

UNCORRECTED DRAFT**Impact of ADHD symptoms on Clinical and Cognitive Aspects of Problem
Gambling**Samuel R Chamberlain¹Katherine Derbyshire²Eric Leppink²Jon E. Grant²

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¹Department of Psychiatry, University of Cambridge, UK; & Cambridge and
Peterborough NHS Foundation Trust, UK

²Department of Psychiatry & Behavioral Neuroscience, University of Chicago

Address correspondence to:

Jon E. Grant, JD, MD, MPH

Professor, Department of Psychiatry & Behavioral Neuroscience

University of Chicago, Pritzker School of Medicine

5841 S. Maryland Avenue, MC 3077, Chicago, IL 60637

Phone: 773-834-1325; Fax: 773-834-6761

Email: jongrant@uchicago.edu

ABSTRACT

Background: Problem gambling is common across cultures, and has been conceptualized in terms of impulsivity. While elevated rates of attention deficit hyperactivity disorder (ADHD) have been observed in problem gamblers, the relationship between these two conditions, and other dissociable forms of impulsivity, has received little research attention.

Methods: N=126 non-treatment seeking young adults with problem gambling were recruited from the community, and were grouped according to the presence or absence of probable current ADHD. Clinical and cognitive measures pertaining to impulsivity were collected via detailed psychiatric assessment, questionnaires, and computerized neuropsychological tests. These variables were compared between groups.

Results: Probable current ADHD was identified in 21.4% of the sample, and was associated with earlier age at onset of gambling behaviors, higher Barratt impulsivity scores (all three subscales), greater caffeine intake, worse response inhibition (Stop-Signal Test), and impaired decision-making (greater proportion of points gambled, Cambridge Gamble Test). Problem gamblers with and without ADHD did not differ on demographic characteristics or the rate of other psychiatric disorders, depression scores, nicotine and alcohol consumption, and body mass index. No significant group differences were found for general response speed, working memory, or executive planning.

Conclusions: ADHD is common in young adults with dysfunctional gambling behaviors and is associated with elevated questionnaire and cognitive based measures of impulsivity, along with heightened caffeine use. Future work should study the causal nature between these factors and the treatment implications of these findings.

Key Words: addiction; cognition; gambling; impulse control disorders; phenomenology;
ADHD; hyperkinetic

INTRODUCTION

Gambling is a commonplace phenomenon across cultures, and approximately 30% of the US adult population has gambled during the past year (e.g. Shaffer and Korn, 2002). Gambling can become excessive and functionally impairing, leading to a shift from recreational gambling to so-termed ‘problem’ gambling, and in extreme forms, full gambling disorder (APA 2013). Unfortunately, only a relatively small proportion of people with problem gambling seek treatment (Erbas & Buchner, 2012), and such behaviors are particularly common in young adults (Petry, 2005). Problem gambling is associated with negative long-term outcomes including poor general health (for example, obesity, headaches, liver disease, hypertension, gastrointestinal problems) (Black et al., 2013) and increased prevalence of other psychiatric morbidities, such as mood and anxiety disorders, and substance use disorders (Bischof et al., 2013; Abdollahnejad et al., 2014). Knowledge of how co-morbidities influence the clinical and cognitive presentation of problem gambling has potential implications not only in terms of psychiatric nosology (understanding the relationship between disorders) but also in terms of neurobiological models and optimizing treatment.

Problem gambling has been conceptualized in terms of ‘impulsivity’ (Chambers & Potenza, 2003; Clark et al., 2013; Goudriaan et al., 2014; Grant & Chamberlain, 2014), a multi-faceted term that broadly refers to behaviors and cognitive processes that are inappropriate, premature, poorly thought-out, and which result in unwanted long-term outcomes (e.g. Moeller et al., 2001; Fineberg et al., 2014). Attention deficit hyperactivity disorder (ADHD) is regarded by many as a prototypical disorder of impulsivity: behavioral impulsivity forms a core part of the symptoms and patients with the condition often show other forms of impulsivity including substance use disorders, forensic contact,

and cognitive dysfunction (Arnsten, 2006; Spencer et al., 2007; Chamberlain et al., 2011; Nigg, 2013). In the background population, ADHD persists into adulthood in 40-60% of cases (Simon et al., 2009).

Early work identified an interesting association between dysfunctional gambling in adults and previous childhood ADHD (or retrospective recall of behavioral problems of childhood suggestive of ADHD) (Carlton et al., 1987; Carlton & Manowitz, 1992). Adolescents and young adults (aged 12-19 years) with problem gambling, recruited from school settings, had elevated rates of ADHD symptoms (Derevensky et al., 2007). A relationship between childhood ADHD and later problem gambling has also been shown longitudinally, particularly when childhood ADHD symptoms persist into adulthood (Breyer et al., 2009).

