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Behavioral addictions in addiction medicine: from mechanisms to practical considerations

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Abstract

Recent progress has been made in our understanding of nonsubstance or "behavioral" addictions, although these conditions and their most appropriate classification remain debated and the knowledge basis for understanding the pathophysiology of and treatments for these conditions includes important gaps. Recent developments include the classification of gambling disorder as a "Substance-Related and Addictive Disorder" in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and proposed diagnostic criteria for Internet Gaming Disorder in Section 3 of DSM-5. This chapter reviews current neuroscientific understandings of behavioral addictions and the potential of neurobiological data to assist in the development of improved policy, prevention, and treatment efforts.

Keywords

Gambling disorder; Internet; Gaming; Addiction; Neuroscience; Treatment

1 INTRODUCTION

While debated, the concept of nonsubstance or "behavioral" addictions has gained traction as evidenced by the recent classification of gambling disorder as a "Substance-Related and Addictive Disorder" in the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) and definition in Section 3 of DSM-5 of diagnostic criteria for Internet gaming disorder (IGD) (American Psychiatric Association, 2013; Petry and O'Brien, 2013). These classification and inclusion efforts have been informed by neuroscientific data. A current challenge exists in translating a neuroscientific understanding of these disorders into

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more effective treatments. Behaviors that may involve excessive or problematic engagement include gambling, Internet use, and gaming. The following chapter reviews the current neurobiological understanding of, and discusses treatment implications with respect to, excessive and interfering patterns of gambling, Internet use, and gaming.

2 GAMBLING DISORDER

The reclassification of gambling disorder in the DSM-5 was based upon evidence of clinical, neurobiological, and other similarities between substance-use and gambling disorders (Potenza, 2006). Due to the recent classification and renaming of "pathological gambling" (PG) in DSM-IV-TR to "gambling disorder" in DSM-5 (American Psychiatric Association, 2000, 2013; Potenza, 2014), this condition will be referred to as gambling disorder in this chapter despite a majority of data emanating from studies of PG.

3 NEURAL FEATURES OF GAMBLING DISORDER

Phenomenological similarities between substance-use and gambling disorders have been observed, leading to inclusionary criteria addressing tolerance, withdrawal, and interference in major areas of life functioning for these conditions. Recently, there have been various other reviews of neural function in gambling disorder (Leeman and Potenza, 2012, 2013; Meng et al., 2014). The current review will describe recent findings related to processes which may be beneficial for advancing treatment of this disorder.

3.1 NEUROCOGNITIVE FACETS

Neurocognitive measures allow for evaluation of possible dysfunction in a variety of cognitive facets and offer insight in to potential underlying neural regions of importance in behavioral addictions (Potenza, 2014). The evaluation of patterns of dysfunction allows for comparisons to healthy comparison subjects, across substance-use disorders, and various other populations of interest which allow for a more in-depth understanding of similarities and differences between these groups (Choi et al., 2014; Leeman and Potenza, 2012; Noël et al., 2013; Yan et al., 2014). Importantly, evaluation of neurocognitive function in PG through neurocognitive tasks has provided insight into the maintenance of this disorder (for review, see Brevers et al., 2013; van Holst et al., 2010). Together, these data inform potential approaches to the identification of those at risk and the development of more effective treatments.

3.2 ELECTROPHYSIOLOGY

Electrophysiological studies involving electroencephalogram (EEG) data and tasks designed to elicit event-related potentials (ERPs) offer insight into neural function linked to sensory or cognitive processing. To date, these methods have not been extensively used within individuals with PG, with existing studies frequently using gambling tasks, as described below.

Feedback-related negativity (FRN), an ERP component elicited through feedback related to subject performance, has been evaluated. Healthy comparison subjects and those with PG presented with similar FRN amplitudes in win and loss conditions; however, in PG subjects,

an additional FRN occurred earlier with latency and amplitude correlated with severity of PG (Oberg et al., 2011). In PG, blunted P3 amplitude and EEG power in theta-band activity were also found in response to high-risk scenarios (Oberg et al., 2011). More recently, Lole and colleagues (2015) found attenuated FRN and feedback-related positivity in response to losses and wins with no difference in P3b amplitude in response to large and small rewards in PG. These data suggest varied sensitivity to risk, reward, and loss in PG which can be evaluated through EEG.

