinking, drunk driving, adverse social consequences, and self-harm (Subbaraman and Kerr, 2015). fMRI studies comparing CSU to mono-substance use (MSU) on reward processing, however, are limited and inconsistent. For instance, Nestor and colleagues (2017) suggested synergistic effects of CSU as compared to MSU, while Karoly and colleagues (2015) suggested neuroprotective effects. Similarly, to our knowledge, there is only one study comparing CSU (abstinent polysubstance-dependent individuals) vs. MSU (abstinent alcoholics) during a behavioral inhibition task across different acute drug conditions (placebo vs. naltrexone; Nestor et al., 2019). For baseline inhibition (placebo), CSU did not significantly differ from MSU on either behavioral performance or neural activation.

O'Leary and colleagues (2019) reported personality differences among standard binge drinkers (sBinge), extreme binge drinkers (eBinge), standard and extreme binge drinkers who also use MJ (MJ+sBinge, MJ+eBinge), and control subjects with no past bingeing/MJ use. Groups were compared on the Barratt Impulsiveness Scale (BIS) and the Zuckerman Sensation Seeking Scale (SSS). When group differences on BIS and SSS subscales were tested separately, eBinge scored higher than sBinge on Thrill and Adventure Seeking. When considering all BIS and SSS subscales together in a logistic regression model, SSS Disinhibition showed group differences, controlling for other subscales, such that MJ+sBinge and MJ+eBinge scored higher than sBinge, and there was a trend toward MJ+sBinge scoring higher than MJ+eBinge.

Following up on O'leary et al.'s 2019 personality study, we sought to better understand the neurobiological differences linked to different patterns of alcohol and marijuana consumption. In this project, we again examined sBinge, eBinge, MJ+sBinge, MJ+eBinge, and control subjects, this time on two fMRI tasks, the Stop Signal Task (SST) and the MID, to assess behavioral inhibition and reward processing, respectively. We hypothesized that, compared to controls, sBinge, and to a greater extent, eBinge would show altered behavioral inhibition and reward sensitivity (without specifying direction of the difference due to inconsistencies in the literature). Comparisons between CSU groups and controls and MSU groups were also examined. However, given the limited and inconsistent findings, no specific hypotheses were formulated.

## 2. Materials and Methods

#### 2.1. Participants

The criteria for the sBinge/eBinge groups were having 2+ sBinge/eBinge episodes, respectively, in the past 30 days or since the semester began and using MJ 3 times or less in the past month (no more than 30 occasions of lifetime MJ use). The CSU groups had to meet criteria for sBinge and eBinge outlined previously and have 4+ episodes of MJ use in the past month. The control group had to have no history of MJ or standard/extreme binge use, but alcohol use consisting of 1–2 drinks per occasion was allowed. In addition, all 4 substance use groups had to have limited lifetime use (<15 times) of other substances except nicotine. All subjects passed a breathalyzer test and had negative urine screens for all drugs except for MJ (due to its long half-life). Other exclusion criteria included: history of seizure disorders, head injury, neurologic, metabolic, or cardiovascular disease, cerebrovascular events, or meeting DSM-IV criteria for major psychiatric disorders (including substance use disorder for all binge groups, and MJ use disorder in the two MJ+Binge groups), based on the Mini International Neuropsychiatric Interview (Hergueta et al., 1998).

The final sample included 221 freshmen and sophomores (40 controls, 62 sBinge, 59 eBinge, 35 MJ+sBinge, and 25 MJ+eBinge). All participants were right-handed, and there was no group difference on age, sex, race, ethnicity, or parental occupation/highest education level.

#### 2.2. Procedures

All procedures were approved by the University of Iowa Institutional Review Board. All participants signed informed consent forms, completed a brief medical history screening, web-based self-reported measures, and fMRI scans.

**2.2.1. Substance Use**—Participants reported total days of standard/extreme bingeing, MJ and tobacco use before and during college, which were combined to represent lifetime use. Recent use was calculated by dividing total days of use (current academic year) by the number of months each participant had been in school when they completed the study. Group membership was based on a screening questionnaire developed by our lab. Substance use was assessed again at the study visit, which sometimes occurred several weeks after the screening questionnaire. There were 14 subjects (4 sBinge, 3 eBinge, 2 MJ+sBinge, and 5 MJ+eBinge) who had inconsistent responses between the screen and study visit. Excluding these individuals resulted in largely unchanged group differences in self-reported substance use. Consequently, we report results based on the screening categorization.

