J Gambl Stud (2018) 34:673–688
https://doi.org/10.1007/s10899-018-9757-z

ORIGINAL PAPER

Problem and Pathological Gambling in Schizophrenia: Exploring Links with Substance Use and Impulsivity

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Published online: 16 February 2018

Abstract High rates of both problem and pathological gambling (PPG) and substance-use disorders (SUDs) have been reported in schizophrenia, and yet PPG frequently goes undetected in clinical practice and unexamined in research. Here, we aimed to examine the relationship between PPG and SUDs in a large sample of patients across several factors related to both gambling and substance use, including poly-substance use. Additionally, delay discounting is a form of impulsivity known to positively associate with both PPG and SUDs and thought to underlie mechanisms of addiction in both contexts. We aimed to investigate the relationship between PPG and delay discounting in schizophrenia. 337 individuals with schizophrenia completed structured face-to-face interviews regarding gambling behaviors, substance use, and delay discounting. PPG in schizophrenia was associated with substance use, in particular with poly-substance use, and with delay discounting among males. Factors related to substance use were strongly linked with gambling in this sample, but not always with PPG more than recreational gambling. Our findings overall support the notions that multiple forms of gambling in schizophrenia are clinically relevant, that gambling may share common substrates with substance use, and that delay discounting represents a potential mechanism of this association in males.

Keywords Delay discounting · Addiction · Behavioral addiction · Psychosis · Schizophrenia

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Introduction

Problem and pathological gambling (PPG) is more prevalent in individuals with schizophrenia than in the general population—frequencies ranging from 5 to 20% have been reported in clinical samples (Desai and Potenza 2009; Haydock et al. 2015). PPG has been associated with increased odds (over three times greater) of psychosis in a community sample (Cunningham-Williams et al. 1998) and more recently in a disordered gambling patient sample (Cassetta et al. 2017). Nonetheless, gambling problems frequently go undetected and untreated in individuals with schizophrenia, and little is known about gambling in this population (Echeburúa et al. 2011). PPG can result in serious consequences, including social, legal, financial, and occupational costs (Bergh and Kühlhorn 1994; Ladouceur et al. 1994), making it a relevant domain to assess and address in general and particularly with patients at risk for impairment in these areas. Information about which patients are at risk for PPG could help to target clinical assessments, and more understanding of potential mechanisms of the association could inform interventions.

Schizophrenia is associated with elevated rates of substance-use disorders (SUDs), which are frequently comorbid with PPG in the general population and may develop via shared mechanisms. The frequent co-occurrence between PPG and SUDs suggest shared mechanisms in schizophrenia (Desai and Potenza 2009). Non-tobacco SUDs occur in 40–50% of individuals with schizophrenia and are associated with negative outcomes such as suicide, violence, homelessness, and incarceration (Thoma et al. 2007). In comparison with the general population, odds of having a SUD are over four times higher in schizophrenia—a figure similar to the increase in odds of PPG (Clarke 2006). SUDs are among the most important predictors for course of illness in schizophrenia patients (Blanchard et al. 2000; Haywood et al. 1995; Swofford et al. 1996; Winklbaur et al. 2006).

In a previous study, PPG was associated with increased scores on the Addiction Severity Index (ASI) for alcohol and marginally increased on the ASI for drug use, but it was not associated with increased likelihood of a diagnosis of nicotine dependence (Desai and Potenza 2009). In a separate study, problem gambling was associated with use of multiple substances including cannabis, other drugs and alcohol at problematic levels (Haydock et al. 2015). Given these findings, more specific information about the relationship between SUDs and PPG in schizophrenia is needed.

Poly-Substance Use

In addition to SUDs broadly, schizophrenia has been associated with high rates of poly-substance use, or PSU (Arndt et al. 1992). PSU is the use of multiple drugs over a defined period of time and is of interest to clinical researchers due to its prevalence and its association with poorer health outcomes and psychopathology (Connor et al. 2014). Among cannabis users, poly-substance users reported higher levels of positive psychotic symptoms, as well as other psychiatric symptoms (Connor et al. 2013). PSU may also relate to PPG in schizophrenia, as it suggests a broader susceptibility to seeking rewarding and potentially addictive outlets. At present writing, no study has examined PSU in relation to PPG in schizophrenia.

