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An Epidemiologic, Longitudinal, and Discordant-Twin Study of the Association Between Gambling Disorder and Suicidal Behaviors

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Abstract

Gambling disorder is associated with suicidal behaviors, but it is not clear whether the association is due to common etiologic factors or to gambling disorder being causally related to suicidality. This question was examined from epidemiologic, longitudinal, and discordant twin study perspectives. The results suggested that the causes of the association with disordered gambling differed for suicidal ideation, plan, and attempt, and differed for men and women. The association of suicidal thoughts with disordered gambling was non-causally explained by common genetic influences among women (but not men). Conversely, there was evidence consistent with a potentially causal influence of disordered gambling on suicide attempt among men (but not women), which might have been related to gambling-related financial problems. The use of monetary data to identify individuals experiencing financial harms associated with their gambling may represent a more practicable target for screening, intervention, and prevention and may reduce gambling-related financial crises, thereby warding off a potential gambling-related suicide attempt.

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Authorship

W.S.S. developed the study concept and the study design. Testing and data collection were performed by W.S.S., A.C.H., M.T.L., and N.G.M. C.N.D. and W.S.S. performed the data analysis and interpretation. W.S.S. and C.N.D. drafted the paper, and A.C.H., M.T.L., and N.G.M. provided critical revisions. All authors approved the final version of the paper for submission.

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Keywords

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Gambling disorder is a pattern of gambling behavior, sometimes recurrent or persistent (Slutske, 2006), that is associated with substantial distress or impairment and that affects about 1% of the population (Potenza et al, 2019). Individuals with gambling disorder experience higher rates, relative to those without a gambling disorder, of nearly every other psychiatric disorder (Petry et al, 2005). Especially alarming is the elevated rate of suicide. For example, in a comprehensive national Swedish study of 2,099 individuals who had received treatment for gambling disorder between 2005 and 2016, 22 of 67 deaths (31%) were due to suicide. Suicide was the leading cause of death in this population-based sample of individuals who had received treatment for a gambling disorder (Karlsson & Håkansson, 2018).

It may be tempting to draw a causal link between gambling disorder and suicide. Individuals with a gambling disorder may accumulate unmanageable financial debt or be forced to face dire legal consequences – both factors that may lead some to consider suicide (Blaszczynski & Farrell, 1998; Chen et al, 2006; Wong et al, 2010). Although there is the necessary temporal order between gambling disorder and suicide mortality consistent with causality, suicides are often preceded by thoughts about suicide, plans to commit suicide, and previous attempts (Kessler et al, 1999; Wong et al, 2010).

The focus of the current investigation was on the relation between gambling disorder and these nonfatal potential precursors to suicide, that is, suicidal thoughts, plans, and attempts. To our knowledge, there have been only five previous general population surveys that focused on the association between gambling disorder and suicidal behaviors¹. Only three assessed suicidal thoughts (Meltzer et al, 2011; Moghaddam et al, 2015; Park et al, 2010), one assessed suicidal plans (Park et al, 2010), and four assessed suicide attempts (Moghaddam et al, 2015; Newman & Thompson, 2003; Newman & Thompson, 2007; Park et al, 2010). Unfortunately, three of the five studies did not assess suicidal behaviors outside of the context of a screening for major depression (Moghaddam et al, 2015; Newman & Thompson, 2003; Newman & Thompson, 2007). That is, suicidal behaviors were only assessed among those who endorsed a two-week period of depressed mood or anhedonia. This leads to measures of suicidal behaviors that are confounded with depressed mood/ anhedonia and excludes suicidal behaviors that occur outside of the context of depression². (Other than the present study), the only study that examined the relation between gambling disorder and suicidal thoughts, plans, and attempts assessed outside of the context of a depression screening in a representative sample of the general population was a study of 5,333 Korean individuals (Park et al, 2010) in which there were significant associations of gambling disorder with suicidal thoughts and plans, but not attempts. This counter-intuitive

¹The use of the term “suicidal behavior” to collectively refer to suicidal thoughts, plans, and attempts has been agreed upon by expert consensus (Nock et al, 2008b).

²A non-trivial percentage of suicidal thoughts and behaviors occur outside of the context of depression. In the present study sample, 47%, 31%, and 28% of those who reported lifetime suicidal thoughts, plans or attempts, respectively, did not have a history of major depression.

result can probably be explained by the lower prevalence of suicide attempt and the small number of individuals ($n = 43$) with gambling disorder.

Although cross-sectional studies have documented substantial associations between gambling disorder and suicidal behaviors, they cannot tell us the temporal relation between the two. There are no longitudinal studies that have tracked the occurrence of suicidal behaviors and disordered gambling over time. In the absence of longitudinal data, researchers have used retrospectively recalled ages-of-onset obtained in a cross-sectional study to examine the temporal priority of co-occurring disorders. For example, in the National Comorbidity Survey Replication, gambling disorder had a later onset than did the co-occurring disorder (including mood, anxiety, impulse-control, and substance use disorders) 74% of the time, an earlier onset 24% of the time, and first occurred in the same year 2% of the time (Kessler et al, 2008). In a small sample of 35 individuals with co-occurring gambling disorder and suicidal behaviors selected from a Swedish population-based study, gambling disorder had a later onset than did suicidal behaviors 63% of the time, an earlier onset 31% of the time, and first occurred in the same year 6% of the time (Sundqvist & Rosendahl, 2019). However, even these data on the relative timing of the onsets of gambling disorder and suicidal behaviors are unsatisfactory because later-emerging gambling disorder could still precipitate a subsequent suicidal event among those with a pre-existing history of suicidal behavior. The existing epidemiologic evidence is insufficient to rule-in or rule-out a potential causal relation between gambling disorder and suicidal behavior.

An alternate explanation for the relation between gambling disorder and suicidal behavior is that they have a shared etiology. For example, Hodgins, Mansley, and Thygesen (2006) proposed that a common factor shared between gambling, substance use, and mood disorders was related to the propensity to attempt, and ultimately, to commit suicide. This is supported by the results of an epidemiologic survey demonstrating that a significant relation between gambling disorder and suicidal behavior was substantially reduced after controlling for substance use disorders, major depression, phobia, and antisocial personality disorder (Newman & Thompson, 2003). Other evidence comes from a family study in which there was a significantly higher rate of suicide attempts (9% versus 1%; odds ratio [OR] = 12.35) among 103 offspring of 95 parents affected with a gambling disorder compared to 130 offspring of 91 unaffected control parents (Black et al, 2015), suggesting that there is a shared familial risk (that may include genetic and shared family environmental factors) common to gambling disorder and suicidal behavior.

Multilevel discordant twin modelling can provide insight into whether the association between gambling disorder and suicidal behavior is potentially causal or due to common genetic and family environmental risk factors. The discordant-twin design is a natural experiment in which a gambling disordered unaffected twin serves as the control for the gambling disordered affected co-twin (McGue et al., 2010). This individual-level effect controls for genetic and shared environmental factors and therefore can be attributed to the unique or individual-specific environment; it is consistent with a possible causal influence of gambling disorder on suicidal behaviors. Multi-level discordant twin modeling (Turkheimer & Harden, 2014) also allows one to model effects at the familial (between-twin pairs) as

well as the individual (within-twin pairs) levels. This familial-level effect represents a non-causal influence of systematic genetic or environmental differences between families that are related to both gambling disorder and suicidal behaviors. The inclusion of psychiatric covariates of interest in the model also can test whether this familial-level effect can be explained by comorbid psychiatric disorders.

The current study was based on data from a large national community-based sample of adult Australian twins that was used to explore the reasons for the elevated rates of suicidal behaviors (thoughts, plan, and attempt) among individuals with a gambling disorder. We examined cross-sectional and longitudinal epidemiologic associations between gambling disorder and suicidal behaviors and conducted multilevel discordant twin modeling predicting suicidal behaviors from gambling disorder. Significant between-twin-pair associations would provide support for a familial influence shared with gambling disorder and suicidal behavior, whereas significant within-twin-pair associations would be consistent with an individual level and a potentially causal relation. Indicators of socioeconomic status and comorbid psychiatric disorders were covaried to eliminate alternate explanations for between-twin-pair and within-twin-pair associations.

