J Gambl Stud. 2016 Nov 8.

Sub-clinical Alcohol Consumption and Gambling Disorder.

Harries MD, Redden SA, Leppink EW, Chamberlain SR, Grant JE.

Authors final version of submitted manuscript.

Abstract

While it is well established that gambling disorder is associated with alcohol use disorder, less is known regarding whether sub-clinical alcohol consumption increases gambling behavior. This study examined the effects of varying levels of alcohol consumption on clinical and cognitive measures. The sample consisted of 572 non-treatment seeking gamblers age 18-29 who were divided into three groups: non-current drinkers, current drinkers who did not qualify for an alcohol use disorder, and those with an alcohol use disorder (AUD). All subjects were assessed on gambling pathology, severity and impulsivity using the Structured Clinical Interview for Gambling Disorder, Yale Brown Obsessive Compulsive Scale for Pathologic Gambling and the Barratt Impulsive Scale-11 and select cognitive tests. In all of the clinical measures, controlling for age, gender and education, the AUD group was significantly more likely than the non-current and current drinkers to be a pathologic gambler and to be impulsive, compulsive and depressed. On cognitive tasks, controlling for age, gender and education, the AUD group had significantly worse strategy use on a spatial working memory task than both other groups. This study suggests that the relationship between alcohol and gambling may only exist when pathology in both alcohol consumption and gambling behavior is present. Examining this relationship with alcohol consumption as a continuous variable would provide additional insight into the potential effects alcohol consumption has on gambling behavior.

1. Introduction

Gambling is a common pastime among adults, with approximately 86% of adults having gambled at some point in their lifetimes and 63% having gambled at some point in the last year (National Opinion Research Center 1999). Gambling usually starts in adolescence, with approximately 60% of 14-15 year olds and 72% of 20 to 21 year olds having gambled. In fact, gambling behavior appears to peak between the ages of 22-30 years (Welte et al. 2008). Although the vast majority of these young people gamble without problems, some progress to a pathological form of the behavior. Understanding the progression from recreational gambling to gambling disorder may allow for earlier interventions.

Young people who tend to develop problems with gambling behavior are frequently male, younger in age, black, and of lower socioeconomic status (Barnes et al. 2015; Welte et al. 2001; Petry et al. 2005; French et al. 2008). Impulsivity is also a risk factor for the development of problematic gambling behavior (Hodgins et al. 2015). A recent study examining clinical characteristics of non-treatment young adult gamblers found that those with higher impulsivity scores on the Barratt Impulsiveness Scale 11 tended to have less formal education, more symptoms of anxiety and depression, and exhibited more severe gambling symptoms (Leppink et al. 2016).

What role do other problematic behaviors (substance use and mental illness) play in young adult gambling behavior? Studies have found that alcohol, tobacco and marijuana use are all significant predictors (OR = 3.22, 1.8 and 2.35 respectively) of overall gambling (Barnes et al. 2015). In addition, Moghaddam and colleagues found that a range of unhealthy behaviors, i.e. stealing, homelessness, fighting, legal issues have also been associated with increased gambling severity (2015). In addition, problem gamblers report increased levels of nicotine and alcohol use, as well as psychological distress, in comparison to moderate-risk gamblers (Shen 2015). The risk of developing severe gambling behavior appears to be 1.7 times more likely for people with mood or anxiety disorders and 2.9 times more likely for those with alcohol or other substance dependence (el-Guably et al. 2006).

With 67.6% of adults in the U.S. consuming alcohol over the past year, questions regarding the influence of alcohol consumption on gambling behavior are particularly important (Barnes et al. 2015). Preclinical and clinical research suggests that alcohol may impair decision-making in both the short and long term, which by implication could contribute to increased gambling (Spoelder et al. 2015; White et al. 2011; Filmore 2007). White et al. found impulsive behavior to increase over a year in heavy drinking adolescents who were moderately impulsive at the start of the study (2011). In fact, it is well established that pathological gamblers often have concurrent alcohol use disorders, sometimes at rates as high as 73.2% (Lorains et al. 2011). Few studies, however, have examined how varying degrees of alcohol consumption may affect clinical and cognitive characteristics of gamblers at all levels of severity. Cronce and colleagues showed alcohol consumption is associated with larger average bets while gambling amongst recreational, non-pathologic gamblers (2010). In contrast, another study showed non-problem gamblers who consumed any alcohol were less likely to participate in electronic gambling compared with those who did not drink alcohol (Markham et al. 2012).