Impulsivity

Given the plausible relationship between SUDs and gambling in schizophrenia, mechanisms related to SUDs in this population may also relate to PPG. Impulsivity is a correlate of—and potentially a vulnerability marker for—both SUDs and PPG (e.g. Fuentes et al. 2006), potentially representing a shared mechanism (Leeman and Potenza 2012; Petry 2001; Verdejo-García et al. 2008). Schizophrenia has also been associated with increased impulsivity and impaired response inhibition (Dursun et al. 2000; Enticott et al. 2008; Fortgang et al. 2016; Kaladjian et al. 2011; Ouzir 2013), and impulsivity has specifically been linked to SUDs in this population (Dervaux et al. 2001). Impulsivity has also been shown to mediate the relationship between depression, often a component of schizophrenia, and PPG (Clarke 2006).

In particular, delay discounting is an aspect of impulsivity related to the devaluing of future rewards according to the length of the wait, signifying a preference for "smaller sooner" as opposed to "larger later" rewards. This form of impulsivity seems to relate clearly to gambling behaviors and has been associated with PPG and with SUDs (e.g. Alessi and Petry 2003; Leeman and Potenza 2012). Individuals with schizophrenia also show steeper rates of delay discounting (Heerey et al. 2007, 2011). Taken together, existing evidence suggests that PPG in schizophrenia could be related to increased delay discounting.

Additionally, there may be a differential association between impulsivity and substance use across genders (Nower et al. 2004; Waldeck and Miller 1997) or as a function of nicotine dependence. Regarding gender, Martin et al. (1997) found that impulsivity was associated with problematic substance use in male but not female adolescents. Therefore, gender is important to examine both as a covariate and as an independent variable potentially revealing different relationships between gambling and impulsivity.

Regarding nicotine dependence, group differences in delay discounting between individuals with schizophrenia and healthy comparison subjects have shown less consistency when accounting for smoking status or nicotine dependence. Though steeper discounting in schizophrenia has been identified even when controlling for overall current substance use (Ahn et al. 2011), two other studies found no significant differences in delay discounting between cigarette smokers with or without schizophrenia (MacKillop and Tidey 2011; Wing et al. 2012). Weller et al. (2014) found that this effect was attributable to elevated delay discounting among healthy control smokers in particular, as delay discounting rates were actually lower among smokers among only patients with schizophrenia. Still, available evidence suggests both gender and nicotine dependence are relevant factors to consider when evaluating delay discounting in schizophrenia.

Previous Findings

Previously in the same sample (Desai and Potenza 2009), 65 participants (19.3%) were categorized as having PPG, 117 (34.7%) reported recreational gambling (RG), and 155 (46%) reported no gambling (NG). Of participants with PPG, 33 (50.77%) met criteria for pathological gambling. There were no significant gender or demographic differences across gambling groups except that more individuals with PPG reported never having been married. This study also found significant group differences in histories of arrest, incarceration, threatening behavior, and use of mental health services, such that the non-gambling group had the lowest frequencies, and the PPG group had frequencies higher than or equivalent

to the RG group. Alcohol abuse was specifically associated with PPG but not with recreational gambling. In addition, scores on the Addiction Severity Index (ASI) for Alcohol were significantly different across gambling groups, ASI Drug use scores were marginally different, and there were marginal group differences in diagnosis of nicotine dependence. Additional variables related to substance use and delay discounting were not explored.

Present Study

Though PPG is a significant concern among individuals with schizophrenia, little research has investigated their relationship and clinical correlates. Multiple studies have targeted schizophrenia and SUDs, but the precise relationships between PPG and SUDs in this population remain poorly understood. Additionally, schizophrenia has been associated with elevated choice impulsivity, including delay discounting. Whether delay discounting relates to PPG in schizophrenia, as it does in the general population, is yet unknown. In the present investigation, we aimed to address these knowledge gaps with an exploratory study examining relationships among gambling behaviors, substance use, and impulsivity in a group of individuals with schizophrenia that was stratified into PPG, RG and NG groups. We believe that this information will be useful clinically to detect possible risk factors for PPG in schizophrenia, and it also may inform our understanding of mechanisms underlying associations between PPG and SUDs in this population.

We hypothesized that PPG would be positively associated with substance-use behaviors (especially PSU) and delay discounting. In line with previous findings in other populations, we hypothesized the latter relationship would be stronger in males.