During simulated blackjack, reward resulted in more positive reactivity in PG compared to healthy comparison subjects during a window after the FRN (between 270 and 320 ms); a difference in positivity was found within PG subjects between responses to rewards and losses, with no differences in healthy comparison subjects (Hewig et al., 2010). However, during varying loss conditions, PG subjects did not show differences in reactivity during conditions of near or full losses during this same window of activity, unlike healthy comparison subjects (Kreussel et al., 2013). When comparing occasional gamblers and PG subjects during a blackjack task, reactivity in these two groups differed in both low- and high-risk conditions during risk assessment, and PG subjects presented with greater negativity during reward processing (Miedl et al., 2014). Together, these studies differences in the electrophysiological brain correlates of reward/loss processing and suggest a need for additional study of cue-related craving effects on risk assessment, loss, and reward processing in PG.

3.3 FUNCTIONAL MAGNETIC RESONANCE IMAGING

Functional magnetic resonance imaging (fMRI) tasks offer insight into the neural circuitry associated with different neuropsychological processes that may be targeted in the treatment of gambling disorder. These tasks permit the evaluation of the neural underpinnings of cognitive processes, such as decision-making or processing of monetary rewards and losses (reviewed in Potenza, 2014). Data from fMRI studies implicate similar brain regions in both substance and behavioral addictions (Leeman and Potenza, 2013; Potenza, 2013). For example, several studies of monetary-reward processing have identified blunted activation of the ventral striatum (VS) during reward anticipation in gambling disorder (Balodis et al, 2012; Choi et al., 2012), resonating with findings in alcohol-, tobacco-, and cannabis-use disorders (reviewed in Balodis and Potenza, 2015). Below, we will highlight findings from fMRI recent studies not covered in recent reviews.

In a recent study examining decision-making when varying risk and ambiguity, healthy control participants but not those with PG showed greater striatal, insular, and prefrontal cortical activations during decision-making under risk as compared to ambiguity, and individuals with PG as compared to those without showed greater striatal activation during betting as compared to “safe” choices (Brevers et al., 2015). Using a different task, Miedl and colleagues demonstrated that processing delayed rewards during decision-making involves widespread, bilateral activation in PG subjects compared to left side activation of healthy controls. In addition, indifferent compared to sure decisions elicited greater widespread activation in PG versus control subjects, where sure decisions for PG subjects only elicited activity in the inferior parietal and superior temporal areas, and greater activity

in the cingulate gyrus, insula, and medial frontal gyrus in healthy control subjects (Miedl et al., 2015). Together, findings suggest a complex relationship between striatal activation and gambling disorder. It is likely that between-study differences in task design (e.g., delay-discounting vs. risky choice tasks) may relate to differences in findings.

Reward type may also impact neural reactivity. Monetary and erotic rewards have been used in order to assess possible differences between reward types. VS activation during reward anticipation for erotic stimuli was lower compared to monetary rewards in PG subjects, and this activation was correlated to subjective ratings for erotic but not monetary rewards in PG subjects (Sescousse et al., 2013). Posterior orbitofrontal cortical activation was greater during reward outcome for PG subjects for monetary gains (Sescousse et al., 2013). Differences based on reward type related to stress systems as VS activation and cortisol levels were correlated in PG subjects in response to monetary cues (Li et al., 2014).

fMRI tasks may model aspects of electronic-gambling machines including “near-miss” events that occur when symbols on two of three reels match. These tasks may relate more closely to specific gambling behaviors compared to other decision-making tasks. During near-miss events, both cocaine-dependent and PG subjects showed greater reactivity in ventrocortical and mesolimbic areas compared to those without either diagnosis, with PG subjects having greatest reactivity (Worhunsky et al., 2014). During a similar task, near-miss events elicited activity in the insula and right inferior frontal gyrus, and increased theta-band oscillations in the right orbitofrontal cortex (OFC) and insula (Dymond et al., 2014). These data suggest task content is also relevant to activity when comparing across addictions. Therefore, future studies should attempt to incorporate tasks which may be more ecologically valid.