Method

Participants

Participants were 8,327 members of the Australian Twin Registry (ATR) Cohorts II and III (ATR-II and ATR-III). They represented a broad cross-section of the general population of Australia. Similar to most community-based twin cohorts, however, the sample was relatively socio-economically advantaged with an average yearly income of 87,066 (SD = 40,804) Australian dollars (equivalent to about \$56,853 in the United States in 2006).

ATR Cohort II—ATR-II members included adult twins ($n = 4,542$) born between 1964 and 1971; 57.8% of the participants were female. Nearly all the participants were of European (mostly Northern European) ancestry; 2.0% of the participants had at least one grandparent of indigenous Australian or New Zealand ancestry, and 2.7% reported Asian or Pacific Islander ancestry. For additional details see Slutske et al. (2009).

ATR Cohort III—The ATR-III members included adult twins ($n = 3,298$) and siblings ($n = 487$) born between 1972 and 1979; 63.9% of the participants were female. Nearly all the participants were of European (mostly Northern European) ancestry; slightly less than 2% of the participants had at least one grandparent of indigenous Australian ancestry, and less than 1% reported Asian ancestry. For additional details see Lynskey et al. (2012).

ATR Cohorts II and III Combined Twin Sample—The combined sample included 2,995 complete twin pairs (1,403 MZ [903 female, 500 male], 1,592 DZ [647 female-female, 327 male-male, and 618 female-male]), 1,844 individual twins from incomplete pairs (608 MZ [324 female, 284 male], 1,236 DZ [309 females and 345 males from same-sex pairs, 409 females and 173 males from opposite-sex pairs]), and six individual twins of unknown zygosity.

Procedure

In both cohorts, interviews were administered by trained lay interviewers who were supervised by project editors. All interviews were tape-recorded and a random sample of 5% of the interview tapes was reviewed for quality control.

ATR Cohort II—Two Phases of assessment were conducted with ATR-II (see Table 1). At the Phase 1 assessment, participants reported on suicidal behaviors, and at the Phase 2 assessment, an in-depth assessment of gambling behaviors and a brief assessment of suicidal behaviors were conducted. The mean age was 29.9 years (range = 24-36) at Phase 1 and 37.7 years (range = 32-43) at Phase 2. The average time interval between the Phase 1 and Phase 2 interviews was 7.8 years (SD = 1.4, range = 4-11). The ATR-II studies were approved by the Institutional Review Boards at Washington University, the University of Missouri, and QIMR. All participants provided informed consent.

ATR Cohort III—Gambling and suicidal behaviors were assessed via computer-assisted telephone interviews conducted between 2005 and 2009 (see Table 1). The mean age at assessment was 32.1 years (range = 21-46). The ATR-III study was approved by the Institutional Review Boards at Washington University and Berghofer QIMR, and secondary analysis of the data was approved by the University of Missouri. All participants provided informed consent.

Measures

Gambling Disorder—The nine DSM-5 lifetime symptoms of gambling disorder were assessed using the National Opinion Research Center DSM Screen for Gambling Problems (Gerstein et al., 1999) in both cohorts. From these symptoms, two categorical phenotypes were created: a diagnosis of DSM-5 gambling disorder³ and having at least one symptom of gambling disorder (“disordered gambling”)⁴. In ATR-II, the age of onset of each symptom of disordered gambling was also ascertained. Age of onset of gambling disorders was the age at which the first symptom occurred. Age of onset of gambling disorder symptoms was not queried in ATR-III. The internal consistency reliability of the nine-item gambling disorder symptom count was excellent: $\alpha = 0.86$. The three-month test-retest reliabilities among 166 participants from ATR-II were also very good: gambling disorder: $r = .95$, disordered gambling: $r = .95$ (tetrachoric correlations), and age of onset of gambling disorders: $r = .63$ (Pearson correlation).

Suicidal Behaviors—At Phase 1, the assessment of suicidal behaviors was the same in both cohorts. Suicidal thoughts (ideation) were assessed with the following question, “Have you ever thought about taking your own life?” Those who endorsed suicidal thoughts were asked about plans of suicide with the question “Did you ever have a [suicide] plan?” Suicide attempts were assessed for all participants, even those without suicidal thoughts or plans, by asking “Have you ever tried to take your own life?” Participants who reported

³The data collection pre-dated the release of the DSM-5. Because the DSM-5 symptom set was identical to that of the DSM-IV with the exception of one eliminated symptom (committed illegal acts to finance gambling), we were able to create a DSM-5 symptom set.

⁴Termed “gambling disorders” when referring to gambling disorder or disordered gambling in aggregate.

suicidal thoughts or attempts were also asked to indicate the ages when each of these experiences first and last occurred (the age of first suicide plan was not queried). The four-year test-retest reliabilities among 216 participants from ATR-II were generally very good: suicidal thoughts: $r = .85$, suicidal plans: $r = .56$, suicide attempt: $r = .97$ (tetrachoric correlations), age of first suicidal thought: $r = 0.67$, and age of first suicide attempt: $r = .96$ (Pearson correlations).

At Phase 2, ATR-II participants were asked “Have you ever tried to or made a plan to take your own life?” Participants who endorsed this symptom were asked to indicate the ages at which this behavior first and last occurred and whether it was “ever related to your gambling.” A composite age-of-onset of suicidality variable was created based on the earliest age reported for the three items of suicidal thoughts, suicide attempts (both from Phase 1), or suicide plans/attempts (from Phase 2).

Other Psychiatric Disorders—Interviews with both cohorts were based on the Australian version of the Semi-Structured Assessment for the Genetics of Alcoholism (Bucholz et al., 1994) and using the DSM-IV diagnostic criteria (American Psychiatric Association, 2000). The following psychiatric disorders were included: major depression, alcohol use disorder, cannabis use disorder, nicotine dependence, and conduct disorder. The diagnosis of alcohol use disorder combined abuse and dependence in accordance with changes in the DSM-5 (because craving was not assessed, it could not be included). The diagnosis of cannabis use disorder was based on an abbreviated 6-item assessment that was included in the ATR-II study (Lynskey et al, 2006), and used in the ATR-III study to harmonize the assessments in the two samples (Richmond-Rakerd et al, 2016). The four-year test-retest reliabilities (tetrachoric correlations) among 216 participants from ATR-II were very good: major depression: $r = .81$, alcohol use disorder: $r = .72$, cannabis use disorder $r = .93$, nicotine dependence: $r = .91$, and conduct disorder: $r = .84$.

Socioeconomic Status—Participants were asked to report their current combined household gross income before taxes using a respondent booklet with a list of 12 (ATR-II) or 11 (ATR-III) income ranges to use as response options. These were harmonized across the two cohorts into 11 ordered categories that were used as an ordinal income variable in analyses. Participants also reported the highest educational level attained with a list of 5 (ATR-II) or 10 (ATR-III) response options that were harmonized across the two cohorts into the 5 ordered categories of 8-10 years schooling (coded ‘1’), matriculation/year 12 (‘2’), technical, teachers' college, TAFE, business or secretarial college (‘3’), university under-graduate training (‘4’) and university post-graduate training (‘5’). These ordered categories were treated as an ordinal educational attainment variable in analyses. Childhood socioeconomic status was based on the response to a question regarding perceived relative financial stability compared to the average family in the community (“better off,” “about average,” or “worse off”) when the participants were 6-13 years of age.

Data Analysis

Cross-Sectional Phenotypic Analyses—Prevalences of gambling disorder and suicidal behaviors were evaluated. Mixed effects logistic regression was conducted within

SAS v9.4 (SAS Institute Inc., 2013) to account for the clustering of data within families. To test whether the effects differed for men and women, interaction terms between sex and gambling disorders were included. We tested whether the cross-sectional phenotypic associations between gambling disorders and suicidal behaviors remained after accounting for other frequently comorbid disorders (major depression, nicotine dependence, alcohol use disorder, cannabis use disorder, and conduct disorder). Additionally, given the differing timing of assessments across cohorts, we tested whether the effects of gambling disorders on suicidal behaviors were moderated by cohort.