Several studies have examined the relationship between dysfunctional gambling and ADHD in adults, some of which also considered other aspects of impulsivity. In a sample receiving on-going treatment for pathological gambling, 20% had comorbid ADHD (Specker et al., 1995). In subjects seeking treatment for pathological gambling, >25% had a history of childhood ADHD, while 10.5% showed persisting ADHD; history of ADHD (childhood and/or adult) was associated with significantly higher severity of gambling disorder symptoms, more psychiatric disorders (including mood, anxiety, and alcohol use disorders), and higher urgency scores on the UPPS Impulsive Behavior Scale (Grall-Bronnec et al., 2011). The study was not sufficiently large to explore relationships between current ADHD and these measures. In adult pathological gamblers who had taken part in gambling research (many of whom were likely to have been treatment-seeking) individuals with comorbid ADHD showed higher neuroticism and openness, and

lower conscientiousness, compared to those without ADHD (indexed using the NEO Personality Inventory Revised; Davtian et al., 2012).

Few studies have examined the influence of ADHD over cognitive functioning in dysfunctional gambling. In individuals with pathological gambling attending a treatment unit, those with a history of childhood ADHD history (defined retrospectively, N=16) were compared to those without (N=39), on the Barratt Impulsivity Scale (BIS), the Stop-Signal Test of inhibitory control, the Differential Reinforcement of Low Rate Responding Test (DRLRR, a measure of gratification deferment), and a Continuous Performance Test (sustained attention) (Rodriguez-Jiminez et al., 2006). Pathological gamblers with a history of ADHD showed significantly worse response inhibition (Stop-Signal Test), abnormal DRLRR performance, and higher scores on the BIS subscales, than those without a history of ADHD. The two groups did not differ in terms of gambling severity or sustained attention.

The majority of the above studies recruited gambling disordered subjects from treatment settings, and included only limited measures of impulsivity (for example, measuring substance use related behaviors but not cognitive measures; or vice versa). Therefore, the aim of this study was to examine the influence of ADHD symptoms over multiple dissociable aspects of impulsivity in problem gamblers recruited from a community setting. It was hypothesized that ADHD in problem gamblers would be associated with more severe gambling symptoms, higher rates of nicotine and alcohol use, and an impulsive cognitive profile (elevated stop-signal reaction times and decision-making impairment).

METHODS

Subjects

Non-treatment-seeking young adults aged 18-29 years were recruited from the general community as part of a longitudinal study of impulsive behaviors. Subjects were self-selected in response to media announcements in a metropolitan area (“have you ever gambled?”). The only inclusion criterion was presence of problem gambling, while the exclusion criteria were an inability to understand/undertake the procedures, and an inability to provide written informed consent (or refusal of consent). Subjects with problem gambling were grouped according to probable presence of current ADHD or no ADHD. Since we sought to examine a naturalistic sample, individuals with psychiatric and substance use comorbidity, as well as those taking psychotropic medications, were allowed to participate.

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 consent statement. After all study procedures were explained, subjects provided voluntary written informed consent. Participants were compensated with a \$50 gift card to a local department store.

Clinical Assessments

Psychiatric assessment included the modified Structured Clinical Interview for Gambling Disorder (SCI-GD) in order to quantify problem gambling (Grant et al. 2004), and the Mini-International Neuropsychiatric Interview (Sheehan et al. 1998) to examine psychiatric morbidity. Problem gambling was defined as a score of 1 or more on the SCI-GD (Desai et al. 2004; Grant et al. 2011; Odlaug et al. 2011). The Adult ADHD Self-

Report Scale (ASRS v1.1) part A was used to screen for ADHD symptoms: a score of four or more on this instrument is consistent with a diagnosis of probable ADHD and was used to define the two study groups (hereafter referred to as ‘problem gamblers with ADHD’ and ‘problem gamblers without ADHD’) (Kessler et al., 2005). Caffeine consumption was quantified via the Beverage and Caffeine Questionnaire (Modi et al., 2010). Subjects reported frequency of gambling behavior, money lost to gambling in the past year, age of first gambling, age of regular gambling, number of alcoholic beverages consumed per week, and amount of smoking per day (packs per day). Each subject completed the Barratt Impulsivity Scale, Version 11 (BIS-11) (Patton et al. 1995), a 30-item, self-report measure that assesses broad aspects of impulsivity. Subscores of the BIS-11 are: attentional impulsivity (inability to concentrate attention), motor impulsivity (acting without thinking), and non-planning impulsivity (being present in the moment, lack of future thinking).