Resting-state fMRI studies may offer valuable insight into functional brain connectivity at rest. In PG subjects, the supplementary motor area and paracingulate cortex show reduced connectivity at rest (Tschernegg et al., 2014). The right caudate appears more involved and the hippocampus less involved in information integration in PG versus control subjects (Tschernegg et al., 2014). These data suggest differences in PG and non-PG groups in networks involved in self-regulation and reward processing.

3.4 STRUCTURAL MRI

Structural MRI allows for volumetric comparison of tissue structures across different diagnostic groups. Using this method, comparisons between PG, substance-addicted and nonaddicted groups may improve understanding of the neural structural under-pinnings of various addictions. Recently, smaller left hippocampal and right amygdalar volumes were found in PG versus control subjects (Rahman et al., 2014). Regional volumes were related to behavioral inhibition scores grouping PG subjects (Rahman et al., 2014). Additionally, problem-gambling subjects displayed similar gray matter volumes as did subjects with alcohol use disorder: lower volumes in left superior frontal cortex, bilateral precentral cortex, right insula, left thalamus, bilateral superior parietal cortex, and right supramarginal cortex (van Holst et al., 2012).

3.5 DIFFUSION TENSOR IMAGING

Diffusion tensor imaging (DTI) may assess white matter integrity. To date, two studies have used DTI to study PG. In PG versus control subjects, lower fractional anisotropy (FA) was present in the right and left genu of the corpus callosum, a pattern also seen in substance abuse (Yip et al., 2011). Lower FA in the corpus callosum was also seen in an independent study which reported widespread lower FA in PG (Jousta et al., 2011). Together, these studies suggest microstructural deficits present in PG which appear not to be accounted for by neurotoxic effects of substances.

3.6 NEUROCHEMISTRY

Preclinical, ligand-based imaging, and molecular genetic research methods may all be used to inform understanding of the role of different neurotransmitters systems in PG (reviewed in Potenza, 2013). In this section, we will focus on recent findings from human ligand-based and genetic studies, with an emphasis on dopamine and serotonin (5-HT). For a discussion of findings from pharmacological treatment studies conducted in gambling disorder, see Section 5.2.

The role of dopamine in PG remains poorly understood. Dopamine has been implicated in substance addictions and reward processing, among other behaviors. Positron emission tomography (PET) permits study of neurochemical and metabolic measures. As reviewed in Potenza (2013), data from PET studies using [11C]-raclopride suggest that individual differences in dopamine release and $D_{2/3}$ receptor availability are related to individual differences in clinical features of PG, such as positive urgency (Clark et al., 2012) and task performance (Linnet et al., 2012) or subjective experiences during gambling tasks (Jousta et al., 2012).

There have been two recent PET studies using the D_3-preferring radioligand [^{11}C]-(+)-propyl-hexahydro-naphtho-oxazin (Boileau et al., 2013, 2014). While no significant differences in D_3 receptor availability were found between individuals with and without PG (Boileau et al., 2013, 2014), significant decreases in receptor binding subsequent to amphetamine challenge were observed among individuals with PG (Boileau et al., 2014).

Problem-gambling severity has been linked to the serotonin system (reviewed in Leeman and Potenza, 2013; Potenza, 2013). A positive association between serotonin 1B receptor availability and problem-gambling severity (Potenza, 2013) and a genetic link between serotonin 2A receptors and PG have been reported; see genetic studies, below (Wilson et al., 2013).

The relationship between dopamine and serotonin and their complementary roles in value-adaptation and loss-chasing may be relevant to PG (Campbell-Meiklejohn et al., 2011). Other neurotransmitter systems (e.g., opioid, cannabinoid, glutamate) require consideration in PG.

4 GENETICS

Polymorphisms in genes encoding for dopamine-related moieties, including *DRD1* DdeI, *DRD2* Taq I A, and *DRD4* (exon III), have been reported, although negative results have also been reported (reviewed in Leeman and Potenza, 2013). Studies also suggest genes coding for the serotonin transporter, *5HTTLPR,* and MAO enzymes (e.g., *MAO-A, MAO-B*) may contribute to PG (reviewed in Leeman and Potenza, 2013). An association between the C/C genotype of the 5-HT-2A receptor gene and PG has also been reported recently (Wilson et al., 2013). Below, we review findings from recent genetic studies, focusing on findings not covered in recent reviews (Gyollai et al., 2014; Leeman and Potenza, 2013; Yau et al., 2014).

