Authors' final version of manuscript - in press, J Psych Res 2016

Cognitive Flexibility as a Salient Predictor of Gambling Severity in Young Adults

Eric W. Leppink, BA[a] *

Sarah A. Redden, BA[a]

Samuel R. Chamberlain, MD, PhD,[b]

Jon E. Grant, JD, MD, MPH[a]

[a]University of Chicago, Department of Psychiatry & Behavioral Neuroscience, 5841 S. Maryland Ave., MC3077, Chicago, IL 60637

[b]Department of Psychiatry, University of Cambridge, Herchel Smith Building, Robinson Way, Cambridge, CB2 0SZ, UK; & Cambridge and Peterborough NHS Foundation Trust (CPFT), Cambridge Road, Fulbourne, Cambridge, CB21 5HH, UK

* denotes corresponding author

Email: eleppink@uchicago.edu; sredden@uchicago.edu; srchamb@gmail.com; jongrant@uchicago.edu;

Abstract

Although gambling disorder (GD) is often characterized as a problem of impulsivity, compulsivity has recently been proposed as a potentially important feature of addictive disorders. The present analysis assessed the neurocognitive and clinical relationship between compulsivity on gambling behavior. A sample of 552 non-treatment seeking gamblers age 18-29 was recruited from the community for a study on gambling in young adults. Gambling severity levels included both casual and disordered gamblers. All participants completed the Intra/Extra-Dimensional Set Shift (IED) task, from which the total adjusted errors were correlated with gambling severity measures, and linear regression modeling was used to assess three error measures from the task. The present analysis found significant positive correlations between problems with cognitive flexibility and gambling severity (reflected by the number of DSM-5 criteria, gambling frequency, amount of money lost in the past year, and gambling urge/behavior severity). I~~D~~ED errors also showed a positive correlation with self-reported compulsive behavior scores. A significant correlation was also found between I~~D~~ED errors and non-planning impulsivity from the BIS. Linear regression models based on total I~~D~~ED errors, extra-dimensional (ED) shift errors, or pre-ED shift errors indicated that these factors accounted for a significant portion of the variance noted in several variables. These findings suggest that cognitive flexibility may be an important consideration in the assessment of gamblers. Results from correlational and linear regression analyses support this possibility, but the exact contributions of both impulsivity and cognitive flexibility remain entangled. Future studies will ideally be able to assess the longitudinal relationships between gambling, compulsivity, and impulsivity, helping to clarify the relative contributions of both impulsive and compulsive features.

Keywords: gambling; cognitive flexibility; compulsivity; young adults; neurocognition

Cognitive Flexibility Correlates with Gambling Severity in Young Adults

1. Introduction

Gambling disorder (GD) is defined as persistent problematic gambling behavior that is also associated with significant distress or impairment (American Psychiatric Association, 2013). The clinical aspects of GD have often been regarded as impulsive, in that they are often poorly thought out (or undertaken without adequate forethought), risky, and result in deleterious long-term outcomes (Chamberlain & Sahakian, 2007). Furthermore, neurocognitive research has found that GD is frequently associated with heightened trait impulsivity (for example, measured by the Barratt Impulsiveness Scale-11), although the exact nature of this neurocognitive trait remains somewhat ill-defined, with associations differing by the measures used, the disorder(s) of interest, and the trait versus state aspects of impulsivity (i.e. state impulsivity measured by behavioral tasks such as the Stroop Color Word Test and the Emotional Conflict Task (Leppink et al., 2016; Choi et al., 2014; Grant & Kim, 2014; el-Guebaly et al., 2012; Leeman & Potenza, 2012; Probst & van Eimeren, 2013; Lai et al., 2011). In addition, previous studies have shown that certain measures of impulsivity show significant associations with GD symptom severity, although this has not always been true (Blanco et al., 2009; Bottesi et al., 2014; Grant & Kim, 2014; Ledgerwood et al., 2012).

One conceptualization holds that impulsivity (tendency towards premature, poorly thought out acts) is diametrically opposed to compulsivity (i.e. thoughts and behaviors that are repetitive, and performed in a stereotyped or habitual fashion), with impulsivity and compulsivity representing opposing ends of a behavioral spectrum (Hollander and Cohen, 1996). Alternatively, the two terms may be seen as overlapping, in that they both imply underlying problems with top-down inhibitory control (Fineberg et al., 2014). Compulsivity has mostly been considered in terms of the ‘archetypal’ disorder of compulsivity, namely obsessive compulsive disorder (OCD). Further complicating our understanding of GD, recent genetic research suggests that GD may be linked with OCD (Scherrer et al., 2015), and thus perhaps characterized by compulsive features. While the presentation of compulsivity in GD may not mirror what is typically seen in a disorder such as OCD (Fineberg et al., 2010), a few studies have found elevated compulsive traits and behaviors in gamblers compared to healthy controls (Goudriaan et al., 2006; Ledgerwood et al., 2012; Grant & Potenza, 2006). Thus, while gambling is frequently considered an impulsive behavior, it may also show associations with compulsivity.

