Should addictive disorders include non-substance-related conditions?

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ABSTRACT

Aims In anticipation of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V), to consider whether addictive disorders should include non-substance use disorders. **Methods** The author reviewed data and provided perspective to explore whether disorders such as pathological gambling (PG) should be grouped together with substance dependence, given that they share many features. **Results** PG and substance dependence currently reside in the DSM, fourth edition, text revision (DSM-IV-TR) within separate categories, with PG classified as an impulse control disorder (ICD) and substance dependence as a substance use disorder (SUD). Arguments can be forwarded to support each categorization, as well as to justify their inclusion together as addictions. **Conclusion** The current state of knowledge suggests that there exist substantial similarities between PG and SUDs. Further research is indicated prior to categorizing PG and other ICDs together with SUDs.

Keywords Behavioral addictions, categorization, classification, impulse control disorders, pathological gambling, substance dependence.

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STATEMENT OF THE PROBLEM

This paper seeks to examine the data supporting whether or not the scope of addictions should extend beyond substance use disorders (SUDs). Specifically, within *Diagnostic and Statistical Manual of Mental Disorders* (DSM), should specific mental health disorders be grouped together with SUDs within the category of addictions? If so, which mental health disorders? What additional information is needed to move forward in the appropriate categorization of disorders meeting a definition of addiction?

REVIEW OF THE LITERATURE

Addiction and the DSM

The nomenclature system within the DSM, fourth edition, text revision (DSM-IV-TR; American Psychiatric Association [1]) currently lacks the term addiction. Substance use disorders (SUDs) are categorized according to the specific problematic substance within separate groupings: abuse, dependence, withdrawal and intoxication. Of these categories, dependence might be most likened to addiction, and one could consider changing the nomenclature to replace 'dependence' with 'addiction'. As described in greater detail below, there exist both pros (e.g. limiting confusion regarding the use of the term dependence—physical dependence versus DSM-defined, diagnostic dependence) and cons (e.g. the stigma generally associated with the term addiction) of making such a change.

Defining addiction

In order to determine whether addictions should extend beyond SUDs, it is important to have a definition for the term 'addiction'. Derived from the Latin *addicere* meaning 'bound to' or 'enslaved by', the term was used initially without a specific reference to substance use. Over the past several centuries, it has become identified increasingly with impaired control over substance use behaviors [2]. None the less, there has been a recent shift returning toward consideration of non-substance-related disorders as addictive in nature [3,4]. A central element cited typically in defining addiction is 'loss of control' over a behavior with associated adverse consequences [2,3,5], although 'impaired control' has been cited as a more

appropriate description [2]. Arguments have been forwarded to move toward the use of 'addiction' rather than the current term 'dependence' given confusion over different definitions of dependence. For example, physical dependence can be achieved upon chronic administration of a drug (e.g. a beta-blocker for hypertension) and can include aspects of tolerance and withdrawal but is generally not associated with the harmful effects of an addiction (e.g. drug-seeking and drug-using that interferes with major areas of life functioning—see definition of core elements of addiction in the next paragraph). In other words, a change in terminology might shift the focus of the disorder from chronic use of a substance and the associated physical dependence to the harmful effects of the addictive process on the individuals, their friends, families, society, etc. Thus, more precise terminology might help to reduce controversy over such interventions as methadone maintenance that are associated with physical dependence but reduce the impact of addiction, and would be consistent with the shift following DSM-III away from aspects of physical dependence as the core features of substance dependence.

One description of the core elements of addiction includes (modified from [3]): (1) craving state prior to behavioral engagement, or a compulsive engagement; (2) impaired control over behavioral engagement; and (3) continued behavioral engagement despite adverse consequences. If one adopts these components as core elements of addiction, other behavioral disorders, particularly those currently classified as impulse control disorders (ICDs), warrant consideration as addictions. Consistently, the National Institute on Drug Abuse (NIDA), a research funding agency in the United States, has recently cited as important the study of non-drug behaviors/disorders (pathological gambling, obesity) in understanding substance dependence [6].

