

**Gambling Disorder and Its Relationship with Substance Use Disorders:
Implications for Nosological Revisions and Treatment**

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- Abstract: 143
- Narrative: 3073
- Number of Tables: 0
- Number of Figures: 0
- Number of References: 78

Abstract

Background: Gambling disorder, recognized by the DSM-5 as a behavioral addiction, affects 0.4 to 1.6% of adults worldwide, and is highly comorbid with other mental health disorders, particularly substance use disorders (SUDs). Objectives: to provide a concise primer on the relationship between gambling disorder and SUDs, focusing on phenomenology/clinical presentation, co-morbidity, familiarity, cognition, neuroanatomy/neurochemistry, and treatment. Methods: Selective review of the literature. Results: Scientific evidence shows that gambling and SUDs have consistently high rates of comorbidity, similar clinical presentations, and some genetic and physiological overlap. Several treatment approaches show promise for gambling disorder, some of which have previously been effective for SUDs. Scientific Significance: It is hoped that recognition of overlap between gambling disorder and SUDs in terms of phenomenology and neurobiology will signal novel treatment approaches and raise the profile of this neglected condition.

Introduction

Gambling disorder (otherwise known as pathological gambling) is a psychiatric condition characterized by persistent and recurrent maladaptive patterns of gambling behavior, leading to impaired functioning. It is associated with reduced quality of life, and high rates of bankruptcy, divorce, and incarceration.¹ Although most people who engage in one or more forms of gambling do so responsibly and without undue negative impact on life, some individuals find that they become preoccupied with gambling and it has multiple negative consequences. For these people, their gambling behavior has devastating consequences that impact the individual, his or her family, and society.² National studies and one meta-analysis of state and regional surveys suggest that the prevalence of gambling disorder in the general United States population ranges from 0.42% to 1.9%.^{3,4} Similar rates of gambling disorder have been reported in other countries.² Data also suggest that money spent on gambling around the world, both online and in gambling establishments, has grown steadily over the last twenty years.⁵ With the growth of gambling opportunities may come increased problematic gambling behavior. Individuals seeking treatment for substance use disorders (SUDs) may be particularly vulnerable to developing a gambling disorder.⁶ As such, recognition of gambling disorder, its relationship to SUDs, and its treatment appear worth of attention from a global public health perspective.

Far from being an exclusively modern formulation, excessive gambling behaviors have been reported for millennia across cultures and have been discussed in the medical literature since the early 1800s.² However, pathological forms of gambling have only been recognized fairly recently by psychiatric nosological classification systems. Though recognized by both Kraepelin and Bleuler, disordered gambling behavior was first formally recognized with the inclusion of pathological gambling as a 'Disorder of Impulse Control' in the Diagnostic and

Statistical Manual Version III (DSM-III).⁷ Subsequent revisions of DSM modeled the diagnostic criteria on those of substance dependence, recognizing the phenomenological parallels between these two types of disorder. The disorder was categorized as an “Impulse-Control Disorders Not Elsewhere Classified,” along with other disorders such as kleptomania, pyromania, and trichotillomania. The Diagnostic and Statistical Manual version 5 (DSM-5)⁸ reflects an important departure from DSM-IV-TR⁹ as the current chapter “Substance-Related and Addictive Disorders” now includes *Gambling Disorder*, formerly listed with the “Impulse Control Disorders Not Elsewhere Classified.”⁸

The placement of gambling disorder in the most recent nosological revision is likely to improve recognition of the disorder, especially among substance abusers who are at high risk for gambling problems.⁶ The name has been changed from pathological gambling to “gambling disorder,” mainly to reduce stigma attached to the word “pathological.” The DSM-5 diagnosis requires that 4 of 9 symptoms be endorsed to qualify for the diagnosis of gambling disorder. This is a change from DSM-IV-TR wherein 5 of 10 symptoms were required. DSM-5 eliminated the symptoms that the gambling resulted in illegal acts as it has been shown to have a low prevalence with its elimination having little or no effect on the information associated with the diagnosis. As with the DSM-IV, the criteria for gambling disorder mirror those used for the SUDs: tolerance (needing to gamble with increasing amount of money), withdrawal (restless or irritable when cutting back), and compulsive use (preoccupied with gambling, chasing losses, repeated unsuccessful attempts to cut control gambling, and gambling as a way of escaping from problems) are the cardinal features. The adverse consequences of addiction are also reflected in the remaining symptoms (lying to others, jeopardizing important relationships, and relying on others financially). Unlike the DSM-5 substance use disorders which have been modified to

include craving or urge as a possible diagnostic criterion, no such addition was made for gambling disorder.