**2.2.2. Stop Signal Task**—There were two SST runs, each consisting of 96 Go and 32 Stop trials (Rao et al., 2014). All trials started with a central fixation cross (500 ms) followed by the Go stimulus (left or right arrow). On Go trials, participants were instructed to indicate the arrow's direction. On Stop trials, a pure tone (900 Hz; 500 ms) – the stop signal – was presented after the Go stimulus. Participants were asked to withhold responding when presented with the stop signal. The interval between the Go and the Stop stimuli is the stop signal duration, which changed according to participants' performance (increased/decreased by 50ms for successful/unsuccessful inhibition).

**2.2.3. Monetary Incentive Delay Task**—The MID task was similar to the one used by Knutson and colleague (2003). There were three runs; each had 48 trials (24 gain, 24 loss), 6 trials for each level of gain/loss (\$0.00, \$0.20, \$1.00, and \$5.00). Within a trial, a cue signifying the valence (gain/loss) and level appeared (250 ms), followed by a delay period (2000-2500ms). Participants were then asked to respond to a target as quickly as possible. Afterward, there was another delay, after which participants saw feedback for their performance (1750 ms). Task difficulty was calibrated for each participant based on a practice performance in a mock scanner so that the success rate would be approximately 66%.

**2.2.4. FMRI Acquisition**—MRI scans were conducted on a Siemens Tim Trio 3T MRI scanner (Erlangen, Germany) equipped with a 12-channel phased array head coil. High-resolution T1-weighted MP-RAGE images (TR = 2,530 ms, TE = 2.8 ms, flip angle = 10 degrees, voxel size =  $1.0 \times 1.0 \times 1.0 \text{ mm}$ , series = interleaved) were collected. For the SST runs, a standard AC-PC acquisition was employed with in plane resolution of 2.0mm and the following parameters: TE = 30ms, TR = 2,800ms, Flip Angle =  $80^\circ$ , FOV =  $220 \times 220$ mm, Matrix =  $128 \times 128$ , slice thickness/gap = 4.0/.5mm, BW = 1954 Hz/pixel. For the MID runs, a 30-degree tipped acquisition sequence was used to recover signal in ventral PFC and VS (Deichmann et al., 2003). fMRI scans were acquired with in plane resolution of

3.4mm and the following parameters: TE = 30ms, TR = 2,000ms, Flip Angle = 77°, FOV = 220×220mm, Matrix = 64×64, slice thickness/gap = 3.5/0.875mm, BW = 2004 Hz/pixel.

#### 2.3. FMRI Statistical Analysis

**2.3.1. Preprocessing**—Prior to all analysis, dummy TRs (the first five volumes of each SST run, and the first six volumes of each MID run) were discarded to remove artifacts associated with scanner disequilibrium. Afterward, all preprocessing steps for both tasks were run with fMRIPrep version 1.1.1 (Esteban et al., 2019). The following steps were applied to T1-weighted images: correction for intensity non-uniformity, skull stripping, spatial normalization to the ICBM 152 Nonlinear Asymmetrical template version 2009c using ANTs (Avants et al., 2009), and tissue segmentation using FSL (Smith et al., 2004). For fMRI data, the following steps were taken: slice time correction using AFNI (Cox, 1996), motion correction using FSL, ANTs "fieldmap-less" distortion correction, and corregistration using boundary-based registration.

**2.3.2. Subject Level Analysis**—For both tasks, each run was analyzed separately. After running fMRIPrep, the subject-level analysis was conducted with FSL FEAT with the following steps: spatial smoothing with a Gaussian kernel of 6-mm full width at half maximum, high-pass filtering with .01 Hz cutoff, and regression. For both tasks, nuisance regressors included the six motion regressors. Task regressors (described below) and their first temporal derivatives were also included.