Although considerable research has focused on fractionating impulsivity such as in terms of cognitive tests and disorders (Dalley et al., 2011), the concept of compulsivity is perhaps less fully developed. Flexible responding, arguably one important aspect of compulsivity, has traditionally been assessed with the Wisconsin Card Sorting Test (WCST) and its variants, which are dependent on distributed neural circuitry including the ventromedial and ventrolateral prefrontal cortices (Hampshire & Owen, 2006; Buckley et al. 2009). Consequently, the majority of available studies have reported on WCST performance in gambling disorder compared with healthy controls. Results are conflicting, with some studies reporting deficits among gamblers (Rugle & Melamed, 1993; Goudriaan et al. 2006; Forbush et al. 2008; Marazziti et al. 2008) and others showing no deficits (Cavedini et al. 2002; Brand et al. 2005) in overall cognitive flexibility. Previous research has found that adults with problem gambling behavior exhibit reversal learning perseveration, another way to examine compulsivity, compared with controls (Leeman and Potenza, 2012). Finally, problem gamblers exhibit reduced flexibility after reversal of previously rewarded contingencies (Vanes et al., 2014).

The goal of the present study was to assess whether compulsivity, rather than impulsivity, has different and perhaps clinically more useful associations with gambling severity. This study, therefore, examined the concept of compulsivity using the Intra-/Extradimensional Set Shifting task (IDED) (Owen et al., 1991), a computer-based measure of cognitive flexibility which has previously been proposed as a meaningful domain of compulsivity (Fineberg et al., 2015; Wu et al., 2014), and the Padua inventory, a questionnaire-based measure of obsessionality/compulsivity typically associated with compulsive disorders. Several studies have found significant associations between elevated questionnaire-based measures of compulsivity and impaired cognitive flexibility (using the WCST) (Gershuny and Sher, 1995; Goodwin and Sher, 1992).

We hypothesized that as the number of errors gamblers made during the I~~D~~ED increased (i.e. greater cognitive inflexibility) there would be a there would be a corresponding increase in gambling symptoms severity as well as psychosocial variables. We also predicted a significant association between I~~D~~ED errors and scores on the Padua Inventory, as both assess certain facets obsessionality/compulsivity.

2. Methods

2.1. Subjects

Subjects were 552 non-treatment seeking young adults age 18 to 29 recruited from the surrounding community near two urban universities in the Midwest for a study on gambling behavior in young adults. Inclusion criteria were a gambling frequency of at least five times in the past year and ability to provide written informed consent for all study procedures. Exclusion criteria were an inability to understand/undertake the assessments, and failure to provide written informed consent. 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.

2.2. Assessments

2.2.1. Demographics and Psychiatric

All participants provided basic demographic information at baseline, including age, sex, race, and education. Participants were also asked about current nicotine, alcohol, and cannabis use. All participants were screened using the Mini International Neuropsychiatric Inventory (MINI) (Sheehan et al., 1998) by trained raters. Raters also assessed participant history of other impulse control disorders using the Minnesota Impulse Disorders Interview (MIDI) (Grant, 2008).

2.2.2. Gambling

Structured Clinical Interview for Pathological Gambling, DSM-5 (SCI-PG): The SCI-PG is a nine question, clinician-administered scale for the diagnosis of GD based on DSM-5 criteria. A total of 4+ current symptoms is consistent with a diagnosis of current GD (Grant et al., 2004). The scale examined symptoms over the past 12 months.

Yale-Brown Obsessive-Compulsive Scale modified for Pathological Gambling (PG-YBOCS): The PG-YBOCS is a ten question clinician-administered measure of gambling severity which assesses urges and behavior related to gambling independently. Questions are scored from 0 (none) to 4 (extreme). Behavior and urge scores are then added to provide a total severity score (Pallanti et al., 2005). The PG-YBOCS measures severity of gambling over the last seven days.

In addition to structured assessments, participants completed assessments of social, financial, legal, and work problems stemming from gambling, as well as the total amount of money lost gambling in the past year and average gambling frequency per week.

2.2.3. Compulsivity/Cognitive Flexibility

Intra-/Extradimensional Set Shifting Task (I~~D~~ED): The I~~D~~ED is a computerized set shifting task which assesses cognitive flexibility (Owen et al., 1991). The I~~D~~ED paradigm, which decomposes different aspects of rule learning and flexible responding, was derived from the Wisconsin Card Sorting Test, and .was taken from the computerized Cambridge Neuropsychological Test Automated Battery (CANTABeclipse, version 3, Cambridge Cognition Ltd, UK). During the task, participants are initially presented with a screen showing four boxes, two of which are blank, and two of which contain distinct pink shapes. Participants are informed that one shape displayed is “correct”, and the other is “incorrect”, based on a rule set by the computer, and their goal is to select the correct shape as many times as possible. After a set number of correct selections, the computer automatically changes which shape is correct, which is defined as the intradimensional set shift (ID), a process which is then repeated several times. After another period of correct responses, the task introduces a second set of stimuli, distinct white shapes, as another variable that are overlaid on top of the pink shapes. During this phase, the computer begins to identify the white shapes as the correct and incorrect variables, rather than the pink shapes, which is described as the extradimensional set shift (ED). The target variable for this analysis was the total number of errors made during the task adjusted for the total number of stages successfully completed.