Methods

Individuals diagnosed with either schizophrenia or schizoaffective disorder were recruited through the Connecticut Mental Health Center (CMHC) and the VA Connecticut Healthcare system. The investigation was conducted in accordance with the Declaration of Helsinki, and the study design was approved by the institutional review boards of the West Haven VA in Connecticut and Yale University. Administrative patient rosters were used to identify individuals with schizophrenia or schizoaffective disorder, and study staff

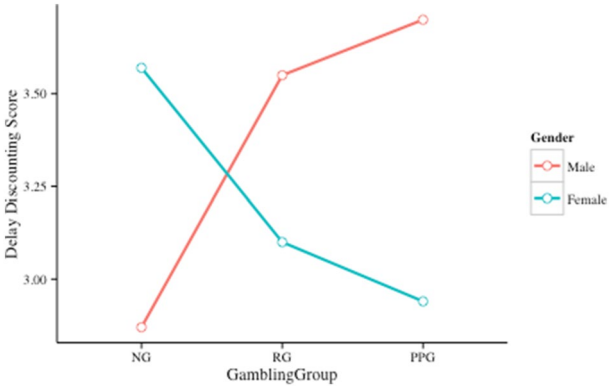

Fig. 1 Delay discounting: Interaction between gambling group and gender. Delay discounting scores (range: 0–6) for individuals reporting histories consistent with non-gambling (NG), recreational gambling (RG), and problem and pathological gambling (PPG)

contacted clinicians to confirm each patient's diagnosis and interest in participation. The response rate was 80.6%. Interested qualifying patients gave written informed consent and were paid $15 for their participation. Data were obtained from face-to-face interviews, which generally lasted between 1 and 1.5 h and included information on sociodemographic information, housing, social support, and functioning.

Measures

Widely used, validated measures were used to assess symptoms, substance use, and gambling-related behaviors.

Gambling Behaviors

Gambling behaviors were assessed using items from the Gambling Impact and Behavior Study (GIBS), a national population-based study of gambling in the United States (Desai and Potenza 2009; Gerstein et al. 1999). Included items assessed forms of gambling, frequency, amounts of money won and lost, motivations for gambling, age of initial gambling, and with whom participants typically gambled. We used the NORC diagnostic Screen (NODS; Gerstein et al. 1999), an instrument that has been found to be valid and reliable (Fager 2007). The NODS assesses Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM IV-TR; American Psychiatric Association 2000) criteria for pathological gambling including tolerance, withdrawal, and impairment in family or social functioning as a result of gambling. Individuals who reported never having gambled more than 5 times in a given year were categorized as "non-gamblers." NODS scores were used to categorize gambling into recreational (NODS = 0–2), and problem/pathological (NODS = 3+) gambling (RG and PPG, respectively) groups, as in prior studies.

Substance Use

To assess substance use, abuse, and dependence, we used the Addiction Severity Index (ASI) for drugs and alcohol (McLellan et al. 1992) and the Diagnostic Interview Schedule (DIS) for nicotine dependence (Robins et al. 1995). The ASI has been shown to be reliable and valid (McLellan et al. 1992). It includes assessment of drugs sampled and drugs of choice, lifetime history and frequency of substance use, presence and severity of symptoms, efforts to reduce use, and treatment history. The DIS for nicotine dependence assesses a comparable history of nicotine use, including withdrawal symptoms and methods of use. Both measures were additionally used to assign current diagnoses (based on 30 days prior to interview) in accordance with DSM IV-TR, and for analyses targeting specific items. As we did not have access to a complete diagnostic history, treatment history served as a proxy for history of SUD diagnosis. We also tested for differences in money spent on alcohol and drug use, due to the relationship between gambling and monetary concerns, in specific drugs used, PSU, and associations between ASI scores and specific NODS PPG criteria.

PSU was calculated by summing the number of substances used over the lifetime and during the 30 days prior to interview, creating two separate indicators. Alcohol, opiates, crack cocaine, powdered cocaine, barbiturates, tranquilizers, amphetamines, hallucinogens, and cannabis were included in these calculations. Tobacco was not included due to the extremely high rates of tobacco use and dependence in schizophrenia and the reduced

propensity for tobacco to interfere with daily functioning as compared with included substances.

Delay Discounting

We used a brief delay-discounting assessment, comprising questions asking participants whether they would prefer a smaller amount of money now or a larger amount later. This brief questionnaire included three items with varying delays. Each item was given a different weight depending on the length of the delay, and the weighted items were summed to create a delay discounting index, such that higher scores indicate greater discounting. Possible scores range from zero to six. Because this brief measure had not previously been shown to be a valid replacement for a longer, standard measure, we also tested the correspondence between this short delay discounting measure and the Monetary Choice Questionnaire (Kirby and Maraković 1996), a commonly used measure of hypothetical delay discounting. We administered both measures to an online sample of 101 individuals using Amazon Mechanical Turk and found that the two measures correlated significantly, $r(99) = .53$, $p < .001$. We therefore find this shortened version of a delay discounting measure to be a valid proxy for longer measures when time is limited.