Task regressors of the SST included Correct Go (pressing correct button on Go trials), Correct Stop (withholding response on Stop trials), Incorrect Stop (pressing correct button on Stop trials), Incorrect Go (pressing incorrect button on Go trials), Miss Go (failing to respond on Go trials), and Fail Stop (pressing incorrect button in Stop trials). We focused on the Correct Stop vs. Correct Go contrast.

Task regressors of the MID included hit and miss trials of both gain and loss conditions with varying levels of money at stake, allowing for modeling of reward/loss anticipation. We focused on Gain \$5.00 vs. Gain \$0.00 and Loss \$5.00 vs. Loss \$0.00 contrasts, as previous studies showed that the largest magnitude (\$5.00) is more trait-like (Wu et al., 2014), showed the most robust effect (e.g., Knutson et al., 2003) and might be the most sensitive to group differences.

**2.3.3. Region of Interest (ROI) Analysis**—Group comparisons were done for each *a priori* ROI (Table S1) separately. Only significant F-tests (False Discovery Rate corrected) were followed up with pairwise comparison. For the SST, ROIs were brain areas activated during action cancellation reported in a meta-analysis (Zhang et al., 2017): Bilateral insula, opercular portion of the inferior frontal gyrus (IFG), SMA, pallidum, and supramarginal gyri. For the MID, ROIs included the ventral striatum, mPFC, and insula (Knutson et al., 2001a, 2001b, 2003; Sescousse et al., 2013; Wu et al., 2014). ROI locations were based on the work by Knutson and colleagues (Knutson et al., 2007). 6mm-radius spherical ROIs were created, from which median activation was extracted for each participant using FSL Featquery.

**2.3.4.** Whole-Brain Permutation Analysis—All whole-brain analyses were assessed using Randomise (5000 permutations of the data to build the null distribution). Prior to thresholding with the Threshold-Free Cluster Enhancement method, a gray matter mask was used.

#### 3.1. Substance Use

Table 1 shows recent (days/month) and lifetime (days) substance use data for each group. The following group comparisons were reported for recent substance use using Kruskal-Wallis tests. Only significant Kruskal-Wallis tests were followed up with pairwise Wilcox tests. Controls were excluded for the group comparison on standard/extreme bingeing and MJ use.

There was a significant group difference in standard bingeing ( $\chi^2(3) = 15.12, p = .002$ ), with sBinge showing the lowest frequency (p's < .05). The groups also differed in extreme bingeing ( $\chi^2(3) = 57.33, p < .001$ ), such that sBinge showed the lowest frequency (p's < .01), MJ+eBinge showed the highest (p's < .02), and MJ+sBinge extreme binged less than eBinge (p = .002). Additionally, MJ use also showed a group effect ( $\chi^2(3) = 125.13, p < .001$ ). Given the study criteria, it is not surprising that both MSU groups showed lower MJ use than the two CSU groups (p's < .001); however, it is notable that there was no difference in MJ use between the two MSU groups, or between the two CSU groups (p's < .001). The Controls group showed the lowest use level (p's < .05). Both MSU groups showed lower tobacco use than the two CSU groups (p's < .05), but there was no difference between the MSU groups, or between the CSU groups (p's < .05), but there was no difference between the MSU groups, or between the CSU groups (p's < .05). The matrix of p's < .05). Both MSU groups showed lower tobacco use than the two CSU groups (p's < .05), but there was no difference between the MSU groups, or between the CSU groups (p's < .05). The matrix of th

#### 3.2. Stop Signal Task

**3.2.1. Quality Control**—For behavioral data, exclusionary criteria proposed by Congdon and colleagues (2012) were used, which involved meeting any of the following: Correct Stop < 25% or > 75%; Correct Go < 60%; Incorrect Go > 10%; negative Stop Signal Reaction Time (SSRT) or SSRT < 50 ms. One participant (MJ+sBinge) was excluded based on these criteria. For imaging data, participants with at least one frame-to-frame movement greater than 3mm in any direction were excluded, resulting in the removal of 18 participants (1 Control, 6 sBinge, 6 eBinge, and 5 MJ+sBinge). Analyses were run after excluding these 19 participants. There were no group differences in framewise displacement (FD).