Padua Inventory (Revised): The Padua is a self-report measure of obsessive and compulsivity symptoms consisting of 39 questions, scored from 0 (not at all) to 4 (very much). The scale yields 5 subscales, as well as a total score, which ranges from 0 to 156 (Burns et al., 1996).

2.2.4. Impulsivity

Barratt Impulsiveness Scale, Version 11 (BIS) (Barratt, 1959; Patton et al., 1995): The BIS is a self-report measure assessing features of impulsivity. The measure consists of 30 items, with responses ranging from 1 (Rarely/Never) to 4 (Almost Always/Always). Responses are broken down into three secondary factors: attentional impulsivity, non-planning impulsivity, and motor impulsivity.

2.3. Data Analysis

Correlational associations were described using Pearson-Product Moment Correlation Coefficients, Point Biserial Correlation Coefficients, and Biserial Correlation Coefficients. Statistical significance was defined as $p < .01$ to account for multiple comparisons, but a Bonferroni correction was not used, as this correction tends to be overly conservative (Rosner, 1995). For further assessment, demographic and clinical data (all variables in Table 1) were entered into three multivariate regression models (method enter, stepping method criteria probability of F, for entry 0.05). The three dependent variables were total I~~D~~ED errors (adjusted), pre-ED errors, and ED errors. Absence of autocorrelation was confirmed using the Durbin-Watson test (value $1.5<d<2.5$), and absence of multicollinearity with collinearity statistics (tolerance >0.10). Homoscedasticity and normality of residuals were inspected using manual plots. For the purposes of the regression models, statistical significance for individual variables was defined as p<0.05 uncorrected, subject to a given model being significant overall at p<0.01.

3. Results

Correlation Analysis: Means and standard deviations for the sample are summarized in **Table 1**. Higher total I~~D~~ED errors (i.e. greater cognitive inflexibility) showed a positive correlation with likelihood of being non-Caucasian (*p*<.001) and female (*p*<.001). Higher total I~~D~~ED errors also showed significant positive correlations with rates of substance dependence (*p*=.001), anxiety disorders (*p*=.008), depression (*p*=.001), and current impulse control disorder (*p*=.004).

For gambling variables, a higher number of I~~D~~ED errors showed positive correlations with gambling frequency (*p*<.001), number of SCI-PG criteria (*p*<.001), and PG-YBOCS urges (*p*<.001), behavior (*p*=.001), and total score (*p*<.001). A positive correlation was also evident between PADUA scores and I~~D~~ED errors (*p*<.001). A significant positive correlation was also identified with the non-planning subscale of the BIS (*p*=.002).

Linear regression with total I~~D~~ED errors (adjusted) as the dependent variable: A significant model was identified (F=3.995, p<0.001) that accounted for 14.2% of the variance (according to the R square statistic). Results are indicated in Table 2 below. Higher I~~D~~ED total errors (adjusted) was significantly associated with female gender, racial-ethnic status of not being White, higher gambling frequency per week, more money lost to gambling in the past year, and higher Barratt attentional and non-planning sub-scores.

Linear regression with Pre-ED errors as the dependent variable: A significant model was identified (F=2.309, p<0.001) that identified for 8.4% of the variance (according to the R square statistic). Results are indicated in Table 3. Higher pre-ED errors was significantly associated with racial-ethnic status being non-White, more money lost to gambling in the past year, and more work problems due to gambling.

Linear regression with ED errors as the dependent variable: A significant model was identified ($F=3.1375$, $p<0.001$) that accounted for 11.5% of the variance (according to the R square statistic). Results are indicated in Table 4 below. A ~~H~~higher number of ED errors was significantly associated with female gender, higher frequency of gambling per week, and higher PADUA total scores.

4. Discussion

While previous comparisons of high and low impulsivity in GD have shown select associations with gambling severity (Ginley et al., 2014; Goudriaan et al., 2008), no study to date has examined the association between an objective cognitive measure of compulsivity and clinical symptoms in individuals across multiple levels of gambling severity. The present analysis found several significant positive correlations between the number of ~~IDE~~ IED errors a gambler makes and distinct measures of gambling severity, such as the number of DSM-5 criteria, gambling frequency, amount of money lost in the past year, and gambling urge/behavior severity. The ~~IDE~~ IED errors also showed a positive correlation with the total Padua Inventory score, a measure of compulsivity and obsessionality. This association suggests that aspects of cognitive flexibility assessed using the ~~IDE~~ IED may be related to certain facets of compulsivity. Furthermore, linear regression analyses across the various error types (ED, pre-ED, Total) showed associations with several facets of gambling behavior, although specific associations did show variations by error type used in the model, with total errors during the ~~IDE~~ IED accounting for the greatest percentage of variance.