Analyses

Chi square tests of independence were used to test associations between gambling group status and history of substance use and specific self-reported symptoms. Univariate analyses of variance (ANOVAs) covarying for age and gender were used to test group differences in scores on the ASI Alcohol and Drug scales and amount of money spent on substance use. Logistic regression covarying for age and gender were used to test associations between ASI scores and specific PPG symptoms among individuals with RG or PPG. To assess group, gender, and nicotine-related differences in delay discounting, we used univariate ANOVAs covarying for age and including group, gender, and history of nicotine dependence as independent variables. Effect sizes are reported using partial eta squared for ANOVAs and Phi for Chi square tests, with thresholds for small, medium and large effects considered to be 0.01, 0.06, and 0.14, respectively.

Results

Individuals diagnosed with schizophrenia or schizoaffective disorder (n = 337) participated in the study (Table 1). Sixty-five participants (19%) met criteria for PPG, and 117 (34%) reported RG. Most individuals with PPG reported never receiving treatment for PPG, consistent with studies in other populations (Leonhard et al. 2000; Slutske 2006). Results of Chi square tests and ANOVAs are reported in Table 2 and described below. In the sample, 146 individuals (60.6%) were prescribed only atypical antipsychotic medication, 23 (9.5%) were prescribed only a typical antipsychotic, 12 (5.0%) were prescribed both, and 60 (24.9%) were not currently prescribed antipsychotic medication. Gambling groups did not differ in distribution of prescription of antipsychotics or types of antipsychotic prescribed. Additional sample characteristics are reported by Desai and Potenza (2009).

Table 1 Demographic data of a sample of individuals with schizophrenia/schizoaffective disorder, separately for gambling groups (PPG, RG, NG)

	Groups			Statistics
	Prob/path gambling	Recreational gambling	Non gambling	
N	65	117	155	
Age (years) M (SD)	45.17 (8.67)	46.89 (11.80)	47.70 (11.27)	$F(2334) = 1.20$, $p = .300$
Gender (%Male)	72.30	75.20	68.40	$\chi^2(N = 337, df = 2) = 1.55$, $p = .461$
Race/ethnicity				
% White	52.30	60.70	55.50	$\chi^2(N = 337, df = 6) = 7.63$, $p = .267$
% Black	41.50	35.90	36.10	
% Hispanic	6.20	0.90	4.50	
% Other	0.00	2.60	3.90	
Marital status				
% Married	9.20	16.20	11.00	$\chi^2(N = 336, df = 8) = 10.50$, $p = .234$
% Separated/divorced	23.10	34.20	32.30	
% Widowed	0.00	3.40	1.90	
% Never married	67.70	45.30	54.80	
Education (years) M (SD)	11.86 (2.52)	12.32 (2.09)	12.64 (2.48)	$F(2334) = 2.52$, $p = .082$
Housing (% housed)	50.80	64.10	56.80	$\chi^2(N = 337, df = 2) = 3.28$, $p = .194$
Employment (% unemployed)	78.50	82.10	80.00	$\chi^2(N = 337, df = 2) = 0.37$, $p = .830$

Table 2 Substance use characteristics of a sample of individuals with schizophrenia/schizoaffective disorder, separately for gambling groups (PPG, RG, NG)