**3.2.2. Behavioral data**—SSRT was calculated using the integration method, as recommended by Verbruggen and colleagues (2013). A one-way ANCOVA did not reveal any Group main effect on the log-transformed SSRT (F(4, 196) = 0.17, p = 0.95, partial  $\eta^2 = 0.003$ ), Percent Correct Stop (F(4, 196) = 0.47, p = 0.76, partial  $\eta^2 = 0.01$ ), or Go RT (F(4, 196) = 1.28, p = 0.28, partial  $\eta^2 = 0.03$ ; Table 2). Exploratory grouping schemes (Controls vs. MSU vs. CSU – grouping regardless of bingeing levels; and Controls vs. sBinge vs. eBinge – grouping regardless of mono- or combined-substance usage) were also run but revealed no significant differences.

**3.2.3. Imaging data**—For each of the 5 groups, one-sample t-tests for the Correct Stop vs. Correct Go contrast showed strong activation in expected regions (IFG, anterior insula, ACC, precuneus, supramarginal; Figure S1). However, voxel-wise 5-group nonparametric analysis of the same contrast revealed no differences. For the ROI analyses, one-way ANCOVAs revealed no significant group differences in any ROIs (Table S2; see Figures 1A and 1B for left and right IFG). Exploratory whole-brain and ROI analyses for additional grouping schemes (Controls vs. MSU vs. CSU; Controls vs. sBinge vs. eBinge) revealed no group differences. Lastly, a whole-brain comparison between Controls vs. all Bingers combined also did not reveal any difference. Additionally, tobacco use was not significantly associated with any of the behavioral or imaging variables.

## 3.3. Monetary Incentive Delay Task

**3.3.1. Quality Control**—The same exclusionary criteria due to excessive motion outlined in the SST section was used and resulted in the exclusion of 6 participants for the MID (3 eBinge, 1 MJ+sBinge, and 2 MJ+eBinge). FD did not show a group difference.

**3.3.2. Behavioral data**—Separate mixed Type (Reward, Loss) x Levels (\$0.00, \$0.20, \$1.00, \$5.00) x Group (Controls, sBinge, eBinge, MJ+sBinge, MJ+sBinge) ANCOVAs were run to detect group differences in RT and accuracy. There was no significant main effect of group, or significant group interaction for RT (all p's > .05, Table 3). For accuracy, there was a significant Type x Group interaction (F(4, 209) = 2,51, p = 0.04, partial  $\eta^2 = 0.05$ ), but there was no significant pairwise group comparison for either Gain or Loss trial types (all p's > .05). There was no other significant group interaction or group main effect for accuracy (all p's > .05).

**3.3.3. Imaging data**—One-sample t-tests (Gain \$5.00 vs. Gain \$0.00) were run separately for each group and revealed activation in expected regions such as insula, dorsal and ventral striatum (Figure S2). Whole brain non-parametric (Gain \$5.00 vs Gain \$0.00 and Loss \$5.00 vs Loss \$0.00) with different grouping schemes (5 groups, Controls vs. MSU vs. CSU, Controls vs. sBinge vs. eBinge, and Controls vs. all Bingers combined) revealed no significant group differences. ROI analyses (5 groups, Controls vs. MSU vs. CSU, Controls vs. eBinge) for these gain/loss contrasts also did not reveal any group differences (see Table S3 for the 5-group analysis). Figures 1C and 1D show percent signal change in left and right VS for Gain \$5.00 vs. Gain \$0.00. As with the SST, tobacco use was not significantly associated with the behavioral or imaging variables.

## 4. Discussion

The current study examined behavioral inhibition (SST) and reward processing (MID) in standard and extreme binge drinking individuals with and without regular MJ co-use. We found no evidence for group differences in behavioral performance or brain activation on either task. Although prior studies have reported brain activation differences in binge drinkers, sample sizes have been relatively small – most consisting of approximately 20 binge and 20 control subjects – and the results have been inconsistent (Cservenka and Brumback, 2017). Using this larger sample, we couldn't replicate the previously reported

findings: the voxel-wise analyses of both tasks did not reveal any difference between 181 binge drinkers and 40 non-bingeing controls. This discrepancy may reflect a bias in reporting positive findings, not only in brain imaging studies (Cservenka and Brumback, 2017) but also in non-imaging neuropsychological studies (Carbia et al., 2018; Lees et al., 2019). Specifically, a quantitative review with 18 non-imaging studies using behavioral inhibition tasks among youth aged 10-24 reported associations between binge drinking and inhibition deficit. However, there were significant concerns with risk of publication bias (significant Egger's test), and with the inconsistency of results (Lees et al., 2019).