While previous studies have suggested a link between GD and impulsivity, compulsivity may also be an important clinical aspect of GD. In particular, salient associations across measures of symptom severity and associated personal/interpersonal dysfunction emphasize the potential clinical importance of compulsivity in GD. Previous work using alternative tasks to the IED, such as the Wisconsin Card Sort Task, have suggested that cognitive flexibility, as a proxy for compulsivity, may be a mediating factor in the clinical presentation of GD (van Holst et al., 2010)~~-~~. Furthermore, this association between gambling severity and compulsivity may corroborate findings from clinical studies assessing medications to reduce gambling symptom severity. Animal research suggests that the opioid antagonist naltrexone, a medication often considered first-line pharmacotherapy treatment for GD (Yip and Potenza, 2014) may improve attentional set-shifting (Rodefer and Nguyen, 2008) In a double-blind study of trichotillomania, another impulse control disorder, naltrexone compared to placebo resulted in significantly greater improvement in cognitive flexibility using the IED~~DE~~ (Grant et al., 2014). The relationship between the opiate system and cognitive flexibility, however, may be more complicated than these studies suggest. Quednow and colleagues (2008) showed that morphine, a ~~n~~ mu~~-opiate~~ opioid ~~agonist~~receptor agonist, selectively improved the error rate in the IED~~DE~~ when undertaken by health control participants, Even more notably, a treatment study using memantine, an N-methyl D-aspartate receptor antagonist, for GD showed that significant improvements in cognitive flexibility on the IED~~DE~~ coincided with GD symptom reduction (Grant et al., 2010). While not necessarily assessed directly in available research, the findings from previous research suggests that compulsivity/cognitive flexibility can be modulated, at least to some extent, by specific pharmacological agents, and, in the case of GD, potentially yield corresponding improvements in symptom severity. Given this possibility, future studies assessing treatments for GD, particularly opioid antagonists and N-methyl D-aspartate receptor antagonists, may consider specifically targeting cases of GD characterized by high compulsivity, as this population may be more likely to respond to these types of pharmacological treatments.

While the present analysis did not include measures to assess potential pathways by which compulsivity and gambling may interact, one possibility is that greater compulsivity/cognitive inflexibility makes it harder for gamblers to shift their attention to alternative activities and sources of stimulation. Once attention is set on gambling, highly compulsive gamblers may struggle to divert attention away from these urges related to gambling. Problems with cognitive inflexibility could potentially make focusing on other important areas, such as work and social obligations, more difficult.

The limited associations between IED~~E~~ errors and the BIS may highlight a distinction between impulsivity and compulsivity in the case of GD. While previous findings with impulsivity (Alessi & Petry, 2003; Blanco et al., 2009; Brevers et al., 2012; Leppink et al., 2016) and current findings on compulsivity suggest that both influence gambling severity, results could indicate that they represent distinct processes that could operate independently (Odlaug et al., 2011), but with a potential intersection in planning. One possible explanation for this distinction is that high impulsivity and high compulsivity represent unique endophenotypes within the more general classification of GD. While some gamblers may present with high levels of impulsivity, there may be an additional subset for which a high level of compulsivity contributes to persistent gambling problems. Thus, rather than characterizing GD as either a compulsive or impulsive disorder, this population may instead be characterized by two distinct endophenotypes distinguished by high and low compulsivity and impulsivity. This characterization may be supported by a recent study assessing the relationship between gambling behavior and certain facets of OCD in a sample of identical twins (Scherrer et al., 2015). Although previous studies have shown that GD does not show increased rates of comorbidity with OCD, this study assessed gamblers relative to different subsets of OCD profiles and severity, irrespective of whether they had a diagnosis of OCD. Furthermore, this study found that OCD and GD shared 19.4% of genetic variance, which is indicative of a common genetic contributor between the two problems. The authors suggest that this association is indicative of a potential association between GD and OCD that has not been as evident in previous studies, one they theorized might be mediated by compulsivity. These findings appear consistent with the present analysis, suggesting that while impulsivity is a common feature in GD, specific aspects of compulsivity may give rise to distinct cognitive endophenotypes. Between genetic associations and differences in clinical presentation, these data suggest that the association between GD and compulsivity merits more extensive investigation.

There were several limitations to the present analysis. One of these was that only a self-report measure of impulsivity was included in the analysis, while the I~~D~~ED is a computerized cognitive assessment of cognitive flexibility. The use of two kinds of instruments, the self-report scale and computerized cognitive assessment, however, could also be considered. Secondly, the present analysis only assessed participants at a single time-point, and thus it is not possible to assess the longitudinal effects of heightened. Future research on the possible interaction of gambling and compulsivity over time will help to clarify whether the associations identified in the present analysis are limited to baseline trends, or if they are predictive of persistent gambling severity over time. Finally, the sample for this analysis exclusively included young adults between 18 and 29 years old. Given this sample, there is a smaller amount of time in which participants would have been able to develop problems with gambling, which may limit the generalizability of findings to other populations. Future research will benefit from expanding assessments to address additional populations, including older adults, for example.

The current study suggests that compulsivity may be an important factor in GD. While some patients may present with heightened levels of impulsivity, others may show greater levels of compulsivity. Thus, both of these factors may be important consideration when attempting to optimize treatment for gamblers, as these cognitive differences may predispose certain individuals to responding to one course of treatment or another. By shifting focus to account for the role of compulsivity, it may be possible to improve clinicians' ability to target treatments to particular endophenotypes in GD, ideally creating a system in which treatments are able to better address the unique needs of each patient struggling to control gambling behavior.