To our knowledge, only a few studies have examined the relationship between sub-clinical alcohol use and its relationship with gambling behavior (Welte et al. 2001; Harvanko et al., 2012; Pino Gutierrez et al.; 2016). This study seeks to fill this space in the literature by examining the relationship between levels of alcohol consumption (non-drinkers, recreational drinkers, and those with alcohol use disorders [AUD]), and impulsivity, comorbid conditions and cognition in young adults with varying degrees of gambling participation. We hypothesize that current drinkers would trend towards the AUD group on various clinical symptoms, represented by increased scores on the Structured Clinical Interview for Gambling Disorder (SCI-GD), Yale Brown Obsessive Scale modified for Pathological Gambling (PG-YBOCS), and the Barratt Impulsiveness Scale -11 (BIS-11), as well as higher scores on anxiety and depression related scales. We also hypothesize that current drinkers will trend towards the AUD group on various cognitive tasks, represented by increased errors on the Intra-Extra Dimensional Set Shift task (IED), and decreased scores on the Stop Signal Task (SST), Cambridge Gambling Task (CGT) and Spatial Working Memory (SWM) task.

2. Materials and methods

2.1 Participants

Participants consisted of non-treatment-seeking young adults aged 18-29 years who were recruited as part of an ongoing longitudinal study of impulsive behaviors. To be included, subjects must have gambled at least five times in the past 12 months. Subjects were excluded if they were unable to give informed consent or were unable to understand/undertake the study procedures. Recruitment consisted of media announcements in two large metropolitan areas. Each subject received a $50 gift card to either Amazon or Target as compensation for his or her participation.

Study procedures were carried out in accordance with the most recent version of the Declaration of Helsinki. The Institutional Review Board of the University of Chicago and the University of Minnesota approved the study and the informed consent procedures. After all study procedures were explained and subjects had the opportunity to ask questions, subjects provided voluntary written informed consent.

2.2 Assessments

2.2.1 Categorical Alcohol Use Definitions

Subjects were divided into three groups based on their alcohol consumption. All participants were asked if they were current drinkers and were also asked the alcohol questions from the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al. 1998) to see who met the diagnostic criteria for alcohol dependence or alcohol abuse, which were then combined into the category of alcohol use disorder. Thus we categorized all participants into one of the following three groups: non-current alcohol drinkers, current alcohol drinkers but do not meet criteria for an alcohol use disorder, and alcohol use disorder (AUD).

2.2.2 Demographic and Clinical Variables

Subjects answered a variety of demographic (sex, age, education level, race, employment status) and clinical questions.

Gambling Diagnosis. Research personnel administered the Structured Clinical Interview for Gambling Disorder (SCI-GD) to each participant. The SCI-GD is a nine-item scale used to assess symptoms of Gambling Disorder. A score of 0 meant 'low risk,' a score of 1-3 signified 'at risk,' and a score of 4 met the diagnostic criteria for a gambling disorder (Grant et al. 2004).

Gambling Severity. Gambling severity was assessed using the Yale Brown Obsessive Compulsive Scale modified for Pathological Gambling (PG-YBOCS) (Pallanti et al. 2005). The PG-YBOCS is a 10-item clinician-administered scale that examines gambling urges/thoughts and behavior over the past seven days. Total scores between 0-7 represented subclinical severity, between 8-15 represented mild severity, between 16-23 represented moderate severity, between 24-31 represented severe severity and between 32-40 represented extreme severity.

Personality-Related Impulsiveness. In order to determine impulsiveness levels amongst participants, the Barrett Impulsiveness Scale-11 was used. This scale is a 30 question, self-administered survey identifying impulsive behavior in three specific areas: attention (ability to concentrate), non-motor (ability to think before acting with motor movements) and non-planning (ability to act with the future in mind) (Patton et al., 1995).

Quality of Life Inventory. Quality of life was assessed using the Quality of Life Inventory, a self-administered survey that examines how important and satisfied the subject is with various areas of their life (i.e. health, money, work, etc.) (Frisch et al. 2013).

Depression and Anxiety Symptoms. Current major depressive disorder (MDD) was determined using the MINI. Symptoms of anxiety and depression were examined with the Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Depression Rating Scale (HAM-D) (Hamilton1959; Hamilton 1960).

2.2.3 Cognitive Variables

Cognitive testing was undertaken using computerized paradigms from the Cambridge Neuropsychological Test Automated Battery (CANTAB). Participants completed cognitive testing in a quiet room, using a touch-screen computer. Based on the existing literature we focused on domains of decision-making, set-shifting, working memory, and response inhibition, which have been found to be impaired in people with gambling disorder (e.g. Clark 2010; van Holst et al. 2010; Grant et al. 2011; Odlaug et al. 2011).