Impulsivity and impulse control disorders

The core elements proposed above for addiction share features with a definition proposed for impulsivity [7]: 'a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to the impulsive individual or others'. Applying this definition, impulsivity has relevance to a broad array of psychiatric disorders including substance use, antisocial and borderline personality, bipolar, attention-deficit hyperactivity and impulse control disorders (ICDs) [7]. ICDs are currently grouped together in DSM-IV-TR in the category of 'ICDs Not Elsewhere Classified', and include pathological gambling (PG), kleptomania, pyromania, intermittent explosive disorder, trichotillomania and ICD not specified elsewhere. Similarly, the ICDs are not grouped with SUDs in the International Statistical Classification of Diseases and Related Health Problems–10th Revision (ICD-10) [8], in which PG and other ICDs are grouped in the section of 'Disorders of Adult Personality and Behavior' under the heading of 'Habit and Impulse Disorders'. Additional ICDs have been proposed, including compulsive shopping, compulsive computer use and compulsive sexual behaviors [9,10]. ICDs are particularly relevant to this paper, as ICDs such as PG have been described as 'behavioral addictions' or 'addictions without the drug' because they share similar features with substance dependence [11,12]. The ICDs do not include obsessive compulsive disorder (OCD), another disorder characterized by repetitive interfering behaviors. As discussed later, the relationship between OCD and ICDs is currently incompletely understood.

ICDs are poorly understood in comparison to other psychiatric disorders. Assessments of ICDs have largely been excluded from major psychiatric epidemiological surveys: no ICDs were assessed in the National Comorbidity Survey [13] and only the St Louis site of the Epidemiological Catchment Area study included measures of PG [14]. As such, our understanding of how ICDs fit into the structure of common psychiatry disorders is limited [15,16], and such information would be helpful in determining the most appropriate categorization of PG and other ICDs. One reason for exclusion of ICDs from these studies is that psychometrically validated instruments for assessing these disorders are largely lacking; e.g. the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) does not contain modules for any ICD [17]. However, a SCID-compatible module for PG has been described recently [18], and further psychometric testing of this instrument and development of others will be important. The availability of such instruments could facilitate the inclusion of PG and other ICD measures into routinely conducted national surveys such as the National Household Survey on Drug Abuse, as was recommended Congressionally [19].

The importance of assessing and treating ICDs is highlighted by recent studies suggesting high rates of ICDs in co-occurrence with other psychiatric disorders. For example, a recent study of 204 consecutive psychiatric in-patient admissions observed that following screening over 30% of patients were identified as having a current ICD, in contrast to the less than 2% who were diagnosed upon admission with an ICD [20]. Given that symptoms of ICDs such as PG have been associated with worse treatment outcome in substance use and other psychiatric domains [21], the findings suggest the need for improved identification and treatment of ICDs. Brief screening instruments would be particularly helpful for this purpose [10].

Arguably, PG represents the ICD that has been most studied to date. As such, the remainder of the paper will

focus on PG and provide data relevant to its potential inclusion with substance dependence within a category of addictions.

Diagnostic criteria

The current diagnostic criteria for PG share many features with those for substance dependence [1]. Similar inclusionary criteria exist for interference in major areas of life functioning, tolerance, withdrawal and repeated unsuccessful attempts to cut back or quit. Some differences between the structuring/defining of gambling and substance use disorders currently exist and warrant consideration in DSM-V; e.g. a category for gambling less severe than PG yet still problematic (problem gambling), similar to the DSM structuring of substance abuse versus substance dependence [22].