References

Alessi, S.M., Petry, N.M., 2003. Pathological gambling severity is associated with impulsivity in a delay discounting procedure. Behav. Processes 64, 345-354.

American Psychiatric Association, 2013. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC, American Psychiatric Association.

Barratt, E.S., 1959. Anxiety and impulsiveness related to psychomotor efficiency. Percept. Mot. Skills 9, 191-198.

Blanco, C., Potenza, M.N., Kim, S., Ibáñez, A., Zaninelli, R., Saiz-Ruiz, J., Grant, J.E., 2009. A pilot study of impulsivity and compulsivity in pathological gambling. Psychiatry Res. 167, 161-168.

Boog, M., Höppener, P., Wetering, B.J., Goudriaan, A.E., Boog, M.C., Franken, I.H., 2014. Cognitive inflexibility in gamblers is primarily present in reward-related decision making. Front. Hum. Neurosci. 8, 1-6.

Bottesi, G., Ghisi, M., Ouimet, A.J., Tira, M.D., Sanavio, E., 2014. Compulsivity and Impulsivity in Pathological Gambling: Does a Dimensional-Transdiagnostic Approach Add Clinical Utility to DSM-5 Classification? J. Gambl. Stud. 31, 825-847.

Brand, M., Kalbe, E., Labudda, K., Fujiwara, E., Kessler, J., Markowitsch, H.J., 2005. Decision-making impairments in patients with pathological gambling. Psychiatry Res. 133, 91–99.

Brevers, D., Cleeremans, A., Verbruggen, F., Bechara, A., Kornreich, C., Verbanck, P., Noël, X., 2012. Impulsive Action but Not Impulsive Choice Determines Problem Gambling Severity. PLoS ONE 7, e50647: 1-8.

Buckley, M.J., Mansouri, F.A., Hoda, H., Mahboubi, M., Browning, P.G., Kwok, S.C., Phillips, A., Tanaka, K., 2009. Dissociable components of rule-guided behavior depend on distinct medial and prefrontal regions. Science 325, 52–58.

Burns, G.L., Keortge, S.G., Formea, G.M., Sternberger, L.G., 1996. Revision of the Padua Inventory of obsessive compulsive disorder symptoms: distinction between worry, obsessions, and compulsions. Behav. Res. Ther. 2, 167-173.

Cavedini, P., Riboldi, G., Keller, R., D'Annucci, A., Bellodi, L, 2002. Frontal lobe dysfunction in pathological gambling patients. Biol. Psychiatry 51, 334–341.

Chamberlain, S.R., Sahakian, B.J., 2007. The neuropsychiatry of impulsivity. Curr. Opin. Psychiatry 20, 255-261.

Choi, S.W., Kim, H.S., Kim, G.Y., Jeon, Y., Park, S.M., Lee, J.Y., Jung, H.Y., Sohn, B.K., Choi, J.S., Kim, D.J., 2014. Similarities and differences among Internet gaming disorder, gambling disorder and alcohol use disorder: A focus on impulsivity and compulsivity. J. Behav. Addict. 3, 246-253.

Dalley, J.W., Everitt, B.J., Robbins, T.W., 2011. Impulsivity, compulsivity, and top-down cognitive control. Neuron 69, 680-94.

el-Guebaly, N., Mudry, T., Zohar, J., Tavares, H., Potenza, M.N., 2012. Compulsive features in behavioral addictions: the case of pathological gambling. Addiction 107, 1726-1734.

Fineberg, N.A., Day, G.A., de Koenigswarter, N., Reghunandanan, S., Kolli, S., Jefferies-Sewell, K., Hranov, G., Laws, K.R., 2015. The neuropsychology of obsessive-compulsive personality disorder: a new analysis. CNS Spectr. 20, 490-9.

Fineberg, N.A., Potenza, M.N., Chamberlain, S.R., Berlin, H.A., Menzies, L., Bechara, A., Sahakian, B.J., Robbins, T.W., Bullmore, E.T., Hollander, E., 2010. Probing Compulsive and Impulsive Behaviors, from Animal Models to Endophenotypes: A Narrative Review. Neuropsychopharmacology 35, 591-604.

Fineberg NA, Chamberlain SR, Goudriaan AE et al., 2014. New developments in human neurocognition: clinical, genetic, and brain imaging correlates of impulsivity and compulsivity. CNS Spectr. 19, 69-89.

Forbush, K.T., Shaw, M., Graeber, M.A., Hovick, L., Meyer, V.J., Moser, D.J., Bayless, J., Watson, D., Black, D.W., 2008. Neuropsychological characteristics and personality traits in pathological gambling. CNS Spect. 13, 306–315.

Gershuny, B.S., Sher, K.J., 1995. Compulsive checking and anxiety in a nonclinical sample: differences in cognition, behavior, personality, and affect. J. Psychopath. Behav. Assess. 17, 19-38.

Ginley, M.K., Whelan, J.P., Meyers, A.W., et al., 2014. Exploring a multidimensional approach to impulsivity in predicting college student gambling. J. Gambl. Stud. 2, 521–536.