Intra-Extra Dimensional Set Shift (IED) task. The IED is a computerized version of the Wisconsin Card Sorting task, asking participants to learn and follow an underlying rule given by the computer. After the participant received and understood the feedback from the computer, and answered six tasks correctly, the task changed and the subject was asked to re-learn and apply the new rule until they were able to achieve six correct answers in a row again. The outcome examined was the total number of adjusted errors (Owen et al. 1991).

Stop Signal Task (SST). Participants are presented with an arrow pointing left or right and are asked to press the matching right or left button on the button box. However, at random, a stop signal tone would sound after the presentation of the arrow on the screen. When the stop signal sounded the subject was supposed to refrain from pressing the matching right or left button. This task measures the amount of time it takes the brain to inhibit the already triggered decision to press the matching button. A longer time corresponds to increased impulsivity. The median reaction times for non-stop signal trials were recorded as well to examine whether the possible presence of a stop signal decreases motor response. (Aron et al. 2007; Logan et al. 1984)

Cambridge Gambling Task (CGT). Subjects were told a token existed behind one of ten available boxes. At random, the ten boxes would be colored either red or blue in different ratios. The subject chose which color box they believed the token was behind. Starting with an imaginary 100 points, they were given an opportunity to make a bet on either red or blue. At first, possible bets started at lower values and then increased. Then, the order of presentation for possible bets switched to go from higher bets to lower bets, presented in a decreasing manner. The outcomes measured in this task were the overall proportion bet, risk adjustment, and quality of decision making, i.e. did the subject make bets following the probability resulting from the ratio of red to blue squares? (Rogers et al. 1999).

Spatial Working Memory Tasks (SWM). The SWM measures strategy and working memory. Subjects attempt to find hidden tokens underneath boxes on a computer screen without re-visiting boxes that already have been discovered to hide tokens. This task is given a strategy score which examined the efficacy of the subject's choices when returning to boxes, and a total errors score which tallies the times the subject returns to boxes that already were discovered to hide tokens (Owen et al. 1990).

2.3 Data Analysis

Participants were categorized based on varying levels of alcohol consumption and compared across the three groups on clinical and cognitive measures. Demographic variables were examined using a chi-squared test, with post-hoc analysis to determine between group differences. Statistical significance in post-hoc analysis was determined using Bonferonni correction. Differences between drinking groups were examined using a multivariate analysis of variance (MANOVA), with age, education and gender as covariates to examine differences between drinking groups while controlling for these variables. Cognitive differences between drinking groups were examined using a separate MANOVA with age, education and gender as covariates, which included key outcome measures from IED, SST, CGT, and SWM tasks. We report effect size estimates using Cohen's d. Statistical significance was defined as $p<0.05$, two-tailed, uncorrected. Statistical tests used IBM SPSS software version 22.

3. Results

We examined whether there was any effect of sex, age, education, race, and employment status on the drinking groups (Table 1). The first group consisted of subjects who were not current drinkers (n=110). The second group consisted of subjects who consumed alcohol currently at some frequency, but were not diagnosed with an AUD (n=335). The third group included subjects who were diagnosed with an AUD (n=127). Significant differences existed between drinking groups in sex, with males being more likely to be part of both the current drinker and AUD groups (p=0.008). Non-current drinkers were significantly more likely to be younger in age ($p<0.001$) a student (p=0.001) and in college (p=0.001).

Controlling for age, gender and education as covariates in a multivariate analysis of variance (MANOVA), significant differences existed between drinking groups for gambling disorder (SCI-GD scores) ($p \leq 0.001$), attention impulsiveness ($p<0.001$), motor impulsiveness ($p \leq 0.001$), non-planning impulsiveness ($p \leq 0.001$), and the total and subscale scores of the PG-YBOCS ($p \leq 0.001$) (Figure 1). Statistically significant differences also existed between groups for depressive symptoms (HAM-D; p=0.005). Within this MANOVA (Table 2), we also examined pairwise comparisons between the three drinking groups. No statistical differences existed between the non-current drinkers and current drinkers groups. The AUD group was significantly more likely to be diagnosed with pathological gambling, to be impulsive, to be compulsive and to be depressed then both the non-current drinkers and current drinkers.