	Groups			Statistics (χ^2 or F)			
	NG	RG	PPG	Overall	PPG versus NG	RG versus NG	PPG versus RG
Treatment for SUDs (%)	36.8	48.7	51.3	$\chi^2(2) = 8.63$, $p = .013$, $\varphi = .16$	3.91, $p = .048$	7.60, $p = .006$	1.13, $p = .289$
Alcohol							
Alcohol users (%)	18.10	30.80	33.80	$\chi^2(2) = 8.60$, $p = .014$, $\varphi = .16$	6.50, $p = .011$	5.98, $p = .014$	.18, $p = .669$
Current alcohol use disorder (%)	12.30	17.10	18.50	$\chi^2(2) = 1.91$, $p = .385$, $\varphi = .08$	1.46, $p = .228$	1.27, $p = .260$	.05, $p = .816$
ASI total score M (SD)	0.06 (0.12)	0.08 (0.12)	0.12 (0.15)	$F(2, 332) = 4.39$, $p = .013$, $\eta_p^2 = .03$	8.17, $p = .005$	1.51, $p = .220$	3.22, $p = .074$
$ Spent on alcohol in 30 days prior to interview M (SD)	5.48 (18.44)	8.91 (23.13)	48.03 (141.60)	$F(2, 332) = 10.36$, $p < .001$, $\eta_p^2 = .06$	12.39, $p = .001$	1.93, $p = .166$	8.52, $p = .004$
Illegal drugs							
Current substance use disorder (%)	19.40	28.20	32.30	$\chi^2(2) = 5.14$, $p = .077$, $\varphi = .12$	4.32, $p = .038$	2.93, $p = .087$	.377, $p = .562$
ASI drug total score M (SD)	0.02 (0.05)	0.03 (0.06)	0.04 (0.07)	$F(2, 332) = 2.58$, $p = .077$, $\eta_p^2 = .02$	5.32, $p = .022$	1.35, $p = .246$	1.12, $p = .292$
$ Spent on drugs in 30 days prior to interview M (SD)	59.78 (344.10)	9.33 (42.00)	38.94 (176.57)	$F(2, 200) = .91$, $p = .404$, $\eta_p^2 = .01$	.08, $p = .767$	1.57, $p = .212$	1.97, $p = .163$
Has used opiates (%)	14.90	24.80	29.20	$\chi^2(2) = 7.04$, $p = .030$, $\varphi = .15$	6.03, $p = .014$	4.16, $p = .041$	.43, $p = .514$
Has used crack cocaine (%)	24.00	29.90	49.20	$\chi^2(2) = 13.68$, $p = .001$, $\varphi = .20$	13.56, $p < .001$	1.18, $p = .277$	6.70, $p = .010$
Has used powdered cocaine (%)	24.00	35.90	44.60	$\chi^2(2) = 10.04$, $p = .007$, $\varphi = .17$	9.20, $p = .002$	4.54, $p = .033$	1.34, $p = .248$
Has used cannabis (%)	57.80	62.40	69.20	$\chi^2(2) = 2.58$, $p = .276$, $\varphi = .09$	2.52, $p = .113$	.59, $p = .444$	.86, $p = .355$
Has used barbiturates (%)	9.10	12.80	18.50	$\chi^2(2) = 3.81$, $p = .149$, $\varphi = .11$	3.84, $p = .050$	.97, $p = .325$	1.05, $p = .305$
Has used tranquilizers (%)	8.40	10.30	13.80	$\chi^2(2) = 1.47$, $p = .479$, $\varphi = .07$	1.48, $p = .224$	.29, $p = .593$	.450, $p = .480$
Has used amphetamines (%)	13.60	16.20	21.90	$\chi^2(2) = 2.27$, $p = .321$, $\varphi = .08$	2.28, $p = .131$	.36, $p = .550$	.88, $p = .348$
Has used hallucinogens (%)	16.20	17.10	20.00	$\chi^2(2) = .46$, $p = .796$, $\varphi = .04$	.45, $p = .501$	.04, $p = .850$	.24, $p = .626$
Tobacco							
Smokes (%)	54.80	74.40	78.50	$\chi^2(2) = 16.78$, $p < .001$, $\varphi = .22$	10.83, $p = .001$	10.93, $p = .001$	.38, $p = .536$
Current nicotine use disorder (%)	53.50	65.00	67.70	$\chi^2(2) = 5.49$, $p = .064$, $\varphi = .13$	3.75, $p = .053$	3.57, $p = .059$	3.57, $p = .059$

Table 2 (continued)

	Groups			Statistics (χ^2 or F)			
	NG	RG	PPG	Overall	PPG versus NG	RG versus NG	PPG versus RG
Poly-substance use							
Lifetime (%)	54.20	65.80	78.50	$\chi^2(2) = 12.21, p = .002, \varphi = .19$	11.38, $p = .001$	3.73, $p = .054$	3.20, $p = .073$
Lifetime, including tobacco (%)	79.40	86.30	95.40	$\chi^2(2) = 9.46, p = .009, \varphi = .17$	8.80, $p = .003$	2.23, $p = .135$	3.67, $p = .055$
Last 30 days (%)	4.50	3.40	13.80	$\chi^2(2) = 9.17, p = .010, \varphi = .17$	5.91, $p = .015$	.21, $p = .649$	6.85, $p = .009$
Last 30 days, including tobacco (%)	21.30	32.50	32.30	$\chi^2(2) = 5.22, p = .073, \varphi = .12$	3.00, $p = 083$	4.33, $p = .038$	0.00, $p = .981$
Impulsivity							
Delay discounting score (0–6) M(SD)	3.09 (2.32)	3.44 (2.04)	3.48 (2.30)	$F(2) = 1.23, p = .294, \eta_p^2 = .01$	1.74, $p = .188$	1.74, $p = .188$	0.06, $p = .805$

Substance Use

Treatment for SUDs

Chi square tests of independence revealed a significant relationship between gambling group and history of treatment for SUDs. Both the RG and PPG groups were significantly more likely to have received treatment for SUDs than NG, but there was no significant difference between RG and PPG.