While candidate gene studies often fail to replicate, genome-wide association studies (GWASs) have arguably shown more consistency, although few have been performed in PG (one reported to date). GWAS data collected in a community-based Australian twin sample identified six single-nucleotide polymorphisms (SNPs) as related to disordered gambling, four of which the authors interpreted as "theoretically relevant," although none reached genome-wide significance (Lind et al., 2012). Identified SNPs included rs8064100, located downstream of metallothionein 1X (*MT1X*), previously implicated in alcohol and drug dependence (Lind et al., 2012).

Genetic contributions have been found to relate to the age of onset of gambling but not age of onset of drinking in males; however, in females, genetic contributions link to onsets of both behaviors (Richmond-Rakerd et al., 2014). Conversely, twin studies suggest nondisordered gambling engagement is equally influenced by family environmental factors in men and women (Slutske and Richmond-Rakerd, 2014). Recently, shared environmental and genetic factors have been linked to the age of gambling initiation predicting gambling behavior later in life (Slutske et al., 2014). Taken together, these findings suggest a complicated relationship between genetic contributions, environmental influences, sex, and gambling behaviors and disorders.

Twin studies offer valuable insight into relative genetic and environmental contributions to PG and co-occurring disorders. The Vietnam Era Twin Registry has demonstrated that PG shares genetic factors with both obsessive-compulsive classes (Scherrer et al., 2015) and drug addictions (Xian et al., 2014), with environmental contributions less important for the overlap between PG and stimulant dependence. These findings suggest the need to identify specific genetic factors involved in these relationships and determine the extent to which these may represent appropriate targets for behavioral or pharmacological interventions in subgroups of individuals with PG.

5 TREATMENT OF GAMBLING DISORDER

Treatment of PG involves both pharmacological and nonpharmacological methods, as reviewed elsewhere (Yip and Potenza, 2014). Though various treatments exist, individuals with PG are often unlikely to seek treatment, and those that do have high dropout rates, highlighting the need for enhanced efforts to get individuals into treatment settings and maintain their attendance (Rash and Petry, 2014).

5.1 BEHAVIORAL TREATMENT

Two recent manuscripts have reviewed nonpharmacological therapies for PG (Cowlishaw et al., 2012; Rash and Petry, 2014). Cognitive behavioral therapy (CBT) has arguably the greatest support, with one CBT treatment adapted from that demonstrating efficacy in the treatment of substance-use disorders and another focused on targeting irrational cognitions. As compared to CBT for substance addictions, CBT for PG may also target financial problems and financial management. Other approaches that have shown efficacy in the treatment of PG involve imaginal desensitization, motivational enhancement, and brief interventions like those that show efficacy in the treatment of substance-use disorders. Mindfulness-based approaches for PG have also been proposed and are beginning to be investigated. Active ingredients of these therapies and biological mechanisms relating to their efficacies have been proposed, and further research is needed to investigate how these treatments work and for whom they might work best (Potenza et al., 2013).