We examined cognition between drinking groups using a separate MANOVA, which also included age, gender and education as covariates (Table 3). Significant differences existed between drinking groups for quality of decision-making on the CGT (p=0.039) and the strategy score of the SWM (p=0.003). A significant difference existed between the non-current drinkers and current drinkers for the CGT quality of decision-making task, with current drinkers scoring higher. No significant difference existed on the same task between the other pairwise comparisons. Significant differences also existed between the non-current drinkers and AUD groups, and current drinkers and the AUD groups for the strategy score of the SWM, with AUD patients possessing poorer strategy scores. No significant differences existed between groups, or in the pairwise comparisons, on the IED or SST cognitive tasks.

Table 1
Demographic variables in young adults based on drinking group.

	Non-current drinkers (n=110)	Current drinkers (n=335)	AUD (n=127)	Statistic	p-value
Gender, (n, %, adjusted residual)				χ^2=9.57	**0.008****
Female	36 (32.7%) [-0.4]	**130 (38.8%) [2.7]&**	**30 (23.6%) [-2.9]&**		
Male	74 (67.3%) [0.4]	**205 (61.2%) [-2.7]&**	**97 (76.4%) [2.9]&**		
Age, years (mean, SD)	20.43 (3.24)	22.53 (3.44)	23.15 (3.73)	F=20.53	**<0.001*****
Education (n, %, adjusted residual)				χ^2=26.10	**0.001*****
Less than high school	5 (4.5%) [0.5]	9 (2.7%) [-1.5]	7 (5.5%) [1.3]		
High school grad/GED	8 (7.3%) [-0.1]	24 (7.2%) [-0.4]	11 (8.7%) [0.6]		
Some College	**87 (79.1%) [4.0]&**	197 (58.8%) [-2.1]	73 (57.5%) [-1.3]		
College grad	**5 (4.5%) [-4.0]&**	69 (20.6%) [2.2]	27 (21.3%) [1.2]		
Post-Graduate	5 (4.5%) [-1.7]	36 (10.7%) [2.0]	9 (7.1%) [-0.7]		
Race (n, %, adjusted residual)				χ^2=25.99	**0.011***
Caucasian	82 (75.2%) [0.8]^	250 (74.9%) [1.7]#	79 (62.2%) [-2.8]		
African American	13 (11.9%) [-0.9]^	49 (14.7%) [-0.1]#	22 (17.3%) [0.9]		
Latino/Hispanic	0 (0%) [-2.2]^	10 (3.0%) [-0.5]#	9 (1.6%) [2.7]		
Asian	11 (10.1%) [1.9]^	13 (3.9%) [-2.7]#	11 (1.9%) [1.3]		
Native American	2 (1.8%) [0.9]^	1 (0.2%) [-2.1]#	3 (0.5%) [1.6]		
Middle Eastern	0 (0%) [-0.5]^	1 (0.2%) [0.8]#	0 (0%) [-0.5]		
Mixed	1 (0.9%) [-1.2]^	10 (1.8%) [1.0]#	3 (2.4%) [-0.1]		
Employment status (n, %, adjusted residual)				χ^2=30.94	**0.001*****
Employed – full time	11 (10%) [-2.9]	76 (22.8%) [2.0]+	27 (21.3%) [0.4]		
Employed – part time	9 (8.2%) [-1.1]	37 (11.1%) [0.2]+	17 (13.4%) [0.9]		
Student	**55 (50%) [3.9]&**	102 (30.6%) [-2.3]+	39 (30.7%) [-1.0]		
Unemployed	5 (4.5%) [-2.7]	41 (12.3%) [0.2]+	23 (18.1%) [2.4]		
Retired	0 (0%) [.0.5]	1 (0.3%) [0.8]+	0 (0%) [-0.5]		
Student + employed	30 (27.3%) [1.4]	76 (22.8%) [0.3]+	21 (16.5%) [-1.8]		

*=p<0.05, **p<0.01, ***p<0.001, &p<0.05 with Bonferroni correction [i.e. there were 6 pairwise comparisons in the gender category so a statistically significant value was determined by dividing 0.05/6=0.00833 to give a necessary p value<0.0083] , ^=109, #=334, +=333

Table 2
Clinical variables in young adults based on drinking group with age, gender and education as covariates.