Longitudinal Phenotypic Analyses—These analyses were based on data from ATR-II. The mean ages of onset of suicidal behaviors and gambling behavior and disorder were examined, and the relative temporal precedence of onsets of suicidal behaviors and gambling behavior were compared with a chi-squared test for equality of proportions. The prospective effects of suicidal thoughts, plans, and attempts on later gambling disorder were evaluated with mixed effects logistic regression.

Multilevel Discordant Twin Analyses—Two-level generalized mixed effects logistic regression was conducted using SAS v9.4 PROC GLIMMIX. Mixed effects logistic regression is used for analyzing clustered binary response data, such as the occurrence of at least one suicide attempt (Hedeker, 2003). With twin data, mixed effects models are appropriate given the inherent clustering of individual twins (level 1) within twin pairs (level 2). Level 1 and level 2 variances were estimated, along with a random intercept. Model estimated coefficients were exponentiated to yield odds ratios (ORs).

A series of three (for suicidal thoughts) or four (for suicidal plans and attempts) models were fit for each suicidal behavior. First, models were run at the individual level while accounting for the non-independence of twin-pair observations. These analyses examine evidence for an overall effect of disordered gambling on each suicide outcome and approximate analyses conducted with unrelated individuals. Minimally-adjusted base models were fit predicting each suicide outcome from the presence or absence of disordered gambling and included age, sex, zygosity, childhood socioeconomic status, adult household income, and educational attainment as covariates. Potential sex and zygosity differences in the effect of disordered gambling were evaluated by including interaction terms. If significant, they were carried forward into fully-adjusted analyses. Fully-adjusted models were fit including all covariates from the minimally-adjusted models, as well as psychiatric conditions (major depression, alcohol use disorder, cannabis use disorder, nicotine dependence, and conduct disorder).

Second, discordant twin models among MZ and DZ same-sex twin pairs were fit to remove potential sources of confounding that may contribute to the overall effect observed in individual level models (McGue et al., 2010). Compared to the analysis of unrelated individuals, discordant twin modeling controls for the shared family environment and genetic factors. Because of this, the approach is uniquely suited to parsing familial effects from possible causal effects of a predictor. Discordant twin models were represented by the following equation:

$$Y_{ij} = \beta_0 + \beta_b \bar{x}_i + \beta_w (X_{ij} - \bar{x}_i),$$

where Y_{ij} is the presence or absence of suicidal thoughts, plans, or attempts (depending on the model) for each twin; X_{ij} indicates whether the twin has disordered gambling or not (0 indicates no symptoms, 1 indicates at least one symptom); and \bar{x}_i is the average score of disordered gambling for the twin pair (0 indicates neither twin has disordered gambling, 0.5 indicates one twin has disordered gambling [i.e., discordant twin pairs], and 1 indicates both twins have disordered gambling)⁵. The coefficient β_b refers to a between-twin pair effect and represents variation accounted for by familial factors shared by both twins. The coefficient β_w represents the within-twin pair effect (i.e., potentially causal effect), or the difference in the odds of suicidality between the twin without disordered gambling and the twin with disordered gambling. Minimally- and fully-adjusted models were fit including MZ and same-sex DZ twin pairs. We explored possible sex differences in the effects of between-twin pair and within-twin pair predictors by including interaction terms. Significant interactions were carried forward into fully-adjusted models.

Third, a set of models that were limited to MZ twins were conducted as a more stringent control for genetic confounding. Fourth, in order to differentiate the predictors of suicide plans and attempts from suicidal thoughts (May & Klonsky, 2016), individual level and discordant twin models that were limited to participants who reported suicidal thoughts were fit to predict suicide plan and attempt.

Biometric Twin Analyses—Although not the main focus of this study, biometric twin analyses were conducted to provide insight into any significant between-family effects observed in the multilevel discordant twin analyses. In particular, bivariate twin analyses were employed to determine the extent to which any between-family influences of disordered gambling on suicidal behavior were explained by genetic or shared environmental influences. The logic behind univariate twin modeling is presented in the Supplemental Materials. Below we describe the logic behind bivariate twin modeling.

The logic of bivariate twin modeling is similar to univariate twin modeling (the analysis of a single trait). With bivariate twin modeling, one is interested in the cross-trait as well as the within-trait similarity. For example, one examines the similarity of disordered gambling in one twin with suicidal thoughts in the other twin. If the MZ cross-trait, cross-twin similarity is greater than the DZ cross-trait, cross-twin similarity, then one infers that genetic factors are contributing to the association between disordered gambling and suicidal thoughts. In other words, there is at least one gene that is a risk factor for both disordered gambling and suicidal thoughts. If the DZ cross-trait, cross-twin similarity is greater than half the MZ cross-trait, cross-twin similarity, then one infers that shared environmental factors are contributing to the association between disordered gambling and suicidal thoughts. Unique environmental factors are implicated when the MZ cross-trait, cross-twin similarity is substantially less than the cross-trait within-twin correlation between disordered gambling

⁵An alternative continuous approach to characterizing discordance was also considered. See Supplemental Table S4 and accompanying text for the rationale for adopting a categorical approach.

and suicidal thoughts. This represents the correlation between disordered gambling and suicidal thoughts that remains after controlling for genetic and shared environmental influences, that is, the factors that are not shared between twins. The unique environmental correlation represents the within-twin-pair association between disordered gambling and suicidal thoughts and is consistent with a potentially causal association (Turkheimer & Harden, 2014).

Results

Cross-sectional Phenotypic Analyses in ATR-II and ATR-III

Prevalences—About one quarter of participants (26.05%) reported having had suicidal thoughts, 6.77% reported having made a suicide plan, and 4.04% had attempted suicide. Men and women were equally likely to report having had suicidal thoughts or making a suicide plan, but men were significantly less likely to report having made a suicide attempt (OR = 0.59 [0.47 – 0.76]). Among those who had made a suicide attempt, 61.86% had made a single attempt, and this did not differ for men and women (men: 61.96%; women: 61.83%); the average number of attempts was 2.09 (SD = 2.47, maximum = 20), and this also did not differ for men (M=1.92, SD = 2.41) and women (M=2.15, SD = 2.50). As expected, suicide attempt was strongly correlated with having had suicidal thoughts and having made a plan (Table 2), and it was exceedingly rare to report a suicide attempt without also reporting having had suicidal thoughts (0.89%). On the other hand, suicide attempt was frequently reported in the absence of ever having made a plan (38.39%).

Regarding gambling disorder, 2.50% met the criteria for a lifetime diagnosis of DSM-5 gambling disorder (4.21% of men and 1.39% of women), and 10.47% (16.67% of men and 6.44% of women) met the criteria for disordered gambling. The prevalences of the nine individual symptoms of DSM-5 gambling disorder are presented in Table S1, the prevalences of participation in 11 different gambling activities are presented in Table S2, and the amounts of time and money spent on gambling are presented in Table S3, all in the Supplemental Materials. Of particular interest is the costliness of gambling disorder and disordered gambling in terms of the time and money spent; during the year of peak gambling involvement, individuals with gambling disorder and disordered gambling had spent 105% and 40%, respectively, of their yearly annual household income on gambling (Table S3).

Associations Between Gambling Disorder and Suicidal Behaviors—Individuals with gambling disorder were about three times as likely as those without a diagnosis to report suicidal thoughts (OR = 2.62 [1.95 – 3.51]), plans (OR = 3.48 [2.39 – 5.05]), and attempts (OR = 3.05 [1.91 – 4.87]); 47.60% of those with gambling disorder reported having suicidal thoughts, 19.71% reported having made a suicide plan, and 11.06% had made a suicide attempt. The magnitude of the associations between gambling disorder and suicidal behaviors did not differ for men and women (thoughts: $F_{(1,3386)} = 0.17$, $p = 0.68$; plans: $F_{(1,3386)} = 0.02$, $p = 0.89$; attempts: $F_{(1,3386)} = 0.00$, $p = 0.96$). They also did not differ between the ATR-II and ATR-III cohorts (thoughts: $F_{(1,3386)} = 0.16$, $p = 0.69$; plans: $F_{(1,3386)} = 0.14$, $p = 0.71$; attempts: $F_{(1,3386)} = 1.34$, $p = 0.25$), which suggests that the different timing of assessments for the two cohorts did not affect the results.