There exist several comprehensive reviews of specific aspects of gambling disorder¹⁰⁻¹⁵ In view of recent proposed reclassification of pathological forms of gambling alongside SUDs, the aim of this paper is to provide a concise primer examining overlap between gambling disorder and the SUDs, incorporating very recent evidence derived from the neurosciences. We highlight implications for neurobiological models and new treatment directions, along with limitations of this approach and areas in which research is lacking.

Phenomenology and clinical features

Diagnostic criteria for DSM-5 gambling disorder show substantive parallels with those for SUDs, reflecting the derivation of former criteria from those for the latter. Both sets of criteria include *inter alia* preoccupation, tolerance, repeated unsuccessful attempts to stop the pathological behavior, restlessness/irritability when attempting to resist the pathological behavior, and escalation (e.g. in frequency or ‘amount’) over time. Only a small proportion of the individuals who are suffering from gambling disorder seek formal treatment.¹⁶ Approximately one-third of individuals with gambling disorder recover from their illness episode without accessing formal treatment services¹⁷ (similar to the rates seen in other addictive disorders, such as alcohol use disorders¹⁸).

Gambling usually begins in childhood or adolescence, evolving into pathological forms into early adulthood, with males tending to start at an earlier age.^{1,19} This is also the case for many manifestations of SUDs.²⁰ Both SUDs and gambling disorder are more frequently observed in men, with a telescoping phenomenon observed in females (i.e., women have a later initial engagement in the addictive behavior, but foreshortened time period from initial

engagement to addiction).²¹ Although prospective studies are largely lacking, gambling disorder appears to follow a trajectory similar to that of substance dependence, with high rates in adolescent and young adult groups, lower rates in older adults, and periods of abstinence and relapse.¹⁷

Both female and male gamblers report that advertisements are a common trigger of their urges to gamble,^{1,22} a finding redolent of substance addictions in which conditioning is central to understanding and treatment: exposure to environmental stimuli previously linked with the substance can trigger such urges to re-engage ('craving').^{23,24} Many gamblers experience severe financial, social, and/or legal problems,¹ as do people with SUDs.⁸ Both lead to work-related problems such as absenteeism, poor performance and unemployment.²⁵

Many individuals with gambling disorder report the need for psychiatric hospitalization owing to depression and related suicidality brought on by their gambling losses.²⁶⁻²⁸ The often overwhelming financial consequences and guilt associated with gambling disorder may also contribute to attempted or completed suicide. A study of Gamblers Anonymous participants (recruited through a gambling telephone hotline) found that 17% to 24% reported having attempted suicide due to gambling.²⁹ SUDs are amongst the psychiatric disorders most predictive of suicidality and self-harm, second only to depression, which of course is also common in individuals with gambling disorder.³⁰⁻³²

Comorbidity

Psychiatric comorbidity is common in individuals with gambling disorder. Frequent co-occurrence has been reported between SUDs (including nicotine dependence) and gambling disorder, with the highest odds ratios generally observed between gambling and alcohol use

disorders.^{5,32-36} Among clinical samples, 52% of Gambler's Anonymous participants reported either alcohol or drug abuse, and 35% to 63% of individuals seeking treatment for gambling disorder also screened positive for a lifetime SUD,³⁷ rates notably higher than that found in the general population (26.6%).³⁸ Studies also demonstrate that individuals with gambling disorder have high rates of lifetime mood (60% - 76%), anxiety (16% - 40%), and personality (87%) disorders, particularly anti-social personality disorder.^{39,40} Elevated rates of other behavioral addictions (compulsive buying and compulsive sexual behavior) have also been found.³⁹ In a systematic review and meta-analysis of the available population surveys exploring comorbid disorders in individuals with gambling disorder,⁴¹ the strongest associations were with nicotine dependence (mean co-morbidity of 60.1% of subjects), followed by SUDs in general (57.5%), followed by any mood disorder (37.9%).