	Means (SD)			Statistic (F)	p-values				Effect size (Cohen's D)		
	Non-current drinkers (n=55)	Current drinkers (n=183)	AUD (n=68)		Between Subjects	Non-current vs. current drinkers	Non-current drinkers vs. AUD	Current drinkers vs. AUD	Non-current vs. current drinkers	Non-current drinkers vs. AUD	Current drinkers vs. AUD
SCI-GD	0.87 (1.59)	1.24 (2.06)	2.68 (2.74)	8.76	**<0.001*** **	0.90	**0.002** **	**<0.001*** **	-	0.81	0.59
PG-YBOCS											
Urge	2.20 (2.61)	2.12 (3.08)	4.66 (4.73)	9.99	**<0.001*** **	0.24	**0.018* **	**<0.001*** **	-	0.64	0.64
Behavior	2.31 (2.92)	2.37 (3.25)	4.94 (4.62)	10.44	**<0.001*** **	0.43	**0.006** **	**<0.001*** **	-	0.68	0.64
Total	4.51 (5.33)	4.48 (6.13)	9.60 (8.96)	11.06	**<0.001*** **	0.31	**0.008** **	**<0.001*** **	-	0.69	0.67
BIS-11											
Attention	16.40 (3.78)	16.48 (3.95)	18.34 (4.51)	7.36	**0.001*** **	0.46	**0.001*** **	**<0.001*** **	-	0.47	0.44
Motor	22.31 (4.22)	23.09 (4.39)	26.78 (5.15)	13.75	**<0.001*** **	0.65	**<0.001*** **	**<0.001*** **	-	0.95	0.77
Non-planning	22.47 (5.19)	23.29 (5.24)	26.81 (5.15)	11.08	**<0.001*** **	0.53	**<0.001*** **	**<0.001*** **	-	0.84	0.68
HAM-A	2.60 (3.30)	4.21 (5.46)	5.88 (5.75)	2.79	0.063	0.34	**0.026* **	0.056	-	0.30	-
HAM-D	3.22 (4.19)	3.95 (5.23)	6.78 (7.31)	5.32	**0.005** **	0.85	**0.024* **	**0.001*** **	-	0.60	0.46
Current MDD	0.16 (0.37)	0.23 (0.42)	0.40 (0.49)	2.99	0.052	0.75	**0.046* **	**0.022* **	-	0.55	0.37
QOLI	47.91 (12.11)	46.43 (13.53)	42.19 (11.32)	1.79	0.17	0.83	0.22	0.06	-	-	-

MANOVA p<0.0001, F=2.714, *=p<0.05, **p<0.01, ***p≤0.001
SCI-GD = Structured Clinical Interview for Gambling Disorder, BIS-11 = Barratt Impulsiveness Scale – 11, PG-YBOCS = Yale Brown Obsessive Compulsive Scale for Pathologic Gambling, HAM-A = Hamilton Anxiety Scale, HAM-D = Hamilton Depression Scale, MDD = Major Depressive Disorder, QOLI = Quality of Life Index

Fig. 1 Gambling pathology (SCI-GD, max score=5), gambling severity (PG-YBOCS, max score=40), and impulsivity (BIS-11, max score=30) compared across drinking groups within MANOVA examining clinical variables. Age, gender and education were included as covariates. All measures were statistically significant ($p \leq 0.001$) in the between subjects effect. AUD = Alcohol Use Disorder.

Table 3
Cognitive assessments of young adults based on drinking group with age, gender and education as covariates.

	Means (SD)			Statistic (F)	p-values				Effect size (Cohen's D)		
	Non-current drinkers (n=109)	Current drinkers (n=333)	AUD (n=126)		Between Subjects	Non-current vs. current drinkers	Non-current drinkers vs. AUD	Current drinkers vs. AUD	Non-current vs. current drinkers	Non-current drinkers vs. AUD	Current drinkers vs. AUD
IED total errors adjusted	25.68 (20.34)	24.40 (22.96)	25.16 (23.54)	0.30	0.74	0.45	0.73	0.71	-	-	-
SST											
Median correct	443.84 (143.24)	482.51 (173.83)	495.06 (180.28)	0.78	0.46	0.26	0.26	0.83	-	-	-
SSRT	175.45 (54.44)	180.92 (65.60)	189.70 (67.49)	0.99	0.37	0.52	0.17	0.29	-	-	-
CGT											
Overall proportion bet	0.51 (0.14)	0.54 (0.14)	0.57 (0.13)	2.71	0.068	0.071	**0.023***	0.33	-	0.44	-
Quality of decision	0.94 (0.12)	0.96 (0.73)	0.93 (0.09)	3.27	**0.039***	**0.024***	0.572	0.090	0.04	-	-
Risk adjustment	1.76 (1.31)	1.56 (1.19)	1.55 (1.12)	1.89	0.15	0.59	0.077	0.094	-	-	-
SWM											
Strategy	29.00 (6.38)	29.56 (6.18)	31.63 (5.87)	5.77	**0.003****	0.98	**0.010****	**0.001*****	-	0.43	0.34
Total Errors	17.79 (20.46)	17.70 (17.29)	20.60 (17.38)	1.31	0.27	0.21	0.98	0.19	-	-	-