Alcohol Use

Significantly more individuals reported regularly consuming alcohol in the PPG group and RG group than the NG group, and there was no significant difference between RG and PPG. There was no significant relationship between gambling group and diagnosis of an alcohol-use disorder based on the 30 days prior to the interview. However, among subjects with RG or PPG, individuals with current alcohol-use-disorder diagnoses were more likely to report specifically repetitive thinking about previous gambling wins and losses, $\chi^2(1) = 6.55$, $p = .011$, $\varphi = .27$.

As previously reported, there was a significant group difference in ASI Alcohol score, such that the PPG group had significantly higher scores than non-gamblers and marginally higher scores than the RG group. We also explored relationships with specific ASI items. Notably, there was a significant group difference in money spent on alcohol in the 30 days prior to interview, such that the PPG group spent significantly more than the NG and RG groups, who did not differ from each other. Additionally, among individuals with RG or PPG, higher ASI Alcohol scores were associated with greater likelihood of repetitive thoughts about wins and losses, $B = 5.96$, $p = .002$, using gambling to regulate negative mood, $B = 2.94$, $p = .003$, increased tolerance, $B = 3.21$, $p = .028$, and chasing, $B = 3.16$, $p = .032$, and marginally greater likelihood of risk of job loss as a result of gambling, $B = 15.44$, $p = .073$.

Illegal Drug Use

There was a marginally significant relationship between gambling group and diagnosis of a non-alcohol SUD based on the 30 days prior to interview. The PPG group showed significantly higher rates than the NG group, and the RG group showed a marginal difference from the NG group, and the PPG and RG groups did not differ. There was no significant relationship between gambling group and amount of money spent on drugs in the prior 30 days.

As previously reported, there was also a marginal group difference in ASI Drug score, such that the PPG group had significantly higher scores than the NG group, and there were no differences between the other groups. ASI Drug scores were also associated with higher likelihood of risk of job loss as a result of gambling among individuals with RG or PPG, $B = 23.97$, $p = .048$.

There were also group differences in likelihood of having used particular drugs, including opiates, crack cocaine, and powdered cocaine. In pairwise comparisons, the RG group was more likely to have used opiates and powdered cocaine than the NG group. The PPG group also had a higher likelihood than the NG group of having used opiates, crack cocaine, and powdered cocaine. The PPG group was more likely to have used crack

cocaine than the RG group. There were no group differences in likelihood of having used barbiturates, tranquilizers, amphetamines, hallucinogens, or cannabis.

Tobacco Use

There were significantly more smokers in the PPG group and in the RG group than in the non-gambling group, and there was no significant differences between the RG and PPG groups. There was a marginally significant relationship between nicotine dependence and gambling group. The PPG group showed a marginally higher rate of diagnoses than the NG and RG groups. There were no significant relationships detected between tobacco use and specific PPG symptoms.

Poly-Substance Use

Groups differed with respect to lifetime PSU. Rates were significantly higher in the PPG group than NG one, and marginally higher than in the RG group, with RG rates marginally higher than NG rates. There was also a significant relationship between gambling group and past-30-day PSU. The PPG group was significantly more likely to report past-30-day PSU than the RG and NG groups, who did not differ from each other.

Delay Discounting

In a univariate ANOVA including gambling group, gender, and history of nicotine dependence as fixed effects and age as a covariate, there were no significant main effects of gambling group, gender, or age on delay discounting. There was a significant main effect of nicotine dependence, $F(1) = 6.23$, $p = .013$, $\eta_p^2 = .02$, such that patients with a history of nicotine dependence had significantly higher levels of delay discounting than patients without this history. There was a significant interaction between gambling group and gender, $F(2) = 3.43$, $p = .034$, $\eta_p^2 = .02$ (Fig. 1). Among males, there was a significant effect of gambling group, $F(2) = 4.02$, $p = .019$, $\eta_p^2 = .03$, such that the RG group was more impulsive than NG, $F(1) = 5.59$, $p = .019$, $\eta_p^2 = .03$, as was the PPG group, $F(1) = 4.99$, $p = .027$, $\eta_p^2 = .03$. Though the PPG group was numerically higher in impulsivity than the RG group, this difference did not reach statistical significance. Among females, there was no significant effect of gambling group, $F(2) = .67$, $p = .515$, $\eta_p^2 = .01$.