Alternatively, this inconsistency in the literature might partly be due to the possibility that bingers from different studies were at different stages of substance misuse, associated with different neural alterations. Researchers have argued that hypoactive frontoparietal responses during inhibition might be a predisposing factor of binge drinking initiation, whose neurotoxic effects can later shift the responses of those regions to hyperactivity (Jones et al., 2018; Padilla et al., 2017; Wetherill et al., 2013a, 2013b; Worhunsky et al., 2016; but see Whelan et al., 2014). Similarly, alterations in reward processing may only be prominent in later stages of substance abuse (Nees et al., 2012; Zilverstand et al., 2018). To our knowledge, there is only one paper comparing short-, medium-, and long-term bingers (Ruan et al., 2019); however, the authors employed resting state rather than task fMRI. Characterizing brain activation in binge drinkers during different stages of abuse will be important for future research.

Although additional work is needed, the current findings suggest that emerging adults without a long binge drinking history may not show any behavioral or neurophysiological differences from non-bingers. It's worth noting that meaningful differences on personality measures of impulsivity and sensation seeking were reported in this sample (O'Leary et al., 2019). Personality traits may be better at discriminating between groups because they assess stable traits, whereas task performance and task-related activation are more state-dependent. This is consistent with a review by Padilla and colleagues (2017) in which increased trait (self-report) and choice impulsivity (choose immediate rather than delayed but larger rewards) showed consistent association with alcohol misuse, whereas the association between behavioral inhibition and alcohol misuse was mixed.

There are limitations that may affect the interpretation of the results. Firstly, all substance use data were self-reported, which may introduce deliberate or unintentional inaccuracies. Also, the sample was a group of relatively healthy young college students, which may limit the generalizability of the findings. Additionally, the study was initially designed to look at the effect of CSU regardless of the bingeing levels. However, we wanted to tease apart the effects of different bingeing levels in MSU and CSU, and thus the CSU group was further categorized into two groups with smaller sample sizes than other groups in the study. In addition, we didn't have a marijuana only group, which is needed to better distinguish the effects of MSU (alcohol alone and MJ alone) and CSU (alcohol combined with MJ). This issue could be addressed in future studies by recruiting marijuana users with limited or no alcohol use. Lastly, we do not know how much of the reported CSU was simultaneous or concurrent. Simultaneous use has been shown to be more harmful than concurrent use

(McCabe et al., 2006; Midanik et al., 2007). Future studies are needed to further test the interaction between simultaneous/concurrent alcohol bingeing and marijuana use.

In this study, we found no group differences in either performance or neural correlates of inhibition and reward. Longitudinal studies can investigate how and when chronic MSU and CSU take their toll on those measures over time. In addition, longitudinal data will also help compare people who have consistent substance use patterns with those who don't. This will be extremely informative as we continue to study the characteristics of individuals with different substance use patterns, which is of great importance in developing treatments that fit individual needs.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Highlights

• Investigated inhibition and reward related brain activation in college students.

- Focused on standard/extreme binge drinkers with and without marijuana use.
- Groups did not differ from one another or in comparison to controls.
- Functional brain differences may emerge after greater use of alcohol/ marijuana.

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#### Figure 1.

Regions of interest activation during the Stop Signal Task and the Monetary Incentive Delay task. Left (A) and right (B) Inferior Frontal Gyrus activation in response to Correct Stop relative to Correct Go. Left (C) and right (D) Ventral Striatum activation in response to Gain \$5.00 relative to No Gain. Red circles represent group means.