MANOVA p=0.021, F=1.852, *=p<0.05, ** p≤0.01, *** p≤0.001
IED = Intra Extra-Dimensional Set Shift Task, SST = Stop Signal Task, CGT = Cambridge Gambling Task, SWM = Spatial Working Memory Task

4. Discussion

This study found that there was a significant relationship between drinking level and gambling, both in number of gambling diagnostic criteria (measured by the SCI-GD) and gambling symptom severity (measured by the PG-YBOCS). This adds to the existing literature previously published by Harvanko et al., which also examined the effects of drinking groups on cognitive and impulsive behavior. However, this study had a much larger sample size (572 vs. 155) and also examined gambling pathology and severity via the SCI-GD and PG-YBOCS, which were not looked at in the previous study (2012). The pairwise comparisons further show that these associations were only significant at the level of an AUD. Although current drinkers showed no statistical difference from non-current drinkers, the AUD group showed significant differences compared to both groups in terms of diagnostic criteria, severity of gambling, as well as impulsivity. Our findings suggest that only at the level of alcohol use pathology (i.e. AUD) did alcohol have a significant effect on gambling behavior. Support for our findings can be found in previous research (White et al. 2011; Markham et al. 2012). Thus, although studies have shown shared genetic contributions, as well as shared treatment strategies, between alcohol consumption and problem gambling (Slutske et al; 2000, Shah et al; 2005, Grant et al. 2006; Tamminga et al. 2006), our findings suggest that the relationship between gambling and alcohol may not pertain to sub-clinical gambling and alcohol use. Our findings also indicate that the transition from sub-clinical to pathologic gambling and AUD may reflect a change in neurobiology that is distinct from the biology associated with occasional gambling or alcohol consumption. This finding is supported by Cronce and colleagues who found alcohol consumption in real time resulted in larger average bets, but showed no persistence over time (2010). It is important to recognize that alternative explanations of our findings may exist. While unlikely due to the high significance of the pairwise comparisons, it is possible that drinkers are in fact at risk for developing clinical traits symptomatic of pathologic gamblers, but the relationship between alcohol consumption and gambling severity only presents in a continuous, increasing fashion. It is also possible that our current drinkers group included more drinkers who consumed alcohol very rarely as opposed to heavy, yet non-dependent or abusive drinkers.

On the cognitive tests, there was no significant effect of group except for on the Spatial Working Memory (SWM) strategy scores, and quality of decision-making on the Cambridge Gamble Task (CGT). AUD was associated with inferior strategy use on SWM compared to both other groups (higher strategy scores indicate worse use of strategy); while the AUD group also made numerically more errors on the task, the main effect of group on errors was not significant, suggesting that the impact of this sub-optimal strategy use on the task in AUD was relatively subtle. This finding correlates with a previous study that found heavy drinking, and not moderate drinking, to increase brain shrinkage, particularly in the frontal regions (Kubota 2001). The main effect of group on quality of decision-making on CGT was due to significantly better decision-making in the current alcohol use group versus the non-alcohol use group, a finding opposite to the expected direction, perhaps reflecting a false positive. In this regard, it is noteworthy that the standard deviation on quality of decision-making was unusually high in the alcohol use group, and so findings may also have been driven by chance extreme performance in some individuals. Contrary to our expectation, groups did not differ significantly in terms of set-shifting or stop-signal performance. The SWM findings raise the question, does behavior change cognition or does a certain level of cognition predispose an individual to express a specific cognitive approach to a task?

There were several limitations to this analysis. First, the current drinkers group potentially included subjects who drink alcohol rarely, yet still qualify themselves as active drinkers, to subjects who drink heavily on a consistent basis. There is inherently a large variation in this group, while the other two groups have narrow inclusion criteria. Additionally, when asking subjects if they drink or do not drink, we assumed all subjects interpreted the question similarly; an answer of yes meant the subject currently was consuming alcohol at some type of regular frequency, no matter how high or low. Similarly, an answer of no meant the subject currently was not consuming alcohol with any frequency. Including this question, many of the scales used in this study are self-reported measures leading one to potentially question the accuracy of various measures. This includes the MINI, which is how AUD was determined. However, the literature suggests that self-reported alcohol consumption measures are often reliable (Del Boca et al., 2003). Another limitation is that our analyses co-varied for potential confounding variables such as age; statistically significant findings are thus likely to be robust against these confounds, but it remains possible that a lack of group effect could reflect loss of power due to correcting for these measures statistically, rather than a true negative effect. Additionally, there was a statistically significant difference in age between groups. This was most likely driven by the non-current drinkers who were mostly under 21 years of age; it may have confounded the statistically significant finding between the non-current drinkers and each of the other two groups. It was also observed that the robust finding in clinical symptomology between groups in this study did not correlate with the cognitive differences between groups. Finally, while the results of this study seem to indicate that current, sub-clinical alcohol consumption does not predispose an individual to becoming a pathologic gambler; this study was unable to properly delineate the temporality of alcohol consumption and gambling.