The associations between the nine individual symptoms of DSM-5 gambling disorder and suicidal thoughts (mean OR = 2.33), plans (mean OR = 3.10) and attempts (mean OR = 2.81) are presented in Table S1, and the association of specific gambling activities with suicide plans or attempts are presented in Table S2. Although all the gambling disorder symptoms were associated with all three suicidal behaviors, the association between the symptom of borrowing money to relieve a desperate financial situation, i.e., “bail out,” was especially strongly associated with suicide attempt (OR = 4.60 [2.64 – 7.99]; Table S1). Of the 11 gambling activities, the only one that was associated with suicidal behaviors was participation in electronic gambling machines (OR = 1.66 [1.20 – 2.29]; Table S2).

Associations Between Disordered Gambling and Suicidal Behaviors—

Participants with at least one symptom of gambling disorder were about twice as likely as those without any symptoms to report suicidal thoughts (OR = 1.78 [1.52 – 2.08]), plans (OR = 2.08 [1.65 – 2.63]) and attempts (OR = 1.89 [1.41 – 2.55])⁶. These associations also did not differ in magnitude for men and women (thoughts: $F_{(1,3386)} = 1.57, p = 0.21$; plans: $F_{(1,3386)} = 0.06, p = 0.81$; attempts: $F_{(1,3386)} = 0.58, p = 0.44$). They also did not differ across the two cohorts (thoughts: $F_{(1,3386)} = 0.38, p = 0.54$; plans: $F_{(1,3386)} = 0.03, p = 0.87$; attempts: $F_{(1,3386)} = 0.33, p = 0.57$), again supporting the decision to combine the two cohorts.

Role of Psychiatric Comorbidity—

There were significant associations between suicidal thoughts, plans, and attempts and psychiatric disorders (see Table 2). There were also significant associations between gambling disorder and psychiatric disorders (see Table 2). After accounting for psychiatric comorbidity, the associations between gambling disorder and suicidal thoughts and attempt became non-significant (thoughts: OR = 1.37 [0.99 – 1.90]; attempt: OR = 1.22 [0.74 – 2.01]), and the association with suicidal plan remained significant but was attenuated (OR = 1.70 [1.13 – 2.55]). On average, the odds ratios of the associations between gambling disorder and the three suicidal behaviors were attenuated by 79.40%, and this did not substantially differ for men (80.87%) and women (68.57%). Among those with a history of gambling disorder, suicidal thoughts (5%), plan (2%), and attempt (0%) never or rarely occurred in the absence of a history of major depression, alcohol use disorder, cannabis use disorder, or conduct disorder (nicotine dependence was not included in this analysis).

Compared to gambling disorder, the magnitudes of the associations between disordered gambling and psychiatric disorders were somewhat weaker (Table 2). As with gambling disorder, the associations between disordered gambling and suicidal thoughts and plans remained but were attenuated (thoughts: OR = 1.28 [1.08 – 1.53]; plans: OR = 1.42 [1.10 – 1.83]), and the association of disordered gambling with suicide attempt became non-significant (OR = 1.11 [0.80 – 1.53]) after accounting for history of major depression, alcohol use disorder, cannabis use disorder, nicotine dependence, and conduct disorder. On average, the odds ratios of the associations between disordered gambling and the three suicidal behaviors were attenuated by 70.95%, and this did not substantially differ for

⁶Even a single symptom of disordered gambling was significantly associated with increased odds of suicidal thoughts (OR = 1.58 [1.30 – 1.93]), plan (OR = 1.54 [1.11 – 2.14]), and attempt (OR = 1.57 [1.04 – 2.36]) relative to zero disordered gambling symptoms.

men (68.41%) and women (68.85%). Among those with a history of disordered gambling, suicidal thoughts (13%), plan (5%), and attempt (3%) rarely occurred in the absence of a history of comorbid major depression, alcohol use disorder, cannabis use disorder, or conduct disorder.

Longitudinal Phenotypic Analyses in ATR-II

Ages of Onset of Gambling Disorder and Suicidal Behaviors—There were 1,251 (27.54%) individuals in ATR-II with a history of any suicidal behavior. The mean age of onset of suicidal behavior was 20.40 (SD = 6.4), and this did not differ for men and women (men: 20.77; women: 20.14; $t = 1.72$, $p = .09$). There were 125 individuals (2.75%) with a history of gambling disorder. The mean age of onset of gambling disorder was 24.40 (SD = 6.39), which differed for men and women (men: $M = 22.87$; women: $M = 27.14$; $t = -3.74$, $p = .0003$).

Temporal Precedence of Gambling Disorder and Suicidal Behavior—Among 66 individuals with co-occurring gambling disorder and suicidal behavior, 61% ($n=40$) of the time gambling disorder had a later onset than did suicidal behavior, 29% ($n=19$) of the time it had an earlier onset, and 11% ($n=7$) of the time gambling disorder and suicidal behavior first occurred in the same year (test of unequal proportions of later versus earlier onset: $\chi^2(1) = 7.47$, $p < 0.006$), and these proportions differed between men and women (men: later = 54%, earlier = 38%, same year = 10%; women: later = 75%, earlier = 13%, same year = 13%; difference between later v. earlier: $\chi^2(1) = 4.79$, $p = 0.03$).

Gambling disorder also had a later *offset* than suicidal behavior 86% ($n=55$) of the time (test of unequal proportions of later versus earlier offset: $\chi^2(1) = 48.50$, $p < 0.0001$)⁷, and 30% ($n=20$) of the time the *first* gambling disorder symptom had occurred 2-17 years (mean = 10.11) after the *last* suicidal behavior had occurred. Gambling disorder was also more persistent than suicidal behaviors, with mean durations from onset to recency of 10.23 (SD = 6.99) and 6.48 years (SD = 7.10), respectively. The average age of the 66 participants with co-occurring gambling disorder and suicidal behavior was 38.03 years; 32 of these (48.48%) had experienced symptoms of disordered gambling within the past year, whereas none had experienced a suicidal thought, plan, or attempt within the past year. The average number of years since the last gambling disorder symptom and suicidal behavior were 2.36 (SD = 3.34) years and 10.57 (SD = 5.65) years, respectively.

A small fraction of individuals attributed their suicidal behavior to gambling. At the Phase 2 interview, 8 of 424 participants who reported a suicide plan or attempt acknowledged that it was related to their gambling. Seven had a lifetime history of gambling disorder, which represented 20.00% of participants with co-occurring gambling disorder and suicidal behavior (based on this single question about suicide plans or attempts).

⁷It was not possible to test sex differences because there were no women who had an earlier gambling disorder than suicidal behavior offset. However, the proportions were quite similar (men: gambling offset later = 88%, earlier = 5%, same year = 3%; women: gambling offset later = 83%, earlier = 0%, same year = 6%).

Longitudinal Associations Between Suicidal Behaviors and Gambling

Disorder—Those who reported suicidal thoughts (OR = 2.58 [1.79 – 3.71]), plans (OR = 3.74 [2.36 – 5.94]) and attempts (OR = 2.41 [1.23 – 4.72]) at Phase 1 were more likely to meet the lifetime criteria for gambling disorder nearly eight years later at Phase 28, and this did not significantly differ for men and women (all $ps > .36$). After accounting for psychiatric comorbidity, the prospective association between suicidal plans and gambling disorder remained significant but was attenuated (OR = 1.83 [1.10 – 3.04]) and the prospective associations between suicidal thoughts and attempt and gambling disorder became non-significant (thoughts: OR = 1.36 [0.91 – 2.03]; attempt: OR = 0.89 [0.41 – 1.92]). Note that these are very similar to the cross-sectional phenotypic associations reported above, which again suggests that the different timing of assessments for the two cohorts did not affect the results and supports combining them in the cross-sectional phenotypic and multilevel discordant twin modeling analyses.

Multilevel Discordant Twin Analyses in ATR-II and ATR-III

Despite the large sample size of over 2,300 complete same-sex twin pairs, there were only 75 pairs discordant for gambling disorder. Therefore, the multilevel discordant twin analyses were based on the broader disordered gambling phenotype. There were 307 same-sex twin pairs discordant for disordered gambling in the full sample, 170 discordant MZ pairs (76 female, 94 male) and 137 discordant DZ pairs (59 female, 78 male). The affected twin in the discordant pairs usually had a single symptom of disordered gambling (59.28%) and the average number of symptoms was 2.23 (SD = 2.05).