Goodwin, A.H., Sher, K.J., 1992. Deficits in set-shifting ability in nonclinical compulsive checkers. J. Psychopath. Behav. Assess. 14, 81-92.

Goudriaan, A.E., Oosterlaan, J., de Beurs, E., van den Brink, W., 2006. Neurocognitive functions in pathological gambling: a comparison with alcohol dependence, Tourette syndrome and normal controls. Addiction 101, 534-547.

Goudriaan, A.E., Oosterlaan, J., De Beurs, E., et al., 2008. The role of self-reported impulsivity and reward sensitivity versus neurocognitive measures of disinhibition and decision-making in the prediction of relapse in pathological gamblers. Psychol. Med. 38, 41–5

Grant, J.E. Impulse Control Disorders: A Clinician's Guide to Understanding and Treating Behavioral Addictions. WW Norton and Company, New York, NY, 2008.

Grant, J.E., Chamberlain, S.R., Odlaug, B.L., Potenza, M.N., Kim, S.W., 2010. Memantine shows promise in reducing gambling severity and cognitive inflexibility in pathological gambling: a pilot study. Psychopharmacol. (Berl.) 212, 603-612.

Grant, J.E., Kim, S.W., 2014. Brain Circuitry of Compulsivity and Impulsivity. CNS Spectr. 19, 21-27.

Grant, J.E., Odlaug, B.L., Schreiber, L.R., Kim, S.W., 2014. The opiate antagonist, naltrexone, in the treatment of trichotillomania: results of a double-blind, placebo-controlled study. J. Clin. Psychopharmacol. 34, 134-138.

Grant, J.E., Potenza, M.N., 2006. Compulsive Aspects of Impulse-Control Disorders. Psychiatr. Clin. North Am. 29, 539-550.

Grant, J.E., Steinberg, M.A., Kim, S.W., Rounsaville, B.J., Potenza, M.N., 2004. Preliminary validity and reliability testing of a structured clinical interview for pathological gambling. Psychiatry Res. 128, 79-88.

Hampshire, A., Owen, A.M., 2006. Fractionating attentional control using event-related fMRI. Cerebral Cortex 16, 1679–1689.

Hollander, E., Cohen, L.J. Impulsivity and Compulsivity, American Psychiatric Press Inc., Washington, D.C., 1996.

Lai, F.D., Ip, A.K., Lee, T.M., 2011. Impulsivity and pathological gambling: Is it a state or a trait problem? BMC Res. Notes 4, 492

Ledgerwood, D.M., Orr, E.S., Kaploun, K.A., Milosevic, A., Frisch, G.R., Rupcich, N., Lundahl, L.H., 2012. Executive Function in Pathological Gamblers and Healthy Controls. J. Gambl. Stud. 28, 89-103.

Leeman, R.F., Potenza, M.N., 2012. Similarities and Differences between Pathological Gambling and Substance Use Disorders: A Focus on Impulsivity and Compulsivity. Psychopharmacol. (Berl) 219, 469-490.

Leppink, E.W., Redden, S.A., Grant, J.E., 2016. Impulsivity and gambling: A complex clinical association across three measures. Am. J. Addict. 25, 138-44.

Marazziti, D., Dell'Osso, M.C., Conversano, C., Consoli, G., Vivarelli, L., Mungai, F., Di Nasso, E., Golia, F., 2008. Executive function abnormalities in pathological gamblers. Clin. Prac. Epidem Mental H. 4, 7.

Odlaug, B.L., Chamberlain, S.R., Kim, S.W., Schreiber, L.R., Grant, J.E., 2011. A neurocognitive comparison of cognitive flexibility and response inhibition in gamblers with varying degrees of clinical severity. Psychol. Med. 41, 2111-2119.

Pallanti, S., DeCaria, C.M., Grant, J.E., 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, 431-443.

Patton, J.H., Stanford, M.S., Barratt, E.S., 1995. Factor structure of the Barratt impulsiveness scale. J. Clin. Psychol. 51, 768-774.

Probst, C.C., van Eimeren, T., 2013. The functional anatomy of impulse control disorders. Curr. Neurol. Neurosci. Rep. 13, 1-10.

Quednow, B.B., Csomor, P.A., Chmiel, J., Beck, T., Vollenweider, F.X., 2008. Sensorimotor gating and attentional set-shifting are improved by the mu-opioid receptor agonist morphine in healthy human volunteers. Int. J. Neuropsychopharmacol. 11, 655-69.

Rosner, B. Fundamentals of Biostatistics. 4th ed. Duxbury Press; Belmont, Calif: 1995

Rugle, L., Melamed, L., 1993. Neuropsychological assessment of attention problems in pathological gamblers. J. Nerv. Mental D. 181, 107–112.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Herqueta, T., Baker, R., Dunbar, G.C., 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 59, 22-33.

Sherrer, J.F., Xian, H., Slutske, W.S., Eisen, S.A., Potenza, M.N., 2015. Associations Between Obsessive-Compulsive Classes and Pathological Gambling in a National Cohort of Male Twins. JAMA 72, 342-349.