Clinical characteristics and social factors

Multiple similarities in clinical characteristics have been cited. High rates of PG have been observed in adolescents and young adults and low rates in older adults [23,24], mirroring the patterns seen in SUDs [25]. The natural histories of PG and SUDs suggest that many people recover on their own following peaks of problem behaviors in adolescence and early adulthood [26]. Like those with SUDs, individuals with PG generally score high on measures of impulsiveness [27,28]. Data suggest that other features of SUDs (e.g. Cloninger's and Babor's typologies of alcoholics, severity of PG associated with early age at onset) might be similarly applicable to PG [29,30]. As these typologies have clinically relevant implications [31], these and other possible subtypes of PG (e.g. those based on specific types or patterns of gambling) warrant further examination [32]. Gender differences also appear similar between PG and SUDs. As with most SUDs, women are less likely than men to experience PG [33]. The gender-related phenomenon of 'telescoping' (in which women have a later initial engagement in the addictive behavior, but foreshortened time period from first engagement to addiction) appears applicable to both PG and SUDs [33–36]. Both SUDs and PG are thought to impact a large social network; for example, it has been suggested that each person with PG influences eight to 10 other people [37]. Data suggest that specific racial/ethnic groups, including African Americans and Native Americans, might have higher rates of PG, similar to the findings of higher rates of some SUDs within these groups [38]. Cultural attitudes may influence gambling behaviors. Certain forms of gambling have relatively greater popularity in specific cultures, e.g. the Mahjong and Pachinko forms of gambling in Asian groups. Differences in cultural attitudes may also influence treatment approaches and treatment-seeking for PG [39]. Social acceptedness of behaviors can influence behavioral engagement; e.g. recent changes in attitudes towards tobacco smoking have been associated with a decline in consumption [40]. Changes in the use of heroin by military personnel during and following the Vietnam war suggest the importance of multiple factors (social acceptedness, drug availability, stress) in influencing substance use behaviors. Substantial changes in the social acceptedness and availability of legalized gambling have occurred recently [41]. Although it is not possible to derive a causal relationship, concurrent with the increased availability and social acceptance of gambling there has been an apparent increase in rates of PG [23]. Given the probable strong influence of multiple environmental factors (e.g. socio-economic status, cultural expectations, etc.) on gambling and substance use behaviors in general and specifically on differences observed between racial and ethnic groups, the extent to which these findings suggest similar diagnostic groupings for PG and SUDs should be considered cautiously [38].

Co-occurring disorders

Studies of multiple clinical samples suggest high rates of co-occurrence between SUDs and PG in both directions [10,42]. Limited data exist from nationally representative samples to investigate the co-occurrence of PG with other psychiatric disorders as studies investigating gambling behaviors have generally had limited psychiatric assessments [24], and those investigating psychiatric disorders had limited or no gambling assessments [12]. Data from the St Louis Epidemiologic Catchment Area (ECA) study indicate that problem gamblers (those with one or more symptom of PG) compared with non-gamblers were more likely to use tobacco and alcohol, meet criteria for abuse or dependence for these substances and meet criteria for multiple other psychiatric disorders including antisocial personality, mood, anxiety and psychotic disorders [13]. Among the strongest associations were those for antisocial personality disorder and alcohol use, suggesting that problem gambling is linked closely to externalizing behaviors [13,14]. A recently conducted survey of over 43 000 individuals found high rates of a broad range of Axis I and Axis II disorders to co-occur frequently with PG [43]. Direct investigation of how PG and other ICDs fit into the structure of mental health disorders is needed [14].

The ECA study found no association (odds ratio of 0.6) between problem gambling and OCD [13]. This finding seems particularly relevant given a proposed categorization of PG as an OCD-spectrum disorder [44]. The lack of a significant association between PG and OCD has also been observed in large samples of individuals with OCD [10]. As such, these data do not support a strong link between OCD and PG and do not support their categorization together. As specific ICDs (such as

trichotillomania) appear to co-occur frequently with OCD, more study is needed to determine the extent to which ICDs are related to one another and SUDs.

Personality features and behavioral measures

Individuals with PG and SUDs have been shown to perform similarly on personality and neurocognitive assessments of impulsivity. Both groups have been shown to score highly on self-reported measures of impulsiveness and sensation-seeking [27,28,45]. In contrast, individuals with OCD tend to score high on measures of harm avoidance. Although both PG and OCD subjects score highly on measures of compulsivity, high scores in PG subjects appear limited to impaired control over mental activities and urges/worries about losing control over motor behaviors [46]. In contrast, in OCD subjects the high scores tend to generalize across more domains, including those on which SUD groups score lower (e.g. washing) [47].