Familiality

Psychiatric disorders are common in the first-degree relatives of those with gambling disorder, particularly mood, anxiety, substance use, and antisocial personality disorders. For example, earlier studies reported alcohol use disorder in 18-50% of first-degree relatives of people with gambling disorder. More recent studies have incorporated control groups. Black and colleagues examined 31 gamblers, 31 control subjects, and first-degree relatives,⁴² thereby quantifying familial aggregation of psychiatric disorders. Lifetime estimates of gambling disorder were significantly higher in family members of gamblers (8.3%) compared to control subjects (2.1%) (odds ratio of 4.49). Similarly elevated estimates were observed for substance use disorders (odds ratio of 4.21). In a separate study conducted in males with gambling disorder (n=52) and their first-degree relatives (n=93), higher prevalence of SUDs, problematic gambling,

depression, and anxiety disorders were found in first-degree relatives of people with gambling disorder versus first-degree relatives of controls.⁴³

Twin studies also support etiological overlap between gambling disorder and SUDs. Using the Vietnam Era Twin Registry (male adults), statistical models were used to determine whether risk factors for DSM-III-R pathological gambling overlapped with those for alcohol dependence.⁴⁴ The authors found that 12-20% of genetic and 3-8% of non-shared environmental variation in risk for pathological gambling was accounted for by risk of alcohol dependence. Data from the national Australian Twin Registry were used in conjunction with statistical models to examine whether genetic risk factors for disordered gambling were shared with alcohol use disorders.⁴⁵ Genetic correlations between these conditions was 0.29-0.44, being particularly strong in males, suggesting that up to two-thirds of the association was attributable to shared genetic vulnerability. The latter study considered both DSM-IV and DSM-5 definitions for gambling disorder /pathological gambling.

Neurocognition

The behaviors that characterize problematic gambling (e.g., chasing losses, preoccupation with gambling, inability to stop) are suggestive of underlying problems with cognitive functions dependent on the integrity of fronto-striatal circuitry.⁴⁸ Such behaviors are impulsive in that they are often premature, poorly thought out, risky, and result in deleterious long-term outcomes.^{49,50} Deficits across multiple dissociable cognitive functions have been identified in people with pathological gambling versus healthy controls, including in aspects of inhibition, working memory, planning, cognitive flexibility, and time management/estimation.^{2,15}

Studies examining gambling disorder and SUDs have found that both groups are characterized by diminished performance on inhibition, time estimation, cognitive flexibility, decision-making, spatial working memory, and planning tasks.⁴⁹ A temporal relationship, however, has not been established between cognitive deficits and clinically significant symptoms, and these deficits could occur in people ‘at risk’ before symptoms develop, or alternatively stem from the disorder itself, perhaps even reflecting a secondary or indeed incidental epiphenomenon. Most likely, some cognitive deficits predispose (perhaps running in families and representing candidate endophenotypes or intermediate markers of risk^{50,51}), while others could be a consequence of recurrent engagement in gambling itself. Certainly some aspects of cognitive dysfunction appear to occur not only in people with SUDs but also in their clinically unaffected first-degree relatives.⁵² While studies of cognitive functioning in unaffected close relatives of people with gambling disorder are lacking, findings from people ‘at risk’ of gambling disorders suggest that deficits in decision-making (dependent on neural circuitry including the orbitofrontal and insular cortices) are evident before the illness, while some other domains may be relatively spared.^{53,54}

Gambling addiction represents a useful heuristic model for exploring the ‘cause versus effect’ issue in addiction more broadly, since gambling of itself is presumably relatively unlikely to subtend toxic effects on the brain, as compared to deleterious effects on brain function expected with recurrent use of (at least some types of) illicit substances.