Vanes, L.D., van Holst, R.J., Jansen, J.M., van den Brink, W., Oosterlaan, J., Goudriaan, A.E., 2014. Contingency learning in alcohol dependence and pathological gambling: learning and unlearning reward contingencies. Alcohol Clin. Exp. Res. 38, 1602-1610.

van Holst, R.J., van den Brink, W., Veltman, D.J., Goudriaan, A.E., 2010. Why gamblers fail to win: A review of cognitive and neuroimaging findings in pathological gambling. Neurosci. Biobehav. Rev. 34, 87-107.

Wu, M., Brockmeyer, T., Hartmann, M., Skunde, M., Herzog, W., Friederich, H.C., 2014. Set-shifting ability across the spectrum of eating disorders and in overweight and obesity: a systematic review and meta-analysis. Psychol. Med. 44, 3365-85.

Yip, S.W., Potenza, M.N., 1995. Treatment of gambling disorders. Curr. Treat. Options Psychiatry 1, 189-203.

Table 1: Sample Characteristics and Correlates of IED errors in 552 Young Adult Gamblers

	Value	**Correlation Coefficient**	***p***	
IED Total errors (adjusted)	24.41 (22.23)	-	-	-
Gender, N (% Male)	361 (65.4)	-.151	<.001	***
Age, Years	22.219 (3.57)	.080	.060	
Education, N (% Some College or More)	491 (88.9)	-.051	.232	
Race, N (% Caucasian)	405 (73.4)	.196	<.001	***
Gambling Frequency, Per Week	1.70 (2.05)	.193	<.001	***
Money Lost, Past Year	1272.00 (3912.61)	.183	<.001	***
Legal Problems from Gambling, N (% Yes)	4 (.7)	-.034	.421	
Social Problems from Gambling, N (% Yes)	49 (8.9)	.061	.152	
Work Problems from Gambling, N (% Yes)	18 (3.3)	.086	.044	*
Financial Problems from Gambling, N (% Yes)	106 (19.2)	.094	.027	*
SCI-PG, Total Score	1.27 (1.92)	.192	<.001	***
PG-YBOCS, Urge Score	2.32 (2.97)	.168	<.001	***
PG-YBOCS, Behavior Score	2.53 (3.24)	.135	.001	***
PG-YBOCS, Total Score	4.86 (5.92)	.158	<.001	***
Major Depression, N (% Current)	21 (3.8)	.143	.001	***
Anxiety Disorder, N (% Current)	64 (11.6)	.113	.008	**
Alcohol Dependence, N (% Current)	79 (14.3)	.042	.321	
Substance Dependence: N; % Current	50 (9.1)	.143	.001	***
Any Impulse Control Disorder, N (% Current)	53 (9.6)	.122	.004	**
BIS: Attentional Impulsivity	16.86 (4.05)	.004	.933	
BIS: Motor Impulsivity	23.80 (4.66)	.062	.145	
BIS: Non-planning Impulsivity	24.24 (5.33)	.130	.002	**
Padua Inventory, Total Score	18.00 (17.32)	.188	<.001	***

All values are Mean (SD) unless otherwise noted

* = Significant at $p \leq .05$; ** = Significant at $p \leq .01$; *** = Significant at $p \leq .001$

SD = Standard Deviation; IED = Intra/Extradimensional Set Shift; SCI-PG = Structured Clinical Interview for Pathological Gambling; YBOCS = Yale-Brown Obsessive-Compulsive Scale adapted for Pathological Gambling; BIS = Barratt Impulsiveness Scale

Table 2. Results from significant linear regression model with total IED errors (adjusted) as the dependent variable.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	28.634	8.646	---	3.312	.001
Gender	-5.796	1.993	-.124	-2.909	.004
Age (years)	-.357	.282	-.057	-1.267	.206
Education (some college or greater)	-1.698	2.935	-.024	-.579	.563
Race	5.591	2.255	.111	2.480	.013
Gambling Frequency, Per Week	1.356	.527	.125	2.571	.010
Money Lost, Past Year	.001	.000	.131	2.929	.004
Legal Problems from Gambling	-8.078	11.264	-.031	-.717	.474
Social Problems from Gambling	-.295	3.857	-.004	-.077	.939
Work Problems from Gambling	.771	5.652	.006	.136	.891
Financial Problems from Gambling	-2.377	2.784	-.042	-.854	.394
SCI-PG, Total Score	.196	.830	.017	.236	.814
PG-YBOCS, Urge Score	.325	.560	.044	.581	.561
PG-YBOCS, Behavior Score	-.585	.523	-.085	-1.118	.264
PG-YBOCS, Total Score#	---	---	---	---	---
Major Depressive Disorder (current)	7.096	5.069	.061	1.400	.162
Anxiety Disorder (current)	2.607	3.076	.038	.848	.397
Alcohol Dependence (current)	.465	2.725	.007	.170	.865
Substance Dependence (current)	6.244	3.360	.081	1.858	.064
Impulse Control Disorder (current)	5.028	3.325	.067	1.512	.131
BIS: Attentional Impulsivity	-.583	.281	-.106	-2.075	.039
BIS: Motor Impulsivity	.027	.252	.006	.106	.916
BIS: Non-planning Impulsivity	.458	.220	.110	2.082	.038
PADUA Inventory, Total Score	.093	.059	.073	1.576	.116

excluded due to failing collinearity test; PG-YBOCS = Yale-Brown Obsessive-Compulsive Scale adapted for Pathological Gambling; BIS = Barratt Impulsiveness Scale; IED = Intra/Extradimensional Set Shift; SCI-PG = Structured Clinical Interview for Pathological Gambling;