PG and SUD groups have demonstrated rapid temporal discounting of rewards, and those with both PG and SUDs tend to show the steepest discounting rates [45,48–50]. Similar to individuals with OCD [51] and SUDs [45,52], individuals with PG have shown disadvantageous performance on the Iowa Gambling Task [53], a paradigm that, by strict definition, does not involve gambling but rather assesses risk–reward decision-making. In people with SUDs, poor performance on the IGT correlates with real-life measures of adverse functioning [52].

Biochemistry

Multiple transmitter systems have been similarly implicated in ICDs and SUDs [8,54]. Many biochemical similarities involving serotonin systems have been observed across disorders linked by impaired impulse control. Low levels of the serotonin metabolite 5-hydroxy-indole-acetic acid have been found in the cerebrospinal fluids of individuals with PG and alcoholism [54]. Levels of platelet monoamine oxidase, considered a peripheral marker of serotonin function, are decreased in subjects with PG, and similar findings have been observed in individuals with SUDs and behaviors characterized by impaired impulse control [54]. Behavioral responses to the partial serotonin $5HT_1/5HT_2$ agonist meta-chlorophenylpiperazine (m-CPP) have been found to distinguish individuals with impaired impulse control, including those with PG and alcohol abuse/dependence, from those without [54]. Specifically, affected individuals report a euphoric response following m-CPP administration whereas unaffected subjects do not. Individuals with impulsive aggression have shown blunted activation of the ventromedial prefrontal cortex (vmPFC) in response to m-CPP and another serotonergic drug (fenfluramine) [55,56]. These findings are similar to those observed in alcoholics following challenge with m-CPP [57]. Further research is needed to examine the extent to which these findings are applicable to PG, other ICDs and other SUDs. Additional biological information, such as that gleaned from biochemical, neuroimaging and genetic studies, is anticipated to have a crucial and expanding role over time in understanding and categorizing disorders appropriately.

Neurocircuitry

Few neuroimaging studies have been performed involving subjects with PG or formal ICDs. Evidence to date suggests similarities between PG, SUDs and other disorders characterized by impaired impulse control. Decreased activation of vmPFC has been observed in PG subjects during the presentation of gambling cues [28] or performance of the Stroop Color–Word Interference Task [58]. Diminished activation of left vmPFC similarly distinguished PG and bipolar subjects from controls during Stroop performance [58,59], and diminished activation of this region has been associated with impulsive aggression in depressed subjects [60]. These findings suggest that vmPFC is involved in impulse regulation across a spectrum of diagnostic disorders. VmPFC has been implicated as a critical component of decision-making circuitry in risk–reward assessment, with abnormal function demonstrated in association with SUDs [52,61].

A brain circuit central to addiction involves the dopaminergic mesolimbic pathway linking the ventral tegmental area to the nucleus accumbens (NAc) or ventral striatum [62]. Developmental models of motivational neurocircuitry underlying PG and SUDs have included dopaminergic activity within the NAc as a focal point [63,64]. Emerging brain imaging data suggest that similar components of the mesolimbic pathway are involved in PG and SUDs. During a guessing task that simulated gambling, PG compared with control subjects showed less ventral striatal activation than did controls, and gambling severity correlated inversely with ventral striatal activation [65]. Similarly, adults with alcohol dependence versus those without have been found to activate ventral striatum less robustly in anticipation of working for monetary reward [66], and similar findings have been observed in subjects' family history positive for alcoholism versus family history negative ones [67]. In that healthy adolescents versus young adults also showed diminished ventral striatal activation during task performance, the findings might help to explain the high rates of addiction observed during adolescence [68]. Diminished ventral striatal activation in addiction also appears relevant to craving states. In a study of gambling urges in PG and cocaine cravings in cocaine dependence (CD), diminished activation of ventral striatum similarly distinguished addicted (PG, CD) from control subjects during

viewing of the respective gambling or drug videotapes [69].

A 'reward deficiency' model of addiction was proposed that is consistent with the recently obtained imaging data [70]. This model could account for the pattern of rapid discounting of rewards that is observed in PG and SUDs. That is, small, immediate rewards have been found to activate preferentially brain regions implicated in PG and SUDs, including the ventral striatum and vmPFC [65,71].