Preliminary descriptive analyses of the association between suicidal behaviors and disordered gambling in discordant twin pairs are presented in Table 3. Among disordered gambling discordant twin pairs, the affected twin was significantly more likely to have experienced suicidal thoughts than the unaffected cotwin (35.50% versus 26.71%), was more likely to have made a suicide plan than the unaffected cotwin, although this difference was not significant (9.45% versus 7.82%) and was more likely to have made a suicide attempt than the unaffected cotwin, although this difference was also not significant (6.51% versus 4.56%). Interestingly, for all three suicidal behaviors, the within-twin pair association with disordered gambling was stronger among men than women. These associations and potential sex differences were more rigorously examined in the multilevel models.

Suicidal Thoughts

Individual Level Model: Disordered gambling was associated with increased odds of having suicidal thoughts (OR = 2.00 [1.65 – 2.41]). This association was attenuated but remained significant after accounting for comorbid psychopathology (OR = 1.37 [1.12 – 1.68]; see Figure 1). Several covariates also showed significant associations with suicidal thoughts (see Table 4 Panel A).

⁸Among those who met the diagnostic criteria for gambling disorder, most onsets actually occurred prior to the Phase 1 interview (76%), so these are not truly prospective associations.

MZ and DZ Discordant Twin Model. In the base model, significant associations with suicidal thoughts were observed at both the within-pair and between-pair levels (within-pair: OR = 1.70 [1.15 – 2.52]; between-pair: OR = 2.89 [1.98 – 4.22]). This means that, within discordant twin pairs, the twin who reported disordered gambling had 70% greater odds of having suicidal thoughts than the unaffected co-twin; compared to pairs where neither twin reported disordered gambling, members of twin pairs where at least one twin engaged in disordered gambling had almost three times the odds of suicidal thoughts. The between-twin-pair effect of disordered gambling differed for men and women (interaction OR = 2.56 [1.21 – 5.41]), with a significantly greater effect in women than men (see Figure 1). The within-twin-pair effect did not significantly differ for MZ and DZ twins (OR = 0.76 [0.34 – 1.66]).

Once comorbid psychopathology was included in the model, the within-twin-pair effect became nonsignificant (OR = 1.52 [1.00 – 2.32]), but the between-pair by sex interaction remained significant (interaction OR = 2.78 [1.28 – 6.01]). Exploring this interaction further, we found that there was a significant between-pair effect for women (OR = 2.77 [1.54 – 4.96]), but not men (OR = 1.05 [0.63 – 1.77]; see Figure 1). The inclusion of comorbid psychopathology in the models attenuated the between-pair effect by 55% in women and 94% in men, with significant effects of major depression, alcohol use disorder, cannabis use disorder, and conduct disorder in both sexes (see Table 4 Panel B). The results of the discordant twin model restricted to MZ twins were consistent with those from the MZ and DZ model (see Table S5 in Supplemental Material).

Suicide Plan

Individual Level Model. In the minimally-adjusted individual level model, disordered gambling was associated with more than three times the odds of reporting a suicide plan in one's lifetime (OR = 3.31 [1.83 – 5.99]). The inclusion of comorbid psychopathology reduced this association, but it remained significant (OR = 2.35 [1.15 – 4.81]). (see Table 4 Panel A).

MZ and DZ Discordant Twin Model. In the minimally-adjusted model including only demographic covariates, the between-pair effect of disordered gambling was significant (OR = 3.76 [1.05 – 13.47]), but the within-twin pair effect was not (OR = 1.48 [0.55 – 4.02]). This means there was no evidence for a potentially causal effect of disordered gambling on suicidal plan, but being a member of a twin pair where at least one twin reported disordered gambling was associated with almost four times the odds of having made a suicide plan. There was no evidence for sex differences in these effects. The within-twin-pair effect did not significantly differ for MZ and DZ twins (OR = 0.58 [0.08 – 4.29]). Comorbid psychopathology, primarily major depression and conduct disorder, appeared to largely explain the between-pair effect of disordered gambling, as this association became nonsignificant and was attenuated by 64% with the inclusion of these covariates (OR = 1.99 [0.46 – 8.65]; see Table 4 Panel B). The results of the discordant twin model restricted to MZ twins was consistent with those from the MZ and DZ model (see Table S5 in Supplemental Material).

Restricting Analyses to Participants with Suicidal Thoughts.: Analyses predicting suicidal plan were conducted in the subset of participants who reported having suicidal thoughts. Of primary interest was the extent to which the original effect sizes from the full samples were attenuated or amplified once suicidal thoughts were held constant. Table S6 in the Supplemental Materials compares the results of the two sets of models.

Individual Level Model.: The results of the individual level analyses of suicide plan controlling for suicidal thoughts were similar to the original analyses. Disordered gambling remained a significant predictor of suicide plan in the minimally- and fully-adjusted models, but with effect sizes attenuated by 79% and 93%, respectively (see Table S6).

MZ and DZ Discordant Twin Model.: The results of the discordant twin analyses of suicide plan controlling for suicidal thoughts were similar to the original analyses. The between-twin-pair effect of disordered gambling remained a significant predictor of suicide plan in the minimally adjusted model, but with the effect size attenuated by 60% (see Table S6).

Suicide Attempt

Individual Level Model.: In the minimally-adjusted individual level model, disordered gambling was associated with almost four times the odds of having made a suicide attempt (OR = 3.76 [1.77 – 8.02]). After comorbid psychopathology was included in the model, the association between disordered gambling and suicide attempt was attenuated and nonsignificant (OR = 1.98 [0.81 – 4.82]).

MZ and DZ Discordant Twin Model.: In the minimally-adjusted discordant twin model, there was not a significant between-pair effect (OR = 1.78 [0.29 – 11.05]), but there was a significant within-twin-pair effect of disordered gambling on lifetime suicide attempt (OR = 5.63 [1.39 – 22.78]). Compared to a co-twin without disordered gambling, the twin with disordered gambling had more than five times the odds of having made a suicide attempt. There was a significant sex difference in the within-pair effect (interaction OR = 0.04 [0.002 – 0.87]), such that the effect was far greater for men than women (men: OR = 136.74 [6.35 – 2944.22]; women: OR = 1.89 [0.36 – 9.87]). The within-twin pair effect did not significantly differ for MZ and DZ twins (OR = 2.60 [0.18 – 38.25]).

With the inclusion of comorbid psychopathology in the model, the within-twin-pair by sex interaction became nonsignificant, although the effect size was still large (OR = 0.25 [0.01 – 5.10]). The within-twin pair effect among men (OR = 23.13 [0.55 – 967.87]) was much larger than among women (OR = 1.38 [0.25 – 7.75]), although both effects were not significant. The results of the discordant twin model restricted to MZ twins were consistent with those from the MZ and DZ model (see Table S5 in Supplemental Material).

Restricting Analyses to Participants with a History of Suicidal Thoughts.: As was done for suicidal plans, analyses predicting suicide attempt were conducted among the subset of participants who reported experiencing suicidal thoughts. Presented in Table S6 in the Supplemental Materials is a comparison of the original results and the results after controlling for suicidal thoughts.

Individual Level Model.: The results of the individual level analyses of suicide attempt controlling for suicidal thoughts were similar to the original analyses. Disordered gambling remained a significant predictor of suicide attempt in the minimally adjusted model, but with the effect size attenuated by 53%. (see Table S6).

MZ and DZ Discordant Twin Model.: The results of the discordant twin analyses of suicide attempt controlling for suicidal thoughts were similar to the original analyses. The within-twin-pair effect of disordered gambling remained a significant predictor of suicide attempt in the minimally-adjusted model with the effect size increasing by 178%; this effect was substantially larger and significant among men but not women. In the fully-adjusted model the within-twin-pair effect was still nonsignificant although the effect size increased by 575% (see Table S6).