Among males, delay discounting also related to substance use, showing significantly higher levels among individuals who had received treatment for use of substances, $F(1) = 9.24$, $p = .003$, $\eta_p^2 = .04$, and among lifetime poly-substance users, $F(1) = 5.61$, $p = .019$, $\eta_p^2 = .02$. These relationships were not significant among females, $F(1) = 0.08$, $p = .775$, $\eta_p^2 < .001$, and $F(1) = 0.52$, $p = .474$, $\eta_p^2 = .01$, respectively.

Discussion

In the current study, the key findings are that PPG in schizophrenia is associated with substance use, in particular with PSU and with delay discounting among males. We find that SUDs are strongly linked with gambling in this sample, across an array of related factors. However, we also found that most indicators related to substance use did not significantly

differ between PPG and RG groups. These findings overall support the notion that gambling in schizophrenia shares common substrates with substance use.

Overall, gambling in schizophrenia was associated with more severe scores on the ASI for alcohol and for drugs, history of treatment for SUDs, and smoking cigarettes. Fewer factors differentiated PPG from RG groups at a statistically significant level; however, the factors distinguishing PPG and RG may hold clinical significance. In our sample, PPG was associated with more money spent on alcohol and higher frequency of cocaine use as compared with RG, as well as marginally higher ASI scores and likelihood of meeting criteria for nicotine dependence. Notably, as predicted, the PPG group was also significantly more likely to report PSU in the 30 days prior to interview than the RG group, and marginally more likely to have a lifetime history of PSU. PSU may suggest a broader susceptibility to potentially addictive stimuli. Overall, money spent on alcohol, use of cocaine, and use of multiple substances may be relevant indicators of increased likelihood of PPG in schizophrenia and may be useful to assess in clinical settings. Substance use also appears to be related overall to gambling in schizophrenia, suggesting that some potential mechanisms of risk for both may be shared in schizophrenia as they are in the general population (McLellan et al. 1992).

To this end, we also tested whether PPG was associated with increased impulsivity, a risk factor for SUDs in the general population and possibly in schizophrenia. Schizophrenia has, as discussed above, been associated with high levels of impulsivity compared with non-affected individuals, showing comparable levels of self-reported impulsivity to bipolar disorder (Fortgang et al. 2016) and steep rates of delay discounting (Heerey et al. 2007). We specifically measured choice impulsivity using an abbreviated delay-discounting questionnaire. As we predicted, we found that PPG was associated with increased impulsivity compared with non-gamblers (and marginally compared with the RG group) in males. No significant relationship was observed in females. In addition, impulsivity was elevated in individuals with history of treatment for SUDs and PSU, but again only in males, and no significant relationship was observed in females. This may suggest differential etiology of PPG in males versus females with schizophrenia, consistent with prior work showing gender-related differences in gambling trajectory, patterns, and motivations (Blanco et al. 2006; Potenza et al. 2001, 2006), and implies that self-control-related interventions may be more effective in males in this population.

An explanation of the relationship between PPG and schizophrenia ultimately must account for the finding that, unlike some other diagnostic groups showing greater odds of PPG, schizophrenia is associated with reduced reward sensitivity (Gard et al. 2007; Juckel et al. 2006) and reduced sensation-seeking (Fortgang et al. 2016; Zhornitsky et al. 2012). Schizophrenia has also been associated with more conservative and fewer risky decisions on the Balloon Analogue Risk Task (BART) and the Risky Gains Task (Cheng et al. 2012). This profile may suggest a reduced likelihood of gambling, and yet we observe the reverse. This presents an apparent inconsistency. Higher levels of sensation-seeking and impulsivity have been identified in individuals with schizophrenia with SUDs than those without (Dervaux et al. 2001; Verdejo-García et al. 2008). Still, given this set of previous findings, it may be that positive reinforcement mechanisms play a smaller role in addictive processes in schizophrenia than in other populations, or that lower levels of these traits create sensitivity to addiction.

Our results suggest that impairment in self-control and decision-making may be related to risk for both substance and behavioral addiction in men with schizophrenia. These findings resonate with those indicating that a cognitive behavioral therapy for individuals with schizophrenia and pathological gambling that includes targeting stimulus control is

effective (Echeburúa et al. 2011), and suggest that this approach may be particularly effective for males and for a broader range of addictive behaviors. Future work may investigate this possibility and also the specific environmental and genetic factors relating to impulsivity, reward sensitivity and other processes in males with schizophrenia as they pertain to PPG. Importantly, other factors may need to be investigated in females with schizophrenia in order to understand and intervene with respect to PPG.