While neuroimaging data suggest similarities between PG and SUDs, they suggest differences between PG and OCD. Multiple cue provocation studies have found increased activity of cortico–striatal–thalamo–cortical circuitry in OCD [72]. In contrast, relatively decreased activation of these brain regions were observed during gambling urges in PG [28].

Genetics

The best support for genetic contributions to PG and SUDs come from studies of the Vietnam Era Twin Registry [73]. These studies indicate heritable contributions to PG [74] and shared environmental and genetic contributions to PG and alcohol dependence [75] and PG and antisocial behaviors [76]. These findings are similar to those suggesting common genetic contributions to a range of drug use disorders [77].

Molecular genetic studies have suggested similarities between PG and SUDs. For example, the D2A1 allele of the D2 dopamine receptor gene (DRD2) has been reported to increase in frequency from non-addicted to PG and co-occurring PG and SUD groups [78]. Similarly, the gene has been implicated in PG with and without SUDs [79]. More conclusive data from genome-wide studies are emerging and similarly implicate genes in PG and SUDs [80]. As genetic factors have been associated with positive outcome for treatment of SUDs [81], genetic sampling should be considered in treatment trials in PG and other ICDs.

Treatment

Pharmacological treatments for PG and other ICDs are at an early stage of testing [9]. No drugs are currently approved by the FDA for the treatment of PG or other ICDs and, of the small number of placebo-controlled trials performed to date, they have generally been short-term, involved small samples and excluded individuals with co-occurring disorders [82]. As with SUDs, serotonin reuptake inhibitors have shown mixed results in the treatment of PG [9]. The mu-opioid-receptor antagonist naltrexone has Food and Drug Administration (FDA) approval for the treatment of opioid and alcohol dependence. Naltrexone is thought to mediate its therapeutic effects in treating addictive disorders through opioid-receptor-mediated, indirect modulation of activity within the mesolimbic dopamine system [82]. Naltrexone has been found to be superior to placebo in the treatment of PG [82]. As in SUDs, naltrexone appears to target addictive urges in PG, as the drug was most efficacious in individuals with strong gambling urges at treatment onset [83]. Data with nalmefene provide further support for a role of opioid receptor antagonism in the treatment of PG [84] and additional evidence for a link between PG and SUDs [85].

Behavioral treatments are at an early stage of testing for PG and other ICDs [86]. As in SUDs, 12-Step self-help groups have long been a mainstay of gambling treatment, with data suggesting high initial dropout rates but improvement related to continued attendance [87]. Existing data support roles for several therapist-driven techniques (motivational interviewing, motivational enhancement, cognitive behavioral therapy) in the treatment of PG [88,89]. These interventions have largely been modeled after those that have been shown to be effective in the treatment of SUDs [90,91]. As data suggest that in the treatment of SUDs combined behavioral and pharmacological intervention is generally more effective than either alone [92], the investigation of such approaches is needed in PG and other ICDs.

Alternative models

An alternative hypothesis has posited that PG represents a mood-spectrum disorder [93]. Consistent with this model, high rates of depressive disorders have been observed in conjunction with PG [13,42], shared genetic contributions to PG and major depression have been found [94], similar brain activation patterns have been observed between PG and bipolar subjects during Stroop performance [58,59] and similar pharmacotherapies have been emerging as effective treatments for PG and bipolar disorder [82,95]. However, many of the clinical features central to PG (e.g. the diagnostic criteria) are more similar to SUDs than to depression, with the exception of gambling to relieve a dysphoric mood [1]. Several of the links between PG and mood disorders also apply to SUDs [96], suggesting the need for further research in the area of co-occurring disorders to identify common contributions to ICDs, SUDs and mood disorders. Other models (e.g. conceptualization of PG along antisocial/conduct or attention-deficit spectrums) could also be considered, and additional studies into the underlying biologies of these psychiatric disorders and their overlap with PG, other ICDs and SUDs should help generate more precise diagnostic categorization.