Cognitive Assessments

Neurocognitive testing was undertaken in a quiet room using a touch-screen computer. Paradigms were included from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Cambridge Cognition Limited 2006). The cognitive domains of interest were: response inhibition, set-shifting, spatial working memory, decision-making, and executive planning. These domains were selected because they have been implicated in the pathophysiology of gambling problems (e.g. Clark 2010; van Holst et al. 2010a; van Holst et al. 2010b; Grant et al. 2011; Odlaug et al. 2011) and because they are often impaired in ADHD (e.g. Chamberlain et al., 2007). Brief descriptions of each task are provided below, and the reader is referred to the references

for more detailed information.

Response inhibition was measured with the Stop-Signal Task (SST, Aron et al. 2004). Subjects viewed a series of directional arrows appearing one per time on-screen, and made quick motor responses depending on the direction of each arrow (left button for a left-facing arrow, and vice versa). On a subset of trials, an auditory stop-signal occurred ('beep') to indicate that the volunteer should attempt to withhold their response for the given trial. By using a tracking algorithm the task estimated the 'stop-signal reaction time' for each subject (longer stop-signal reaction times equate to worse response inhibition). Median reaction times for 'go' trials were also recorded.

Set-shifting was measured using the Intra-Dimensional/Extra-Dimensional test (IDED, Roberts et al., 1982). Subjects were presented with two pictures on-screen per time, and had to work out a rule governing which stimulus was "correct" based on feedback provided by the computer. At various points, the rule governing the "correct" stimulus was changed by the computer, necessitating flexible learning. The key outcome measure from the task was the total number of errors made, adjusted for parts of the task that were failed or not attempted.

On the Spatial Working Memory task (SWM, Owen et al. 1990), participants attempted to locate tokens hidden underneath boxes on-screen whilst avoiding returning to boxes that previously yielded such tokens. The key outcome measure was the total number of errors made on the task.

Decision-making was examined using the Cambridge Gamble Task (CGT, Rogers et al. 1999). On each trial, subjects were presented with a set of red and blue boxes on the screen (ten boxes in total). The ratio of red to blue boxes was varied over the course of the task. Participants were informed that for each trial, the computer had hidden a 'token'

inside one of the boxes, and that they had to indicate whether they felt the token would be hidden behind a red or a blue box. This decision was made by selecting 'red' or 'blue' using the touch-screen. Participants were then required to gamble a proportion of their points on whether their color choice was correct. The primary outcome measures from the task were overall proportion of points gambled, proportion of rational decisions (quality of decision-making, number of logical choices of block color), and risk adjustment (a measure of the tendency to alter amount bet depending on the degree of statistical risk).

Executive planning was quantified using the One Touch Stockings of Cambridge task (OTS, Owen et al., 1990). For each trial, two sets of snooker balls were shown in pockets on-screen. Volunteers had to work out 'in mind' the minimum possible number of moves it would take to make one set of snooker balls match the appearance of the other set. This process necessitates forward planning and sequencing. The key outcome measure was the number of problems solved correctly on the first attempt.

Data Analysis

Salient demographic, clinical, and cognitive variables were tabulated for the two groups (problem gamblers with ADHD, and problem gamblers without ADHD). Differences between the two study groups were explored using independent sample t-tests (or alternative non-parametric tests were used as appropriate, where indicated in the text). Where significant group differences were found, effect sizes were reported (Cohen's *D*). Statistical significance was defined as $p < 0.05$ two-tailed, uncorrected. IBM SPSS Software, Version 21 was used for the analyses.

RESULTS

Of the 126 problem gamblers enrolled, 27 had probable ADHD (21.4% of the sample). Demographic and clinical measures of the two groups are presented in **Table 1**, where it can be seen that they were well matched in terms of age, gender, and education level. The two groups did not differ significantly in terms of rate of co-morbid psychiatric disorders, depression scores, alcohol consumption, nicotine consumption, or body mass index. Gamblers with ADHD did not differ from the non-ADHD group on overall frequency of gambling, amount lost to gambling, or SCI-GD scores. However, the ADHD group exhibited significantly earlier onset of gambling (age at first gambling, age of first regular gambling), higher BIS-11 scores, and greater caffeine consumption, versus the non-ADHD group.

** TABLE 1 ABOUT HERE PLEASE **

Outcome measures from the neurocognitive assessments are indicated in **Table 2**. It can be seen that the group with ADHD, compared to the non-ADHD group, had significantly worse response inhibition (longer stop-signal reaction times) and gambled a larger proportion of points on the gambling task. The other measures of interest did not differ significantly between the two groups.