5.2 PHARMACOLOGICAL TREATMENT

Serotonin selective reuptake inhibitors, dopaminergic agents, mood stabilizers, glutamatergic agents, opioid-receptor antagonists, and other drugs have been investigated in the treatment of PG (reviewed in Bullock and Potenza, 2012; Yip and Potenza, 2014). Arguably, the most consistent results are from studies of opioid-receptor antagonists (naltrexone, nalmefene), with four randomized clinical trials (RCTs) showing varying degrees of efficacy. However, the effect size of opioid-receptor antagonists in the treatment of PG may be modest (Bartley and Bloch, 2013), although the medication may be most helpful for specific subgroups (those with familial histories of alcoholism or strong gambling urges). Treatment algorithms have been proposed (Bullock and Potenza, 2012) largely based on co-occurring disorders (e.g., lithium in the treatment of individuals with PG and co-occurring bipolar-spectrum disorders) and willingness to take pharmacotherapies. For individuals less willing to consider pharmacotherapies, *n*-acetyl cysteine, a dietary supplement with glutamatergic properties, may represent an important therapeutic possibility. Recently, in a placebo-controlled RCT of *n*-acetyl cysteine in individuals with PG and nicotine dependence in which all participants received a behavioral therapy for gambling involving CBT, motivational, and imaginal-desensitization components, active *n*-acetyl cysteine was superior to placebo with respect to reducing smoking during treatment and reducing gambling behaviors at follow-up (Grant et al., 2014). These findings raise the intriguing possibility that *n*-acetyl cysteine may lead to greater durability of gambling-related behavioral therapies, perhaps augmenting a “sleeper” effect that has been described for CBT in the treatment of substance-use disorders. However, this and other aspects of how behavioral and pharmacological therapies may be used conjointly in the treatment of PG warrant additional investigation.

6 PROBLEMATIC INTERNET USE AND IGD

The extent to which Internet use may be considered the focus of a disorder has been debated, with some contending that the Internet may represent a vehicle for other behaviors (e.g., gambling) that constitute the true diagnostic focus (Petry and O’Brien, 2013). Additionally, if considered a disorder, debate exists regarding the extent to which problematic Internet use

(PIU) may represent an addiction or not. Given these debates, we will use the term PIU in this review although other terms (e.g., Internet addiction) have been used in the literature. PIU may be conceptualized as involving the excessive or poorly controlled urges and behaviors relating to Internet use that lead to subjective distress and/or interference in major areas of life functioning. It is a heterogeneous construct that may include a multitude features relating to sexual, social networking, and gaming behaviors. Currently, IGD is included in Section 3 of the DSM-5 as this was determined to need more research, despite being considered the most well studied and interfering type of Internet use at the time of DSM-5 deliberations (Petry and O'Brien, 2013).

7 NEURAL FEATURES OF PIU

7.1 NEUROCOGNITIVE FACETS

Few neurocognitive studies have been used to assess PIU and IGD; however, differences in impulsivity have been noted. High urgency, a facet of impulsivity, has been shown to relate to PIU (Billeux et al., 2011). Higher self-reported impulsivity was also found in IGD and alcohol use disorder (AUD) compared to healthy controls and GD (Choi et al., 2014). Interestingly, IGD, AUD, and healthy controls displayed less compulsivity than did GD on a set-shifting task (Choi et al., 2014). Additional neurocognitive differences have been observed (see following sections). Together, these data suggest differences between IGD and healthy populations as well as between IGD and other behavioral addictions, and these may be important considerations for treatment development (Dong and Potenza, 2014).

7.2 ELECTROPHYSIOLOGY

Resting-state EEG studies are used to evaluate intrinsic neural activity which is not elicited through a task. In a PIU population, lower absolute beta-band and greater absolute gamma-band activities related to disorder severity and impulsivity measures (Choi et al., 2013). In those with comorbid depression, increased theta and decreased alpha-band power was found compared to nondepressed individuals with PIU where nondepressed individuals presented with decreased delta- and beta-band power compared to depressed individuals (Lee et al., 2014). These resting-state data suggest these neurobiological differences may be markers for PIU.

Studies evaluating ERP activity, such as a Go/No-Go or Stroop task, may reflect facets related to impulsivity and error processing. In a Go/No-Go task, N2 amplitude was lower in PIU and P3 amplitude was larger with a longer latency, and decreased activity in conflict detection was observed compared to healthy comparison subjects (Dong et al., 2010). Relative to healthy comparison subjects, an incorrect response during the No-Go condition elicited a decreased amplitude of error-related negativity in individuals with IGD which was associated with impulsivity assessed via task performance and self-report (Littel et al., 2012). Similarly, during Stroop performance, decreased medial frontal negativity, greater reaction times, and response errors were found during incongruent trials in the PIU group to the healthy comparison subjects (Dong et al., 2011). Together, these studies suggest differences in impulsivity which may be evaluated through ERP tasks, and which may relate

to deficits in conflict processing and have implications for treatment development (Dong and Potenza, 2014).