Conclusions

Existing data suggest that: (1) PG shares many features with SUDs (supporting their grouping together as addictions); (2) PG does not share as many features with

OCD (not supporting the grouping of PG with OCD as an OCD-spectrum disorder); and (3) PG and mood disorders share features (suggesting the need for more investigation into the underlying mechanisms). The current categorization of PG as an ICD is not inconsistent with these other categorizations, and increased impulsivity or disadvantageous risk-reward decision-making appears to be a common link across PG, other ICDs and SUDs.

IDENTIFICATION OF RESEARCH GAPS AND SPECIFIC RECOMMENDATIONS

Research gap 1: assessing and categorizing ICDs

Although substantial data exist for the inclusion of PG within the framework of addictions, less data are available for other ICDs. More work is needed to characterize the formal ICDs currently grouped together in the DSM, as well as those currently under various stages of consideration (compulsive shopping, compulsive computer use, compulsive sexual behaviors). Other disorders characterized by impaired impulse control (e.g. attention-deficit hyperactivity and binge-eating disorder) should be examined further with respect to their relationship to formal ICDs and SUDs. Empirically validated instruments for assessment of ICDs are needed, such that these disorders can be routinely assessed in large epidemiological studies and on-going surveys of risk behaviors (e.g. the National Household Drug Abuse, Monitoring the Future and CDC Youth Risk Behavior Surveys). Information from such studies would be helpful in monitoring the relationship over time between ICDs and other psychiatric disorders, including SUDs. Formal analysis of where PG and other ICDs fit within the structure of common psychiatric disorders is needed. Such studies should help to clarify the extent to which disorders such as PG, other ICDs, major depression, SUDs and other psychiatric disorders should be grouped together or separately. Longitudinal assessments would be important in gathering more information on the natural histories of PG and other ICDs with respect to SUDs and other psychiatric disorders. Specific questions investigating the relationship between risk behaviors (e.g. does one usually gamble when drinking or smoking and vice-versa) would help to define aspects that have until now been largely only associated. Inclusion of subsyndromal measures are important given concerns regarding the most appropriate threshold for diagnosing PG and the observation of increased psychopathology in groups engaging in subsyndromal levels of gambling. Such information would be helpful in determining the extent to which additional diagnostic categories (e.g. problem gambling) should be considered in DSM-V, as well as the extent to which public health guidelines should be considered for gambling as currently exist for alcohol consumption. The readiness of psychiatrists, other health-care providers and patients to define PG and other ICDs as addictions warrants consideration. For example, the term 'addiction' has historically carried negative connotations, and resistance might be encountered regarding incorporation of the term into the DSM. Additionally, given the small amount of data on ICDs other than PG, should PG be removed from its current categorization as an ICD or would the entire category be moved with less data to justify a shift?

Research gap 2: special populations

Most research performed to date in PG has involved predominantly or exclusively Caucasian men, generating a deficiency in our understanding of other groups. As with SUDs, in studies in which subgroups have been identified, differences have often been observed. As with SUDs, certain groups (adolescents and young adults, males) appear to have higher rates of PG. Other groups also warrant specific consideration: women may be considered in some ways more susceptible than men to PG and SUDs given the telescoping phenomenon, and older adults despite lower rates of PG and SUDs may be particularly vulnerable given limited abilities to regain lost money. More research is needed to substantiate links between PG, other ICDs and SUDs across specific populations, and to investigate the specific factors that influence addictive behaviors within these groups (environmental, biochemical, neural, genetic factors). Both risk (e.g. experiencing of stressful life events) and protective factors (e.g. school attendance or community involvement) should be better characterized for specific populations to assess the extent to which similar processes contribute to PG, other ICDs and SUDs. Research into the applicability of current diagnostic criteria across specific groups (e.g. age and gender) should be performed similarly or concordantly in order to investigate the importance of differences (e.g. in inclusionary criteria or thresholding thereof) across ICDs and SUDs for specific populations.