** TABLE 2 ABOUT HERE PLEASE **

DISCUSSION

This study explored the impact of ADHD on dissociable aspects of impulsivity in non-treatment seeking young adults with problem gambling. The key findings were that ADHD was associated with earlier age of first gambling (and regular gambling), elevated questionnaire measures of impulsivity, greater caffeine consumption, impaired response inhibition, and gambling excess points during the gambling task.

Overall, we identified probable current ADHD in 21.4% of the sample, a rate similar to that reported in another study in adults (Specker et al., 1995; but see also Grall-Bronnec et al., 2011). This adds weight to the proposition that gambling and ADHD share comorbid overlap and that screening for this comorbidity in disordered gambling is clinically important. Those with and without ADHD did not differ in terms of salient demographic characteristics (age, gender, education), presence of one or more other current psychiatric disorders, or depressive mood scores (Hamilton), meaning that other findings can be interpreted in the absence of potential confounding influences from these variables.

Contrary to our hypothesis, but consistent with at least one previous study (Rodriguez-Jiminez et al., 2006), we did not find that gambling severity was affected by ADHD, in terms of SCI-GD total scores, frequency of gambling, or money lost to gambling. ADHD was associated with earlier age of first gambling, and earlier age of regular gambling, which is what might be anticipated if these two clinical disorders stem from common predisposing etiological factors.

In terms of substance use, contrary to expectations, we did not find elevated rates of alcohol and nicotine consumption in problem gamblers as a function of ADHD status. Significantly higher rates of alcohol use disorders, and trend higher rates of tobacco dependence, were shown in a previous study in problem gamblers with a history of

ADHD versus no such history (Grall-Bronnec et al., 2011). In general, pathological gambling has been associated with high rates of substance use disorders especially over the lifetime (Petry et al., 2005), as has ADHD (e.g. Lee et al., 2011). The current results may indicate that problem gambling and ADHD are not synergistic in terms of their associations with nicotine and alcohol consumption.

The finding that ADHD was linked with higher daily caffeine consumption in problem gamblers is intriguing in view of controversy about the role of caffeine in mental health disorders (Lara, 2010). Early clinical trials found that caffeine showed some efficacy in the treatment of ADHD; furthermore, caffeine has potential cognitive-enhancing effects at least in small-medium doses, and acts as an adenosine antagonist (Ioannidis et al., 2014). Elevated caffeine use in problem gambling with ADHD raises the possibility that such individuals may be ‘self-medicating’ (Ioannidis et al., 2014).

Replicating previous research in gamblers with childhood ADHD assessed retrospectively (Rodriguez-Jiminez et al., 2006), we found that ADHD was associated with elevated impulsivity scores on the Barratt questionnaire, across all three subscales. This finding may also bear similarities to the elevated ‘urgency’ type impulsivity scores found in problem gamblers with a history of ADHD, using a different scale (Grall-Bronnec et al., 2011).

Turning to the cognitive results, consistent with our predictions, problem gamblers with ADHD had worse response inhibition on the Stop-Signal Task (SST), and gambled a greater proportion of points on the Cambridge Gamble Task (CGT), versus their non-ADHD counterparts. Impaired response inhibition was found elsewhere using the SST, in pathological gamblers with a history of childhood ADHD versus those without (Rodriguez-Jiminez et al., 2006). In our study, gamblers with ADHD were not

significantly different from non-ADHD participants on the other cognitive domains including general response speed, set-shifting, working memory, and executive planning. Caution is warranted when making inferences about the functioning of fronto-striatal circuitry based on behavioral cognitive measures alone. Response inhibition is dependent on distributed neural circuitry including the anterior cingulate cortices and right frontal cortex (Aron et al., 2004). Increased proportion gambled on the CGT occurs in neurosurgical patients with ventromedial prefrontal and insular lesions (Clark et al., 2008). Thus these findings collectively may implicate dysregulation of more ventromedial and inferior frontal sectors of the prefrontal lobes in comorbid problem gambling and ADHD; it would be valuable in future work to explore whether this is indeed the case by using neuroimaging techniques.

There are several limitations to the current study. The sample size may have limited power to detect more subtle differences between the groups i.e. differences with small effect size; however, such subtle differences are unlikely to be clinically meaningful. We focused on current ADHD symptoms, measured using a validated scale with high specificity and sensitivity; however, we did not collect information regarding childhood ADHD diagnoses – in the absence of supporting documentation from childhood, such diagnoses would have been subject to potential recall bias and inaccuracies in any event, even had this information been collected. This being an exploratory study, we did not correct for multiple comparisons, hence findings merit confirmation in future larger trials.