Biometric Twin Analyses of Disordered Gambling and Suicidal Thoughts

Biometric twin modeling was conducted to follow up on the between-twin-pair association between disordered gambling and suicidal thoughts that was significant among women but not men. Twin correlations for disordered gambling and suicidal thoughts (Table S7) and the results of univariate twin modeling (Table S8) are presented in the Supplemental Materials. The relative contributions of genetic, shared environmental, and unique environmental influences to disordered gambling liability were 0.54, 0, and 0.46, respectively, and were 0.51, 0, and 0.49, respectively, for the propensity to experience suicidal thoughts. The estimates for men and women did not significantly differ (see Table S8).

The MZ cross-trait twin correlation for disordered gambling and suicidal thoughts was significant among women ($r = 0.25$), but not among men ($r = 0.09$; see Table S7). When a bivariate biometric twin model was fit to the data allowing the parameter estimates to differ for men and women, there was not a significant reduction in model fit when the contributions of shared environmental influences were dropped: $\chi^2(6) = 0.92, p = 0.99$, and a model that included genetic and unique environmental influences provided an adequate fit to the data: $\chi^2(24) = 28.87, p = 0.23$. The genetic contributions to disordered gambling and suicidal thoughts were significantly correlated in women ($r_a = 0.42$ [0.26 to 0.63]), but not in men ($r_a = 0.15$ [-0.15 to 0.45]), and the unique environmental contributions to disordered gambling and suicidal thoughts were significantly correlated in men ($r_e = 0.26$ [0.03 to 0.48]), but not in women ($r_e = -0.04$ [-0.42 to 0.17]); these estimates were relatively unchanged when shared environmental influences were included in the model. These results are consistent with the multilevel discordant twin model showing that the between-twin-pair effects of disordered gambling were associated with suicidal thoughts among women, but not among men, and extends these findings by demonstrating that the between-twin-pair effects were due to common genetic influences.

Discussion

The present study establishes significant associations between gambling disorders and suicidal thoughts, plan, and attempt in a general population sample for the first time. It also is the first study to dissect these associations into family-level (including genetic and

shared environmental factors) and individual-level (including a potentially causal relation) components.

Differences Between Suicidal Thoughts, Plan, and Attempt

The causes of the associations with disordered gambling differed for suicidal thoughts, plan, and attempt. In the multilevel discordant twin models, the between-twin-pair associations between disordered gambling and suicidal thoughts and plan were larger than the within-twin-pair associations. The opposite was true for suicide attempt where the within-twin-pair association was larger than the between-twin-pair association. This means that the associations of disordered gambling with suicidal ideation or plan were mainly due to genetic or shared environmental influences that differed between families, whereas the association with suicide attempt was mainly due to unique environmental influences that varied within twin pairs. Combining suicidal behaviors together into an overall “suicidality” measure may obscure important differences.

There were also important sex differences in these associations. The between-twin-pair association of disordered gambling with suicidal thoughts differed among men and women, with the association being larger and only significant among women; follow-up biometric analyses narrowed down the source of the between-family effect to shared genes. The within-twin-pair association of disordered gambling with suicide attempt was larger and only significant among men. This means that there is something that differs within male twin pairs discordant for disordered gambling that contributes to the association with suicide attempt and is consistent with a potentially causal relation.

From Suicidal Thoughts to Suicide Plan and Attempt

There is a concern that much of the extant suicidality literature has conflated the correlates of suicide attempt with the correlates of suicidal thoughts, with convincing evidence that many of the correlates of suicide attempt disappear or are substantially reduced after accounting for the presence of suicidal ideation (Klonsky et al, 2016; May & Klonsky, 2015). Therefore, we revisited the multilevel analyses of suicide plan and attempt restricted to participants with a history of suicidal thoughts.

At the individual and the between-twin-pair level the associations of disordered gambling with suicide plan remained significant but were substantially attenuated, suggesting that much of the association was with suicidal thinking. Nonetheless, a significant association of disordered gambling with suicide plan remained after accounting for suicidal thoughts. This residual association suggests that disordered gambling may also be related to the progression from suicidal thinking to forming a suicide plan.

The association of disordered gambling with suicide attempt at the individual level was substantially attenuated and no longer significant after accounting for a history of suicidal thoughts. At the within-twin-pair level, however, the association between disordered gambling and suicide attempt was substantially amplified, with the sex difference intact. This suggests that not only is the within-twin-pair difference in disordered gambling associated with suicide attempt among men, but that by stripping away the influence on

suicidal thinking an even stronger association was revealed. This intriguing and novel (yet unpredicted) finding requires replication.

Role of Psychiatric Comorbidity

The cross-sectional associations between gambling disorders and the three suicidal behaviors were attenuated by over 70% after accounting for comorbid psychopathology, but the magnitude of the contribution of psychiatric comorbidity to the associations between disordered gambling and suicide plan and attempt were substantially reduced when analyses were restricted to participants with a history of suicidal thoughts. This is consistent with the results of a massive international survey of 11 nations (Nock et al, 2008a), and a large United States national survey (Hoertel et al, 2015). Comorbid psychopathology is primarily associated with suicidal thoughts but may also play a role in the progression to suicide plan and attempt.

Temporal Relation between Gambling Disorder and Suicidal Behaviors

The ability to draw causal inferences from the multilevel discordant twin analyses was hampered by the reliance on cross-sectional data. We attempted to discern the temporal relation between gambling disorder and suicidal behaviors from retrospectively-reported ages-of-onset and recency. The mean age of onset of suicidal behaviors (20.40) was earlier than the mean age of onset of gambling disorder (24.40), and for the majority of those who experienced both, the onset of suicidal behaviors was more likely to precede the onset of gambling disorder (61%), the offset of suicidal behaviors was more likely to precede the resolution of gambling disorder (86%), and there was a substantial percentage (30%) whose first symptom of gambling disorder post-dated the last suicidal behavior by many years. This suggests that gambling disorder was unlikely to be a predominant cause of suicidal behavior. This is consistent with the finding that only a minority of those with co-occurring gambling disorder and suicidal behavior (20%) attributed the suicidal behavior to gambling. Although this was based on a small number of individuals, it is strikingly similar to the rate observed among those with co-occurring gambling disorder and suicide attempt (21%) in a Canadian study (Hodgins et al, 2006).

Both the present Australian study and a previous Swedish study suggest that there might be important differences between men and women in the sequence of gambling disorder and suicidal behavior. In the present study, men were significantly more likely than women to experience an onset of gambling disorder that preceded the onset of suicidal behavior (38% versus 13%). Although the differences were not statistically significant, the Swedish study (Sundqvist & Rosendahl, 2019) also found that suicidal behavior onset more often came after or in the same year as the onset of gambling disorder among men (42%) than among women (27%). These data raise the possibility that gambling disorder may be more likely to be a cause of suicidal behavior among men than among women, which is consistent with the results of the discordant twin analyses of suicide attempt.

Potentially Causal Effect of Disordered Gambling on Suicide Attempt Among Men

The processes by which disordered gambling may potentially cause a suicide attempt particularly among men remain unclear. We hypothesize that this may have to do with

the uniquely life-altering financial toll that disordered gambling can exact. Historically, population rates of suicide have been associated with major economic downturns, with the highest rate of suicide in the last 100 years in the United States and Australia occurring during the Great Depression of 1929-1933 (Morrell et al, 1993; Tapia Granados & Diez Roux, 2009), with all the excess suicides occurring among men (Macmahon et al, 1963; Morrell et al, 1993). The more recent Great Recession of 2008 similarly led to an uptick in “economic suicides” with a fourfold greater increase among men than among women (Reeves, McKee, & Stuckler, 2014)⁹. A psychological autopsy study conducted in Hong Kong of 150 completed suicides, compared to 150 matched living controls, demonstrated that suicides were more likely to be preceded by unmanageable debt or unemployment (Chen et al, 2006), and of the 17 gambling-related suicides, all were characterized by unmanageable debt (Wong et al, 2010). These financial crises may pose a greater suicide risk among men than women because they may threaten the traditional primary role identities of men as being financially stable and competitive in the labor force (Girard, 1993; Stack, 2000), leading to feelings of burdensomeness and hopelessness (Klonsky & May, 2015; van Orden et al, 2010).