Research gap 3: neuroscience: neurocognition/ neuroimaging

Recent advances in neuroscience have resulted in the rapid acquisition of large amounts of data. However, few ICDs have been studied using these techniques. Specific investigations using brain imaging [magnetic resonance imaging (MRI), functional MRI(fMRI), positron emission topography (PET), single photon emission computed tomography (SPECT)] are needed involving subjects with PG and other ICDs. Structural MRI studies are needed to examine PG and ICD subjects and the relationship between brain structure and symptom severity and other clinical characteristics. Functional imaging studies,

particularly those using paradigms targeting impulsivity and risk–reward decision-making, seem particularly salient to PG, other ICDs and SUDs. Studies investigating patterns of brain connectivity (e.g. using diffusion tensor imaging or independent component analysis techniques) would be helpful in identifying whether similar neural circuits are disrupted in ICDs and SUDs. Ligand-based studies of neurotransmitter systems implicated in PG and other ICDs are needed to evaluate the extent to which specific neurotransmitter systems are similarly dysregulated in ICDs and SUDs. These studies would be of particular relevance to providing an empirical basis for the testing of specific pharmacological treatments across ICDs and SUDs. Using similar assessments and paradigms across multiple, theoretically linked diagnostic groups would facilitate the identification of common elements across diagnostic groups. Genetic factors, particularly commonly occurring, functional allelic variants known to influence brain activity, should be examined in conjunction with neuroimaging in PG, other ICDs and SUDs. The inclusion of personality or neurocognitive measures (e.g. those targeting aspects of impulsivity and compulsivity) would allow for further assessment that could be used in conjunction with imaging methods and treatment trials to better explore PG and other ICDs and their relationships to SUDs and other psychiatric disorders. Incorporation of such measures into treatment studies of ICDs and SUDs could help to determine the extent to which similar pathological processes should be targeted across SUDs and ICDs. Given the high rates of co-occurrence between PG and other psychiatric disorders including SUDs, future imaging studies of individuals with these co-occurring disorders are important. Incorporation of imaging modalities into behavioral and pharmacological treatment studies of ICDs and SUDs could help to identify the extent to which similar brain activation changes are associated with effective outcome across disorders.

Research gap 4: neuroscience: genetics

Few large-scale genetic studies have included measures of PG and other ICDs. A more thorough investigation of existing data from the Vietnam Era Twin Registry could characterize further the relationship between PG, SUDs and other psychiatric disorders. Additional twin studies beyond the exclusively older male Vietnam Era Twin Registry group are needed to examine women and sociocultural influences on expression of PG, other ICDs, SUDs and other psychiatric disorders, as well as to estimate genetic and environmental contributions to the disorders within a current environmental context. Genome-wide, molecular genetic studies using current strategies (e.g. affected sibling-pair designs) are needed for probands with PG and other ICDs to identify specific genetic contributions to the disorders and determine the extent to which they are similar to or distinct from SUDs. Genetic factors contributing to specific stages of progression of PG and other ICDs should be identified and compared with those identified in similar studies of SUDs. Genetic studies should employ measures of environmental influences given data supporting gene × environment interactions in the development of psychiatric disorders. Identification of specific genes similarly contributing to PG, other ICDs and SUDs could facilitate targeting of specific therapies across disorders. Identification of specific genetic factors relating similarly to treatment outcome with similar behavioral or pharmacological therapies across disorders would suggest the correction of similar pathological processes across ICDs and SUDs.

Conclusion

PG and other ICDs have historically received relatively little attention from the mental health research and treatment communities. As such, substantial gaps of knowledge exist in the biological, phenomenological and clinical characteristics of ICDs and in the relationship between specific ICDs and other disorders. As recent studies have suggested that ICDs are relatively common [19], it is important not only to understand better the basic mechanisms underlying the disorders, but also to advance prevention and treatment strategies [9]. Examinations should carefully investigate the relationship between ICDs and other psychiatric disorders given the high rates of co-occurrence observed between ICDs and other disorders in population-based and clinical samples [19,43]. The improved understanding of the relationship between ICDs and other psychiatric disorders, particularly SUDs, has important implications not only for the categorization of ICDs, but also for improving prevention and treatment strategies [85].

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