Table 3. Results from significant linear regression model with pre-ED errors as the dependent variable.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	3.166	1.428	---	2.217	.027
Gender	.610	.328	.082	1.859	.064
Age (years)	.026	.046	.026	.568	.570
Education (some college or greater)	-.858	.484	-.076	-1.772	.077
Race	.972	.373	.121	2.604	.009
Gambling Frequency, Per Week	-.047	.087	-.027	-.538	.591
Money Lost, Past Year	.000	.000	.119	2.596	.010
Legal Problems from Gambling	.216	1.857	.005	.117	.907
Social Problems from Gambling	-.712	.639	-.057	-1.115	.265
Work Problems from Gambling	2.230	.932	.112	2.391	.017
Financial Problems from Gambling	-.039	.459	-.004	-.085	.933
SCI-PG, Total Score	.154	.135	.082	1.140	.255
PG-YBOCS, Urge Score	-.034	.093	-.028	-.364	.716
PG-YBOCS, Behavior Score	-.018	.087	-.016	-.206	.837
PG-YBOCS, Total Score#	---	---	---	---	---
Major Depressive Disorder (current)	-.797	.875	-.041	-.911	.363
Anxiety Disorder (current)	.119	.508	.011	.234	.815
Alcohol Dependence (current)	-.176	.454	-.017	-.387	.699
Substance Dependence (current)	-.446	.556	-.036	-.801	.423
Impulse Control Disorder (current)	.018	.046	.021	.394	.693
BIS: Attentional Impulsivity	.037	.042	.049	.896	.371
BIS: Motor Impulsivity	.042	.036	.063	1.150	.251
BIS: Non-planning Impulsivity	.001	.010	.007	.139	.890

excluded due to failing collinearity test; PG-YBOCS = Yale-Brown Obsessive-Compulsive Scale adapted for Pathological Gambling; BIS = Barratt Impulsiveness Scale; IED = Intra/Extradimensional Set Shift; SCI-PG = Structured Clinical Interview for Pathological Gambling;

Table 4. Results from significant linear regression model with ED errors as the dependent variable.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	11.822	3.905	---	3.027	.003
Gender	-3.082	.900	-.148	-3.424	.001
Age (years)	-.134	.127	-.048	-1.053	.293
Education (some college or greater)	-.634	1.325	-.020	-.479	.632
Race	1.043	1.018	.047	1.024	.306
Gambling Frequency, Per Week	.534	.238	.111	2.244	.025
Money Lost, Past Year	.000	.000	.069	1.523	.128
Legal Problems from Gambling	-2.786	5.087	-.024	-.548	.584
Social Problems from Gambling	-1.399	1.742	-.040	-.803	.422
Work Problems from Gambling	2.183	2.552	.039	.855	.393
Financial Problems from Gambling	-.725	1.258	-.029	-.577	.564
SCI-PG, Total Score	.241	.375	.047	.644	.520
PG-YBOCS, Urge Score	.079	.253	.024	.311	.756
PG-YBOCS, Behavior Score	-.049	.236	-.016	-.206	.837
PG-YBOCS, Total Score#	---	---	---	---	---
Major Depressive Disorder (current)	-2.368	2.289	-.046	-1.034	.301
Anxiety Disorder (current)	2.517	1.389	.082	1.812	.071
Alcohol Dependence (current)	-2.012	1.231	-.071	-1.635	.103
Substance Dependence (current)	2.257	1.517	.066	1.487	.138
Impulse Control Disorder (current)	.734	1.501	.022	.489	.625
BIS: Attentional Impulsivity	-.127	.127	-.052	-1.003	.316
BIS: Motor Impulsivity	-.012	.114	-.006	-.105	.916
BIS: Non-planning Impulsivity	.145	.099	.078	1.461	.145
PADUA Inventory, Total Score	.060	.027	.105	2.242	.025

excluded due to failing collinearity test; PG-YBOCS = Yale-Brown Obsessive-Compulsive Scale adapted for Pathological Gambling; BIS = Barratt Impulsiveness Scale; IED = Intra/Extradimensional Set Shift; SCI-PG = Structured Clinical Interview for Pathological Gambling;

Acknowledgements

None

Contributors

Eric Leppink: Mr. Leppink drafted the manuscript and conducted the data analysis.

Sarah Redden: Ms. Redden collected the data and assisted in drafting the manuscript.

Samuel Chamberlain: Dr. Chamberlain conducted data analysis and assisted in drafting the manuscript.

Jon Grant: Dr. Grant designed the study, collected data, and drafted the manuscript.

Financial Support

This research was supported by the National Center for Responsible Gaming (NCRG). The NCRG did not play any role in the analysis, interpretation, or preparation of this manuscript.