Limitations

There were at least five limitations of the current study. First, the sex-specific multilevel discordant twin models of suicide attempt were underpowered, making it difficult to interrogate the significant difference observed between men and women. Second, potentially important psychiatric disorders, such as bipolar disorder, post-traumatic stress disorder, panic disorder, and generalized anxiety disorder, as well as traits such as impulsivity, were not included. These might have contributed to the between-twin-pair effect of disordered gambling on suicidal thoughts among women, or to the progression to suicide plan or attempt in either sex. Third, although there was adequate test-retest reliability of the measures, they were all based on retrospective reports, which have known weaknesses (e.g., Henry et al, 1994), especially assessments of ages of onset (e.g., Prusoff et al, 1988). Fourth, given the dearth of longitudinal data on suicidal behaviors, the availability of assessments at two time points was a strength of the study. However, the longitudinal nature of the study was extremely limited. The study would have been strengthened by assessing suicidal and gambling behaviors at multiple time points, and this should be a priority for future research. Fifth, the participants represented a narrow age range (27-43 years), were primarily of Northern European ancestry, and resided in Australia. In addition, the data were collected over a decade ago. Thus, it is not clear the extent to which the results of this study can be generalized to other ages, ethnicities, racial groups, countries, or the current milieu. Moving forward, the inclusion of more diverse and contemporary samples will also be an important priority for research.

Conclusions and Future Directions

This study represents the largest and most comprehensive epidemiologic study and the only genetically-informed study of the relation between gambling disorders and suicidal behaviors. The significant association of disordered gambling with suicidal thoughts

⁹A similar uptick in “economic suicides” was predicted in the wake of the COVID-19 pandemic (McIntyre & Lee, 2020).

appeared to be primarily due to common genetic factors (especially among women), and the association of disordered gambling with suicide attempt was potentially due to a causal relation (especially among men).

Great progress had been made in the past decade in elucidating the genetic overlap between different psychiatric disorders by interrogating the results of genome-wide association studies (GWAS; Harden & Koellinger, 2020). Importantly, the genotype-phenotype associations of interest (for example, for gambling disorder and suicidal behavior) do not have to come from the same study. There have now been a handful of large-scale GWASs of suicidality (e.g. Erlangsen et al, 2020; Mullins et al, 2019); a top priority will be to conduct a large-scale GWAS of gambling disorder so that the genetic overlap with suicidal behaviors (and other disorders and traits) can be more thoroughly probed.

In previous research we demonstrated using a discordant twin design that there was a potentially causal relation between neighborhood disadvantage and disordered gambling (Slutske et al, 2019), and that genetic variation in the frequency of gambling was associated with exposure to neighborhood disadvantage (Slutske et al., 2015). Interestingly, exposure to neighborhood disadvantage has also been associated with suicidal behaviors (Wardle et al., 2019). This emerging evidence suggests that disordered gambling and genetic risk for disordered gambling might shape the environment, for example, in the quality of the neighborhood in which one lives and whether one has experienced homelessness and severe financial problems (Roberts et al, 2017; Wong et al, 2010) that might precipitate suicidal behaviors. It remains an important question for future genetically-informed research to determine which aspects of the environment might be critical in explaining the potentially causal and non-causal links between gambling disorders and suicidal behaviors.

Implications for Prevention and Intervention

The results of this study are inconsistent with a causal influence of disordered gambling on thoughts about suicide or plans to commit suicide. Rather, there were non-causal associations between disordered gambling and suicidal thoughts and plans that were explained by common familial influences shared with major depression and conduct disorder. A potentially effective route for preventing disordered gambling and suicidal ideation and the escalation to suicide attempt may be via pharmacological or psychological treatments for depression (Abbott, 2020; Zalsman et al, 2016).

On the other hand, after removing the influence of shared genetic and environmental risk factors, there was evidence consistent with a potentially causal influence of disordered gambling on suicide attempt, especially among men. We speculated that this causal influence may be related to financial problems. There were several clues consistent with this -- household income was inversely related, and the percentage of household income spent on gambling was positively related to the severity of gambling problems, and the DSM-5 gambling disorder symptom of borrowing money to relieve a desperate financial situation, i.e., "bail out," was the symptom most strongly associated with suicide attempt. These clues are buttressed by findings from studies of individuals who have sought treatment for their disordered gambling (Swanton & Gainsbury, 2020). For example, in a study of 202 callers to a state-funded gambling helpline, the best predictor of suicidal ideation or attempt was

financial problems (Carr et al, 2018). A massive study utilizing financial transaction data from the UK's largest retail bank demonstrated that the percentage of financial transactions that were devoted to gambling were significantly associated with a wide range of adverse financial, lifestyle, and health outcomes, including mortality (Muggleton et al, 2021).

Most people struggling with gambling disorders do not seek treatment (Slutske, 2006). Financial problems are often the impetus when help is sought (Swanton & Gainsbury, 2020). Given the difficulties inherent in screening for a disorder that is relatively rare, coupled with the unwillingness of those affected to seek treatment, focusing on the monetary aspect of disordered gambling may represent a more practicable target for screening, intervention, and prevention. The use of monetary data to identify individuals experiencing financial harms associated with their gambling is exemplified by the UK study described above (Muggleton et al, 2021). The proliferation of on-line gambling activities (Gainsbury, 2015) simplifies the identification of individuals who have incurred substantial financial losses due to their gambling (e.g., Gray et al, 2012), and can also make it possible to follow up with a tailored intervention to modify gambling behavior to forestall a financial crisis (e.g., Wohl et al, 2017). Not only would this reduce gambling-related financial crises, but also might ward off a potential gambling-related suicide attempt.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Estimates (and 95% confidence intervals) from multilevel models predicting suicidal thoughts, plan, and attempt from disordered gambling. Individual level effects are in the top panels, within-twin-pair effects (that include potentially causal effects) are in the middle panels, and between-twin-pair effects (that include genetic and shared environmental influences) are in the bottom panels; see Table 4 for a list of the covariates included in the base and adjusted models. Because there was a significant sex difference for the between-pair effects for suicidal thoughts, the effects are plotted separately for men and women. Not shown in the figure is the significant sex difference for the unadjusted within-twin-pair effect for suicide attempt (unadjusted: men odds ratio = 136.74, women odds ratio = 1.89; adjusted: men odds ratio = 23.13, women odds ratio = 1.38).

Note: The upper bounds for the four confidence intervals that exceeded the chart boundaries were: suicide plan between-pair base model: 13.47; suicide attempt within-pair base model: 22.78; suicide attempt within-pair adjusted model: 11.17; suicide attempt between-pair base model: 11.05.

Table 1.

Overview of assessments in the two twin cohorts.

Twin Cohort						
ATR-II			ATR-III			
Phase 1	years	ages	assessments	years	ages	assessments
	1996-2000	24-36	<ul style="list-style-type: none"> • suicidal behaviors -age of onset • other psychiatric disorders 	2005-2009	21-46	<ul style="list-style-type: none"> • suicidal behaviors -age of onset (not used) • gambling disorder • other psychiatric disorders • past year income • educational attainment
	4 year retest interview (<i>n</i> = 216)					
Phase 2	years	ages	assessments	years	ages	assessments
	2004-2007	32-43	<ul style="list-style-type: none"> • suicidal behaviors - age of onset • gambling disorder - gambling activity participation - age of onset • past year income • educational attainment 	NA	NA	NA
	3 month retest interview (<i>n</i> = 166)					

Note: ATR-III also includes siblings, ATR = Australian Twin Registry

Table 2.

Correlations between study variables among men (N=3,281) and women (N=5,046).