Taken together, the clinical and cognitive findings seem to suggest that there is a distinct difference between subjects with AUD and subjects who consume alcohol in non-dependent or non-abusive levels. Therefore, alcohol consumption by itself may not be a good indicator of future pathological gambling. Additional studies are needed that examine other aspects of the relationship between alcohol and gambling, particularly to better understand the linear relationship between alcohol consumption and gambling disorder, as well as the directionality of any causal relationship between alcohol consumption and gambling behavior.

5. References

Aron AR. (2007). The neural basis of inhibition in cognitive control. *Neuroscientist*. 13(3):214-28.

Barnes GM, Welte JW, Tidwell M, Hoffman JH. (2015) Gambling and substance use: Co-occurrence among adults in a recent general population study in the United States. *Int Gambl Stud*. 15(1):55-71.

Clark L. (2010). Decision-making during gambling: an integration of cognitive and psychobiological approaches. *Philos Trans R Soc Lond B Biol Sci.* 365(1538):319-30.

Cronce JM, Corbin WR. (2010). Effects of alcohol and initial gambling outcomes on within-session gambling behavior. Exp Clin *Psycopharmaco*. 18(2):145-157.

Del Boca FK, Darkes J. (2003). The validity of self-reports of alcohol consumption: state of the science and challenges for research. *Addiction.* 98:21-12.

El-Guebaly N, Patten S, Currie S, Williams J, Beck C, Maxwell C, et al. (2006). Epidemiological associations between gambling behavior, substance use & mood and anxiety disorders. *J Gambl Stud.* 22(3):275–287.

Fillmore MT. (2007). Acute alcohol-induced impairment of cognitive functions: past and present findings. *Int J Disabil Hum Dev*. 6:115–125.

French MT, Maclean JC, Ettner SL. (2008). Drinkers and bettors: Investigating the complementarity of alcohol consumption and problem gambling. *Drug Alcohol Depend*. 96:155–164.

Frisch, MB. (2013). Evidence-based well-being/positive psychology assessment and intervention with quality of life therapy and coaching and the quality of life inventory (QOLI). *Soc Indic Res.* 114:193-227.

Grant JE, Potenza MN, Hollander E, Cunningham-Williams R, Nurminen T, Smits G, et al. (2006). Multicenter investigation of the opioid antagonist nalmefene in the treatment of pathological gambling. *Am J Psychiatry.* 163(2):303–312.

Grant JE, Steinberg MA, Kim SW, Rounsaville BJ, Potenza MN. (2004). Preliminary validity reliability testing of a structured clinical interview for pathological gambling. *Psychiatric Res*. 128(1):79-88.

Grant JE, Chamberlain SR, Schreiber LR, Odlaug BL, Kim SW. (2011). Selective decision-making in at-risk gamblers. *Psychiatry Res.* 189(1):115-20.

Hamilton, M. (1959). The assessment of anxiety states by rating. *Brit J Med Psycho*. 32:50–55.

Hamilton, M. (1960). A rating scale for depression. J Neurol Neurosurg *Psychiatry*. 23:56–62.

Harvanko AM, Odlaug BL, Schreiber LR, Grant JE. (2012). Cognitive task performance and frequency of alcohol usage in young adults. *J Addict Med*. 6(2):106-11.

Hodgins DC, Holub A. (2015). Components of impulsivity in gambling disorder. *Int J Ment Health Addict*. 13(6):699-711.

Kubota M, Nakazaki S, Hirai S, Saeki N, Yamaura A, Kusaka T. Alcohol consumption and frontal lobe shrinkage: study of 1432 non-alcoholic subjects. J Neurol Neurosurg Psychiatry 2001; 71: 104–6.

Leppink EW, Redden SA, Grant JE. (2016). Impulsivity and gambling: a complex clinical association across three measures. *Am J Addict.* 25:138-144.