7.3 FUNCTIONAL MRI

Reward circuitry, cognitive control, cue reactivity, and craving fMRI tasks have implicated some similar brain regions in PIU and substance-use disorders (reviewed in van Rooij and Prause, 2014; Yau and Potenza, 2015; Yau et al., 2012). In particular, mesolimbic and cortical regions relating to reward/motivation and behavioral control may contribute to the pathophysiology of PIU. A recent meta-analysis found subjects with IGD showed abnormal activation of the medial frontal, medial temporal, and cingulate gyrus regions in response to a range of cognitive tasks (Meng et al., 2014).

Studies of functional connectivity may provide insight into how brain regions interact in circuits. Resting-state MRI has been used to investigate task-independent functional connectivity between regions of the mesolimbic system. Graph-theoretical approaches have identified connectivity in limbic regions including the amygdala, the insula, and dorsolateral prefrontal cortex (dlPFC) correlated with features of PIU and IGD (Ko et al., 2015; Wang et al., 2015). Similarly, less functional connectivity in executive-control networks was observed among individuals with IGD compared to control subjects (Dong et al., 2015). These brain networks have been implicated in substance addictions and may contribute to the development and maintenance of addictive behaviors. Altered connectivity between regions of the default-mode network has also been observed among individuals with PIU, and degree of connectivity was related to PIU severity (Wee et al., 2014).

7.4 STRUCTURAL MRI

Several studies have also investigated structural abnormalities that may relate to PIU. Reduced regional gray matter volume has been observed in key nodes of executive-control networks (e.g., frontoinsular cortex, anterior cingulate cortex, dlPFC, and posterior parietal cortex) in association with greater PIU severity (Li et al., 2015). Furthermore, these differences correlated with performance on the Stroop task and may, therefore, reflect reduced inhibitory control and cognitive efficiency. Decreased cortical thickness (Hong et al., 2013) has also been observed in regions of the executive-control network among individuals with PIU.

In light of the recent DSM categorization changes relating to conditions with addictive potential, comparing PIU and substance-abusing populations may provide insight into the most appropriate categorization of PIU. Commonalities and differences exist between the two groups and a better understanding of this can help improve diagnosis (Yau et al., 2012). For example, among both IGD and alcohol-dependent populations, negative functional connectivity between the dlPFC and the OFC and positive connectivity between the dlPFC and the ACC have been observed (Han et al., 2015). However, subjects with IGD showed negative connectivity between the dlPFC and regions of the temporal lobe, and the striatum, whereas alcohol-dependent subjects had positive connectivity. Kim and colleagues (2015) recently found increased regional homogeneity in the posterior cingulate cortex in both IGD

and alcohol-dependent individuals; however, regional homogeneity appeared selectively reduced in the superior temporal gyrus in IGD.

7.5 DIFFUSION TENSOR IMAGING

DTI studies have suggested poorer white matter integrity in PIU, although not consistently (Yau et al., 2012). In one study of adolescents, lower FA was observed in the OFC, corpus callosum, cingulum, inferior fronto-occipital fasciculus, corona radiata, and internal and external capsules, with FA measures in the genu of the corpus collusum inversely correlating with measures of anxiety and those in the external capsule relating inversely correlating with PIU severity (Lin et al., 2012). A separate study found lower white matter density in the inferior frontal gyrus, insula, amygdala, and anterior cingulate in IGD subjects relatively to control subjects (Lin et al., 2015).

7.6 NEUROCHEMISTRY

Several neurotransmitter systems may contribute to PIU. Of these, the dopaminergic system has arguably received the most research attention. Years of problematic gaming was negatively correlated with D_2-like receptor availability in the striatum and IGD subjects showed decreased glucose metabolism in the OFC, insula, and limbic regions (Tian et al, 2014). In a separate study, dopamine transporter expression in the striatum was significantly lower in individuals with PIU compared to healthy control subjects (Hou et al., 2012).