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	lifetime prevalence men (%)
1. gambling disorder (4+ sxs)	.95	.. ^a	.26	.31	.27	.33	.29	.30	.30	.36	4.21
2. disordered gambling (1+ sxs)	.. ^a	.95	.17	.21	.16	.14	.29	.18	.27	.29	16.67
3. suicidal thoughts	.26	.21	.85	.. ^a	.83	.52	.22	.35	.21	.40	25.78
4. suicide plan	.30	.21	.. ^a	.56	.78	.50	.24	.32	.21	.38	6.34
5. suicide attempt	.27	.22	.91	.80	.97	.52	.31	.41	.33	.49	2.90
6. major depression	.25	.23	.60	.58	.52	.81	.19	.31	.27	.28	19.72
7. alcohol use disorder	.21	.17	.24	.27	.32	.19	.72	.48	.41	.42	43.16
8. cannabis use disorder	.21	.22	.38	.32	.38	.31	.51	.93	.55	.48	19.48
9. nicotine dependence	.40	.39	.23	.24	.34	.26	.40	.60	.91	.39	35.14
10. conduct disorder	.40	.31	.36	.37	.43	.31	.45	.56	.52	.84	15.79
lifetime prevalence women (%)	1.39	6.44	26.22	7.06	4.78	31.05	21.94	10.23	30.94	4.76	

Note: Cell entries are tetrachoric correlations. Correlations among men are in the upper diagonal, correlations among women are in the lower diagonal, retest reliabilities are on the diagonal (for the first two variables, the mean retest interval was three months, for the remaining variables, the mean retest interval was four years). All correlations are significant at $p < 0.05$.

^a correlations between contingent/nested phenotypes could not be calculated

Table 3. Suicidal thoughts, plan, and attempt among twin pairs discordant for disordered gambling.

Suicidal behavior	Sample	Twin pairs discordant for disordered gambling (n = 307)		McNemar's test (df = 1)	Chi-square	p
		Affected twin % (n)	Unaffected twin % (n)			
Suicidal thoughts	Full sample	35.50 (109)	26.71 (82)	6.45		.0111
	Men	32.56 (56)	22.67 (39)	4.90		.0269
	Women	39.26 (53)	31.85 (43)	1.85		.1736
	MZ twins	34.12 (58)	25.88 (44)	3.63		.0568
	DZ twins	37.23 (51)	27.74 (38)	2.86		.0906
Suicide plan	Full sample	9.45 (29)	7.82 (24)	0.71		.3980
	Men	7.56 (13)	5.23 (9)	1.14		.2850
	Women	11.85 (16)	11.11 (15)	0.05		.8273
	MZ twins	7.06 (12)	5.88 (10)	0.25		.6171
	DZ twins	12.41 (17)	10.22 (14)	0.47		.4913
Suicide attempt	Full sample	6.51 (20)	4.56 (14)	1.50		.2207
	Men	4.65 (8)	1.74 (3)	2.79		.0956
	Women	8.89 (12)	8.15 (11)	0.07		.7963
	MZ twins	7.06 (12)	4.12 (7)	2.27		.1317
	DZ twins	5.84 (8)	5.11 (7)	0.08		.7815

Note: ATR-II and ATR-III same-sex twin pairs

Table 4.

Results of individual level (Panel A) and multilevel discordant twin (Panel B) analyses predicting suicidal thoughts, plan, and attempt from disordered gambling.

Predictor	Suicidal thoughts n = 2033 affected			Suicide plan n = 531 affected			Suicide attempt n = 317 affected					
	Base model	Fully adjusted	95% CI	OR	95% CI	OR	95% CI	OR	95% CI			
PANEL A												
Individual Level Models												
Sex	1.07	0.94, 1.21	1.11	0.96, 1.29	0.81	0.49, 1.32	0.75	0.40, 1.42	0.99	0.50, 1.96	1.64	0.67, 4.00
Age	1.00	0.99, 1.02	1.01	0.99, 1.03	0.98	0.90, 1.06	0.97	0.89, 1.07	0.94	0.85, 1.04	0.94	0.83, 1.07
Zygosity	0.87*	0.77, 0.98	1.04	0.99, 1.08	0.84	0.47, 1.50	1.02	0.81, 1.30	0.91	0.41, 1.98	1.01	0.74, 1.38
Childhood SES	0.86*	0.77, 0.97	0.93	0.83, 1.05	1.07	0.68, 1.68	1.51	0.91, 2.51	0.90	0.49, 1.66	0.94	0.49, 1.82
Adult income	0.88***	0.86, 0.91	0.92***	0.89, 0.95	0.76***	0.69, 0.83	0.77***	0.69, 0.86	0.74***	0.66, 0.83	0.80**	0.70, 0.92
Education	1.15***	1.09, 1.20	1.19***	1.13, 1.26	1.21	1.00, 1.47	1.24	0.99, 1.55	0.89	0.68, 1.15	0.93	0.69, 1.25
Disordered gambling	2.00***	1.65, 2.41	1.37**	1.12, 1.68	3.31***	1.83, 5.99	2.35*	1.15, 4.81	3.76**	1.77, 8.02	1.98	0.81, 4.82
Major depression			5.90***	5.03, 6.90			52.61***	25.91, 106.83			50.23***	19.25, 131.07
Alcohol use disorder			1.40***	1.20, 1.62			2.01*	1.14, 3.55			1.69	0.79, 3.63
Cannabis use disorder			1.97***	1.63, 2.38			1.89	0.98, 3.63			4.31***	1.86, 9.95
Nicotine dependence			1.19*	1.02, 1.37			0.81	0.45, 1.47			1.20	0.55, 2.64
Conduct disorder			2.42***	1.95, 3.03			5.60***	2.67, 11.75			5.25***	2.15, 12.81
PANEL B												
MZ and DZ Multilevel Discordant Twin Models												
n = 1520 affected												
Sex	1.28*	1.06, 1.55	1.07	0.86, 1.34	1.49	0.70, 3.20	1.29	0.53, 3.14	1.79	0.62, 5.15	2.58	0.54, 3.12
Age	1.01	0.98, 1.03	1.01	0.99, 1.04	1.00	0.91, 1.09	1.00	0.90, 1.10	0.95	0.85, 1.07	0.96	0.86, 1.10
Zygosity	0.85	0.71, 1.01	0.85	0.71, 1.02	0.87	0.44, 1.37	0.86	0.41, 1.81	1.08	0.44, 2.65	1.14	0.41, 2.63
Childhood SES	0.92	0.78, 1.07	1.00	0.85, 1.17	1.05	0.64, 1.69	1.31	0.76, 2.26	1.19	0.59, 2.38	1.48	0.61, 2.30
Adult income	0.88***	0.84, 0.91	0.91***	0.88, 0.95	0.74***	0.66, 0.83	0.76***	0.67, 0.86	0.74***	0.65, 0.85	0.81*	0.69, 0.96
Education	1.14***	1.06, 1.22	1.18***	1.09, 1.27	1.29*	1.02, 1.63	1.31*	1.02, 1.69	0.88	0.65, 1.20	0.93	0.64, 1.17
WP disordered gambling	1.70**	1.15, 2.52	1.52*	0.99, 2.32	1.48	0.55, 4.02	1.07	0.37, 3.11	5.63*	1.39, 22.78	2.70	0.65, 11.17

Predictor	Suicidal thoughts n = 2033 affected			Suicide plan n = 531 affected			Suicide attempt n = 317 affected			
	Base model	Fully adjusted	95% CI	Base model	Fully adjusted	95% CI	Base model	Fully adjusted	95% CI	
PANEL A										
Individual Level Models										
WP x sex interaction	---	---	---	---	---	---	0.04*	0.01, 0.87	0.25	0.01, 5.10
BP disordered gambling	2.89***	1.98, 4.22	---	3.76*	1.05, 13.47	1.99	1.78	0.29, 11.05	0.88	0.12, 6.67
BP x sex interaction	---	2.78**	1.28, 6.01	---	---	---	---	---	---	---
Major depression	---	5.85***	4.77, 7.18	---	22.99***	11.59, 55.60	---	---	20.88***	8.00, 54.46
Alcohol use disorder	---	1.60***	1.30, 1.96	---	1.65	0.87, 3.13	---	---	2.10	0.89, 4.91
Cannabis use disorder	---	1.94***	1.49, 2.52	---	1.32	0.61, 2.82	---	---	4.59**	1.74, 12.14
Nicotine dependence	---	1.13	0.92, 1.39	---	1.17	0.61, 2.25	---	---	1.29	0.54, 3.09
Conduct disorder	---	2.26***	1.65, 3.09	---	3.23**	1.33, 7.80	---	---	3.09*	1.03, 9.26

Note: N=7,856 individual twins (individual level models) or N=6,016 individual twins (multilevel discordant twin models) in each set of analyses, OR = odds ratio, CI = confidence interval, WP = within-pair, BP = between-pair

* = p < .05

** = p < .01

*** = p < .001