Logan GD, Cowan WB. (1984). On the ability to inhibit thought and action: a theory of an act of control. *Psychol Rev.* 91:295–327

Lorains F, Cowlishaw S, Thomas S. (2011). Prevalence of comorbid disorders in problem and pathological gambling: systematic review and meta-analysis of population surveys. *Addiction.* 106:490-498.

Markham F, Young M, Doran B. (2012). The relationship between alcohol consumption and gambling behavior during a single visit to a gambling venue. *Drug Alcohol Rev*. 31:770-777.

Moghaddam JF, Gihyun Y, Camposa MD, Fonga TW. (2015). Social and behavioral problems among five gambling severity groups. *Psychiatry Res*. 230:143-149.

National Opinion Research Center. (1999). Gambling Impact and Behavior Study, Chicago, IL: National Opinion Research Center.

Odlaug BL, Chamberlain SR, Kim SW, Schreiber LR, Grant JE. (2011). A neurocognitive comparison of cognitive flexibility and response inhibition in gamblers with varying degrees of clinical severity. *Psychol Med*. 41(10):2111-9.

Owen AM, Downes JJ, Sahakian BJ, Polkey CE, Robbins TW. (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia 28:1021e34.*

Owen AM, Roberts AC, Polkey CE, Sahakian BJ, Robbins TW. (1991). Extra-dimensional versus intra-dimensional set shifting performance following frontal lobe excisions, temporal lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia*. 29(10):993-1006.

Pallanti S, DeCaria SM, Grant JE, Urpe M, Hollander E. (2005). Reliability and validity of the pathological gambling adaptation of the Yale-Brown Obsessive-Compulsive Scale (PG-YBOCS). *J Gambl Stud.* 21(4):431-443.

Patton JH, Stanford MS, Barratt ES. (1995). Factor structure of the Barratt Impulsiveness Scale. *J Clin Psychol.* 51:768-74.

Petry N, Stinson F, Grant B. (2005). Comorbidity of DSM-IV pathological gambling and other psychiatric disorders: Results from the national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry.* 66(5):564–574

Pino-Gutierrez A, Fernandez-Aranda F, Granero R, Tarrega S, Valdeperez A, Aguera Z, et al. (2016). Impact of alcohol consumption on clinical aspects of gambling disorder. *Int J Ment Health Nurs*.

Rogers RD, Owen AM, Middleton HC, Williams EJ, Pickard JD, Sahakian BJ, Robbins TW. (1999). Choosing between small, likely rewards and large, unlikely rewards activates inferior and orbital prefrontal cortex. *J. Neuroci.* 19:9029-9038.

Shah KR, Eisen SA, Xian H, Potenza MN. (2005). Genetic studies of pathological gambling: a review of methodology and analyses of data from the Vietnam era twin registry. *J Gambl Stud*. 21(2):179–203

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry*. 20:22-23;34-57.

Shen Y, Kairouz S, Nadeau L, Robillard C. (2015). Comparing problem gamblers with moderate-risk gamblers in a sample of university students. *J Behav Addict.* 4(2):53-59.

Slutske WS, Eisen S, True WR, Lyons MJ, Goldberg J, Tsuang M. (2000). Common genetic vulnerability for pathological gambling and alcohol dependence in men. *Arch Gen Psychiatry.* 57(7):666–673.

Spoelder M, Lesscher HM, Hesseling P, Baars AM, Lozeman-van t Klooster JG, Mijnsbergen R, et al. (2015). Altered performance in a rat gambling task after acute and repeated alcohol exposure. *Psychopharmacology.* 232:3649-3662.

Tamminga CA, Nestler EJ. (2016). Pathological gambling: focusing on the addiction, not the activity. *Am J Psychiatry*. 163(2):180–181.

van Holst RJ, van den Brink W, Veltman DJ, Goudriaan AE. (2010). Brain imaging studies in pathological gambling. *Curr Psychiatry Rep*. 12(5):418-25.

Welte J, Barnes G, Wieczorek W, Tidwell M, Parker J. (2001). Alcohol and gambling pathology among U.S. adults: Prevalence, demographic patterns and comorbidity. *J Stud Alcohol Drugs*. 62(5):706–712.

Welte JW, Barnes GM, Tidwell MC, Joffman JH. (2008). The prevalence of problem gambling among U.S. adolescents and young adults: results from a national survey. *J Gambl Stud.* 24(2):119-133.

White HR, Marmorstein NR, Crews FT, Bates ME, Mun EY, Loeber R. (2011). Associations between heavy drinking and changes in impulsive behavior among adolescent males. *Alcohol Clin Exp Res*. 35(2):295-303.