Neurobiology and Pharmacotherapy Treatment

Multiple neurotransmitter systems have been implicated in the pathophysiology of gambling disorder and in SUDs. Dopamine is involved in learning, motivation, and the salience

of stimuli, including rewards. Alterations in dopaminergic pathways have been proposed as underlying the seeking of rewards (i.e. gambling; addictive substances) that trigger the release of dopamine and produce feelings of pleasure.⁵⁵ Neuroimaging studies in gambling disorder have demonstrated diminished ventral striatum and ventromedial prefrontal cortex/ventrolateral prefrontal cortex activity during rewarding events.^{56,57} Dopamine antagonists acting on D2/D3 receptors, however, enhance gambling-related motivations and behaviors in patients with gambling disorder and have no efficacy in the treatment of gambling disorder.⁵⁸⁻⁶⁰ There is a strong body of preclinical evidence arising from over two decades of animal studies suggesting a critical role for glutamate transmission and glutamate receptors in drug reward, reinforcement, and relapse.^{61,62} Some data from cerebrospinal fluid studies also suggest a dysfunctional glutamate system in gambling disorder.⁶³ Medications that possess a glutamatergic mechanism of action (acamprosate, N-acetyl cysteine, gabapentin, lamotrigine, memantine, modafinil, and topiramate) have shown benefit for substance use disorders and have some limited but promising data for gambling disorder.^{64,65} Although no medication has received regulatory approval in any jurisdiction as a treatment for gambling disorder, there have been 18 double-blind, placebo-controlled trials of various pharmacological agents (opioid antagonists, glutamatergic agents, antidepressants, mood stabilizers). A meta-analysis of randomized trials included 16 outcome studies, published between 2000 and 2006 found that pharmacological treatments were more effective than placebo treatment at post-treatment (overall effect size = 0.78).⁶⁶

Research on the use of opioid antagonists, which have a long history in the treatment of substance addictions, has yielded the most promising results for gambling disorder. These medications modulate dopaminergic transmission in the mesolimbic pathway and decrease the urges to gamble as well as the gambling behavior itself.⁶⁵ Pooled analyses of those who

responded to opioid antagonists demonstrated significant reduction in gambling urges, particularly among participants with a positive family history of alcohol dependence.⁶⁷ Other agents, such as those that improve glutamatergic tone in the nucleus accumbens and thereby reduce reward-seeking behavior in addictions, or atypical stimulants that reduce impulsivity, may also be promising treatment approaches for gambling disorder just as they are for substance addictions.⁶⁵

Psychosocial Treatments

Brief treatments (for example, telephone-based motivational interviewing, self-help cognitive-behavioral therapy workbook) have shown short and long-term benefit (i.e. at one and two year follow-up) for people with gambling disorder.^{68,69} Positive findings have been reported for similar treatments in SUDs.⁷⁰⁻⁷²

In terms of longer psychosocial treatments, a meta-analysis identified 22 randomized trials in gambling disorder, published between 1968 and 2004.⁷³ Psychological treatments were more effective than no treatment immediately following treatment and/or at follow-up (average follow up was 17 months later) (overall effect size = 1.59). Most of the treatment studies involved behavioral, cognitive or cognitive-behavioral therapy. In a Cochrane review of CBT studies in gambling disorder, meta-analysis was suggestive of medium-large effect sizes.⁷⁴ Meta-analysis of effect sizes for psychosocial treatments for SUDs showed variable effect sizes depending on the type of treatment and particular SUD under scrutiny, with largest effects reported for CBT plus contingency management; and in the context of cannabis misuse.⁷²

Although borrowing from treatment studies for SUDs, the evidence-based psychosocial treatments for gambling disorder have not aligned identically with traditional substance addiction

treatment. Traditional treatment for SUDs has relied on detoxification, group counseling and education, and strong links to 12-step programs. The field of gambling treatment has relied more on the use of individual psychosocial treatment, and research supports the use of many of the same modalities of treatment (e.g., motivational interviewing, CBT, relapse prevention).