Strengths and Limitations

Our findings provide novel information about gambling in schizophrenia. Given the high frequency of PPG in schizophrenia and the potential for adverse outcomes associated with it, more information is urgently needed regarding the relationship between the two pathologies. We use a unique and large sample to explore this relationship at a fine-grained level, using structured assessments. Limitations of our study, however, include the cross-sectional design. This limits our ability to assess true risk factors, as temporal information is only available by retrospective self-report. Future longitudinal work could address these gaps. We were also unable to compare individuals with schizophrenia and PPG with individuals without schizophrenia and with PPG. While comparison with other samples described in the literature helps to understand these findings in context, future work may directly compare these two groups to improve our understanding of whether PPG functions differently in schizophrenia. Another limitation is that the patient sample is not representative of those who are not in treatment, and that we used patient roster information to determine schizophrenia-spectrum-disorder diagnoses rather than administering structured diagnostic interviews in the context of the study.

All information about gambling and substance use relied on self-report, which may have been biased or based on inaccurate recollections. Future work could benefit from using objective measures or diary studies to reduce memory-related interference. We also did not correct for multiple testing, as this was an exploratory study. Additionally, we did not measure sensation-seeking or reward sensitivity at a trait level or overall cognitive ability. In future studies, measures of these constructs could contribute to an understanding of the mechanisms of addictive behaviors in schizophrenia, as could multi-method measurement of the complex entity of impulsivity and related constructs. Delay-discounting has been shown to load onto a component with risk-taking as assessed by the BART in a principal-components analysis (Reynolds et al. 2006), but—like other lab tasks used to measure aspects of impulsivity—it has shown inconsistent and small correlations with self-reported measures of impulsivity (e.g. Cyders and Coskunpinar 2011; Lane et al. 2003; Lewis et al. 2015). As such, additional research is needed in this area to disentangle specific aspects of impulsivity-related constructs that link to clinically relevant phenomena, particularly in specific psychiatric populations. Finally, though we identify specific links among PPG, SUDs, and delay discounting in the current study, at this time we do not offer a prediction regarding the precise relationship among these variables taken together. Future work may use additional modeling techniques to interrogate the structure of these related variables within schizophrenia.

Conclusions and Future Directions

High rates of both PPG and SUDs have been reported in individuals with schizophrenia, but considerably less is known about PPG relative to SUDs in this population. Our findings

suggest a relationship between them. However, simply stratifying by history of SUDs does not provide adequate differentiation between recreational and pathological levels of gambling. We found that a finer-grained distinction helped to uncover unique relationships with PPG, and that this process included assessment of PSU. Assessment of PPG may be beneficial alongside assessment of SUDs in clinical settings, especially for individuals with a history of substance abuse or PSU. Interventions in males with schizophrenia may benefit from a focus on self-control and decision-making. More information is needed to gain a fuller understanding of PPG in schizophrenia, but evidence suggests a need to introduce assessment of this comorbidity in clinical settings.

Acknowledgements Supported in part by: (1) the Veterans Administration, (2) the National Center for Responsible Gaming, (3) the National Center on Addiction and Substance Abuse, and (4) the Connecticut Department of Mental Health and Addiction Services. The funding agencies did not provide input into the content of the manuscript beyond the Grant funding.

Compliance with Ethical Standards

Conflict of interest The authors report no conflicts of interests with respect to the content of this manuscript. Dr. Potenza has received financial support or compensation for the following. Dr. Potenza has consulted for Ironwood, Lundbeck, Shire, INSYS, RiverMend Health, Opiant/Lakelight Therapeutics, and Jazz Pharmaceuticals; has received research support from Mohegan Sun Casino, the National Center for Responsible Gaming, and Pfizer pharmaceuticals; has participated in surveys, mailings or telephone consultations related to drug addiction, impulse control disorders or other health topics; has consulted for law offices and gambling entities on issues related to impulse control disorders; provides clinical care in the Connecticut Department of Mental Health and Addiction Services Problem Gambling Services Program; has performed grant reviews for the National Institutes of Health and other agencies; has guest-edited journal sections; has given academic lectures in grand rounds, CME events and other clinical or scientific venues; and has generated books or book chapters for publishers of mental health texts.

Ethical Approval The investigation was conducted in accordance with the Declaration of Helsinki, and the study design was approved by the institutional review boards of the West Haven VA in Connecticut and Yale University. Thus, all procedures were in accordance with the ethical standards of the institutional review boards and with the 1964 Helsinki declaration and its later amendments.

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