## Table 1

## Participant Characteristics

	Controls Mean (SD)	sBinge Mean (SD)	eBinge Mean (SD)	MJ+sBinge Mean (SD)	MJ+eBinge Mean (SD)	$F/\chi^2$	р
Ν	40	62	59	35	25	-	-
Males (% of N)	20 (50%)	33 (54%)	29 (49%)	19 (54%)	11 (44%)	0.85	.93
Age	18.70 (0.61)	18.65 (0.68)	18.78 (0.72)	18.60 (0.60)	18.72 (0.68)	0.51	.73
Recent Use (Days/Month)							
sBinge	0	2.42 (2.55)	3.58 (3.74)	3.83 (2.70)	6.31 (6.67)	15.12*	.002
eBinge	0	0.35 (0.66)	2.04 (2.43)	0.86 (1.17)	4.25 (4.38)	57.33*	<.001
MJ	0	0.33 (0.60)	0.36 (0.61)	8.68 (5.36)	11.67 (9.41)	125.13*	<.001
Tobacco	0.03 (0.19)	1.02 (4.19)	1.03 (3.99)	2.33 (6.66)	2.72 (5.89)	37.98	< .001
Lifetime (Days)							
sBinge	0	17.76 (18.13)	37.00 (40.25)	48.37 (58.59)	71.96 (69.51)	29.05*	<.001
eBinge	0	2.19 (2.65)	16.31 (20.02)	9.17 (14.68)	39.20 (57.31)	68.47*	<.001
MJ	0	3.29 (6.47)	3.22 (4.71)	99.74 (87.86)	113.92 (76.49)	117.3 1*	<.001
Tobacco	0.28 (1.13)	19.90 (81.68)	10.31 (25.01)	33.20 (122.56)	24.76 (37.87)	50.07	< .001

Group differences in substance use were examined with Kruskal-Wallis tests. sBinge: Standard Bingeing, eBinge: Extreme Bingeing, MJ: marijuana.

 $^{*}$  denoted group comparison between the 4 substance using groups only.

#### Table 2

#### Behavioral Performance of the Stop Signal Task

	Controls Mean (SD)	sBinge Mean (SD)	eBinge Mean (SD)	MJ+sBinge Mean (SD)	MJ+eBinge Mean (SD)	F	р
Ν	39	56	53	29	25	-	-
SSRT	203.40 (41.36)	199.85 (43.76)	208.42 (57.62)	200.59 (36.72)	203.42 (35.23)	0.17	0.95
Correct Stop (%)	53.08 (5.91)	51.14 (7.67)	51.12 (8.70)	51.13 (7.69)	52.00 (7.40)	0.47	0.76
Go RT	577.96 (105.76)	577.38 (95.69)	541.30 (90.41)	554.15 (100.38)	546.67 (110.52)	1.28	0.28

Group differences in behavioral performance of the Stop Signal Task were assessed with one-way ANCOVAs with tobacco use as a covariate (details in the Results section). SSRT: Stop Signal Reaction Time (table showed original SSRT, but test statistics are from ANCOVA with the log transformed SSRT), RT: Reaction Time. All reported means are the original means, not the estimated marginal means from the ANCOVA models.

## Table 3

Behavioral Performance of the Monetary Incentive Delay Task

	Controls Mean (SD)	sBinge Mean (SD)	eBinge Mean (SD)	MJ+sBinge Mean (SD)	MJ+eBinge Mean (SD)	F	р
Ν	40	62	56	34	23	-	-
Gain RT	209.31 (16.34)	204.41 (13.85)	205.71 (15.68)	208.23 (13.86)	206.08 (14.31)	0.60	0.67
Loss RT	210.86 (16.65)	208.07 (16.02)	208.02 (15.68)	210.69 (14.24)	206.73 (15.96)	0.60	0.67
Gain Accuracy (%)	78.37 (6.62)	78.92 (7.19)	80.16 (6.70)	79.25 (6.29)	78.29 (6.54)	0.06	.993
Loss Accuracy (%)	78.02 (7.19)	77.53 (9.28)	76.56 (9.20)	78.23 (7.08)	79.35 (6.17)	0.06	.993

Group differences in behavioral performance of the Monetary Incentive Delay task were assessed with mixed ANCOVAs with tobacco use as a covariate (details in the Results section). All reported means are the original means, not the estimated marginal means from the ANCOVA models.