Although perhaps accessed less frequently than in the case of SUDs, 12-step programs are widely available for individuals with gambling disorder. Gamblers Anonymous (GA) was conceived in 1957 in Los Angeles and currently operates in at least 55 countries worldwide. Individuals use a program of twelve steps and twelve traditions, modified from Alcoholics Anonymous (AA), to acknowledge powerlessness over compulsive gambling and to remain gambling-free. The groups promote a sense of common purpose and understanding as well as reinforcement of each consecutive day of abstinence from gambling. Although some data have shown that individuals affiliated with GA have better gambling outcomes than those who do not,⁷⁵ treatment outcome studies that have used referral to GA as a comparison condition to cognitive behavioral treatment have shown poor GA attendance and outcomes.^{75,76}

Conclusions

This selective review has considered evidence for overlap between gambling disorder and SUDs from several perspectives. These two types of conditions share remarkable parallels in terms of disease onset and course, along with overlapping comorbid expression, and evidence for common etiological (genetic and environmental) factors derived from family (including twin) studies. Though head-to-head comparisons are generally lacking, impairment in certain cognitive functions (e.g. relating to decision-making and reward processing) are likely shared by both types of condition, and may even represent predisposing factors occurring prior to the expression

of clinically significant symptoms. Similarly, overlapping neuroanatomical and chemical systems have been implicated. These streams of research have been complemented by increasing recognition of gambling as a ‘behavioral addiction’ in nosological classification, as indicated by its inclusion in the Substance Related and Addictive Disorders chapter of DSM-5.⁸

While we would argue that viewing gambling from an addiction perspective represents a useful heuristic, it is important to note that this perspective is not without its critics, nor is the salient literature free of methodological difficulties. From a phenomenological perspective, criteria for gambling disorder (and its predecessors) were derived somewhat from SUD criteria; that these two types of condition, thusly defined, share overlap in other domains could to some extent be a natural consequence of this (‘circular reasoning’). Gambling disorder and SUDs show co-morbid overlap, but so too does gambling present concomitantly with other conditions (especially depression). That said, a meta-analysis of survey data found that nicotine dependence and SUDs in general appeared to be more strongly linked with gambling disorder than other disorders.⁴¹ Another potential criticism of the ‘addiction approach’ is that it tends to overlook the heterogeneity in the expression of these disorders. Also, a number of unanswered questions remain in relation to treatments of gambling disorders and whether approaches should differ from those used to treat SUDs. For example, how should concurrent substance addiction be addressed in gambling treatment? Should different subtypes of gamblers receive different treatments? Can someone learn to moderate gambling behavior instead of having to be abstinent? These questions need empirical examination, and it may be possible to improve our treatment outcomes through further investigation of these questions. No study has yet examined whether certain individuals with gambling disorder (such as those with versus without comorbid SUDs) would benefit differentially from specific medications, and no research has yet

determined who would benefit more from pharmacotherapy or cognitive behavioral therapy. Finally, our aim here was to provide a concise overview of key research germane to the debate, rather than a comprehensive and detailed review. As such, by necessity some topics were covered in brief and distilled. We draw the readers' attention to reviews elsewhere providing more detail of specific aspects of gambling disorder.¹⁰⁻¹⁵

It is hoped that reclassification of gambling disorder alongside SUDs, along with complementary tiers of research on overlap derived from neurosciences and clinical trials, will improve recognition, neurobiological models, and treatment approaches. A number of distinct treatment approaches have shown promise in helping those with gambling disorder, with large effect sizes at immediate follow-up. As access to multiple types of gambling activities increase throughout the world, more sophisticated research into gambling disorder and its treatment will be needed.

Acknowledgements.

This research was supported by a Center for Excellence in Gambling Research grant by the National Center for Responsible Gaming.

Declaration of Interest.

The authors declare that there are no competing financial interests in relation to the submitted work. Dr. Grant has received research grant support from NIDA, NCRG, Psyadon Pharmaceuticals, Forest Pharmaceuticals, and Transcept Pharmaceuticals. He has also received royalties from American Psychiatric Publishing Inc, Oxford University Press, Norton, and

McGraw Hill Publishers. Dr. Chamberlain has consulted for Cambridge Cognition, P1Vital, Shire, and Lilly.

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