Beyond the dopaminergic system, other neurochemical systems have shown differences which may underlie PIU. Recently, lower levels of *N*-acetyl aspartate (NAA) and cystolic, choline-containing compound (Cho) levels were observed in the medial temporal cortices of IGD patients. Additionally, lower levels of NAA and Cho in the right frontal cortex were also seen, and the NAA was inversely related to Young Internet Addiction Scale scores and perseverative responses during the Wisconsin Card Sorting Task (Han et al., 2014). Further study of the underlying neurochemical differences among individuals with PIU is needed in order to guide treatment development efforts.

8 GENETICS

Genetic mechanisms underlying PIU are poorly understood and currently only preliminary studies exists. As with disordered gambling, relationships between PIU and the Taq1A1 allele of the *DRD2* gene (Han et al., 2007) and homozygosity of the short allelic variant of the *5-HTTLPR* gene (Lee et al., 2008) have been associated with PIU. However, these studies warrant replication and verification in larger samples, and other approaches (twin and GWAS studies) warrant undertaking.

9 TREATMENT

Few interventions have been systematically tested for PIU or IGD. Treatment strategies may be particularly important for adolescents and young adults given high prevalence estimates among these age groups (Spada, 2014).

9.1 BEHAVIORAL TREATMENT

Behavioral treatments have yet to be systematically studied in the context of PIU. Preliminary studies of CBT adapted for PIU (and more specifically in certain studies of IGD and problematic Internet pornography viewing) has demonstrated preliminary positive benefits (Twohig and Crosby, 2010; Wölfling et al., 2014; Young, 2013). Such CBT approaches aim to help individuals examine emotional motives and identify problematic cognition that may prompt them to engage excessively in online activities. As with disordered gambling, individuals are encouraged to explore alternative ways to satisfy those needs (e.g., developing other recreational pursuits) and to correct maladaptive thinking patterns. Family therapies involving increased socialization efforts have also been examined in PIU (Liu et al., 2015), with preliminary reports of possible treatment-related changes in striatal responsivity (Han et al., 2012). Other behavioral interventions (e.g., solution-focused brief therapy, mindfulness-based interventions) may also be helpful given the proposed addiction model of PIU but their efficacy has yet to be studied directly.

9.2 PHARMACOLOGICAL TREATMENT

Psychostimulants, opioid-receptor antagonists (e.g., naltrexone), antiepileptics, antipsychotics (e.g., olanzapine), antidepressants (e.g., bupropion), and glutamate-receptor antagonists have explored in treatments for PIU (reviewed in Camardese et al., 2012; Przepiorka et al., 2014; Winkler et al., 2013). Successful treatment may link changes in specific domains (e.g., depression, cognitive flexibility), and as in PG, comorbidity may be important to consider (Przepiorka et al., 2014). Although many pharmacotherapies have been explored in the treatment of PIU, placebo-controlled RCTs of significant size and duration are largely lacking, and as is the case with PG, no medications have approval by the U.S. Food and Drug Administration (FDA) with an indication for treating PIU or IGD.

10 FUTURE DIRECTIONS

While much research has been conducted recently on PG, PIU, and IGD, many research gaps exist, with arguably greater gaps and controversies for Internet-related behaviors and disorders. For example, research criteria for IGD have only recently been proposed, and these do not cover other forms of Internet use (e.g., social networking, pornography viewing) that might be problematic for individuals (Rehbein and Mößle, 2013). Additionally, the absence of agreed-upon criteria for PIU has led to marked variations in reported prevalence estimates and assessment of public health impacts (Petry and O'Brien, 2013). While treatment development efforts for PG have led to the availability of efficacious behavioral therapies for PG, such studies are at earlier stages for PIU. For PG, PIU, and IGD, no pharmacotherapy trials have led to the availability of medications with FDA indications for the disorders. With respect to prevention efforts, healthy levels of engagement in gambling, gaming, and Internet use remain discussed and/or debated. In these efforts, potentially vulnerable individuals should be considered, especially youth. Other factors should also be considered; for example, most studies of PG, PIU, and IGD have focused on males, and sex differences warrant consideration, particularly for specific Internet-related behaviors like social networking. Additionally, health disparities related to race/ethnicity should also be considered. In this context, neurobiological findings should be

used to inform advancement of policy, prevention, and treatment efforts relating to behavioral addictions.

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