In summary, we examined a spread of different types of impulsivity as a function of ADHD in non-treatment seeking young adults with dysfunctional gambling. ADHD in problem gambling was associated with earlier onset of gambling behaviors, more

impulsivity on the BIS questionnaire, more caffeine intake, impaired response inhibition, and greater amounts gambled on the gambling task. Future work should explore the clinical implications of these findings in comorbid patients and the neural correlates of the disproportionate cognitive impairment identified.

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Conflicts of Interest: Dr. Grant has received research grants from NIMH, National Center for Responsible Gaming, and Forest and Roche Pharmaceuticals. He receives yearly compensation from Springer Publishing for acting as Editor-in-Chief of the Journal of Gambling Studies and has received royalties from Oxford University Press, American Psychiatric Publishing, Inc., Norton Press, and McGraw Hill. Dr. Chamberlain consults for Cambridge Cognition. Ms. Derbyshire and Mr. Leppink report no financial relationships with commercial interests.

Ethical Standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Table 1. Demographic and Clinical Characteristics of the Study Groups

Variable	Problem gamblers with ADHD (N=27)	Problem gamblers without ADHD (N=99)	p-value	Effect Size
Age, years	23.4 (3.8)	23.1 (3.8)	0.391	
Gender, male, n [%]	15 [55.6%]	64 [64.6%]	0.662	
Education, some college or higher, n [%]	26 [96.3%]	88 [88.9%]	0.428c	
Age at first gambling, years	12.5 (4.0)	14.5 (4.2)	0.032	0.49
Age at regular gambling, years	17.0 (3.2)	18.9 (2.4)	<0.001	0.67
Frequency of Gambling (mean episodes per week)	2.8 (2.8)	2.4 (2.4)	0.455	
Amount lost to gambling in past year (USD)	3144.6 (8057.0)	2549.5 (5629.8)	0.660	
SCI-GD total score	2.5 (2.1)	2.3 (1.9)	0.705	
BIS-11				
Attention Impulsive	19.9 (4.7)	16.5 (4.2)	<0.001	0.76
Motor Impulsive	26.6 (5.7)	23.8 (5.0)	0.014	0.52
Non-planning Impulsive	27.8 (5.0)	24.2 (5.4)	0.002	0.69
Any Current MINI Diagnosis, n [%]	17 [63.0%]	49 [49.5%]	0.214c	
HAM-D total score	7.9 (7.5)	7.2 (7.0)	0.709	
Alcoholic drinks per week	4.0 (3.0)	3.1 (2.1)	0.136	
Caffeine intake per day, mg	237.4 (283.6)	147.2 (136.6)	0.021	0.40
Nicotine consumption, packs per day (equivalent)	0.11 (0.22)	0.12 (0.28)	0.802	
Body Mass Index	23.2 (4.4)	25.0 (6.8)	0.195	

All scores are mean \pm SD unless otherwise noted. Statistic: t-tests except where indicated with 'c' for chi-square. Effect sizes are Cohen's D. SCI-GD = Structured Clinical Interview for Gambling Disorder; BIS-11 = Barratt Impulsivity Scale; MINI = Mini International Neuropsychiatric Inventory; HAM-D = Hamilton Depression Rating Scale.

Table 2. Cognitive Characteristics of the Study Groups

Variables	Problem gamblers with ADHD (N=27)	Problem gamblers without ADHD (N=99)	p-value	Effect Size
SST SSRT	217.8 (97.0)	184.8 (64.7)	0.039	0.40
SST Median Correct RT on GO Trials	490.3 (193.6)	522.8 (205.4)	0.463	
IDED total errors adjusted	25.9 (20.8)	29.4 (26.8)	0.520	
SWM total errors	23.4 (22.5)	20.3 (18.7)	0.463	
CGT Overall Proportion Bet	0.61 (0.12)	0.55 (0.13)	0.030	0.48
CGT Quality of Decision Making	0.94 (0.09)	0.94 (0.08)	0.964	
CGT Risk Adjustment	1.23 (1.20)	1.36 (1.20)	0.616	
OTS problems solved on first attempt	17.6 (4.1)	17.4 (3.8)	0.746	

All scores are mean \pm SD unless otherwise noted. Statistic: t-tests. Effect sizes are Cohen's D. SST = Stop Signal Task; SSRT = Stop-Signal Reaction Time; IDED = Intra-Dimensional/Extra-Dimensional set-shift Task; SWM = Spatial Working Memory task; CGT = Cambridge Gamble Task; OTS = One Touch Stockings of Cambridge task.