A Familial Subtype of Gambling Disorder

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Abstract

Background: Although family history of psychiatric disorders has often been considered potentially useful in understanding clinical presentations in patients, it is less clear what a positive gambling family history means for people with gambling disorder. We sought to understand the clinical impact of having a first-degree relative with gambling disorder in a sample of adults with gambling disorder.

Methods: Data from 455 participants (aged 18-65 years) who had participated in previous pharmacological and psychotherapeutic clinical trials for gambling disorder were pooled in a secondary analysis. Demographic and clinical variables were compared between those who did versus did not have one or more first-degree relative(s) with gambling disorder. Additionally, we examined whether a family history of gambling disorder was associated with treatment outcome.

Results: 223 (49.0%) participants had at least one first-degree family member(s) with gambling disorder. In terms of clinical variables, family history of gambling disorder was significantly associated with being female, having an earlier age of gambling onset, longer duration of untreated gambling illness, a greater likelihood of developing legal problems secondary to gambling, and higher rates of alcohol use disorder in family members. Family history of gambling disorder was also associated with a greater gambling symptom improvement from pharmacotherapy.

Conclusions: These results indicate that gamblers with a first-degree family member with a gambling disorder may have a unique clinical presentation and better response to treatment interventions.

Key Words: family history; gambling; addiction; treatment

**Introduction**

Gambling disorder is a psychiatric disorder with a current global prevalence of 0.4-2% and is associated with impaired psychosocial functioning, reduced quality of life, financial problems, and suicidality (Hodgins et al., 2011; Potenza et al., 2019). Family history is a routine part of a clinical assessment of gambling disorder, as it is with all psychiatric conditions, but the utility of the assessment in the case of gambling disorder remains unclear. In the related condition of alcohol use disorder, family history of alcoholism has helped identify predictive factors that may or may not result in treatment differences (Drake et al., 1995; Garbutt et al., 2014; Hashimoto et al., 2022; Conlin et al., 2023). In the case of gambling disorder, a family history of problem gambling has been associated with greater awareness of a person’s gambling problems (Gooding et al., 2023), perhaps the type of gambling that a gambling disordered person prefers (Sharman et al., 2019), and parental separation/divorce and financial hardship (Dowling et al., 2021). That has been the extent, however, of the examination of family history of gambling disorder in people with this condition. Understanding differences between gambling individuals with positive and negative family histories of gambling disorder may be important in order to identify potentially clinical subtypes and improve treatment outcomes. Family history has found to be important in other areas of mental ill health. For example, in the 1970s George Winokur found that people with positive family histories of major depressive disorder (i.e. a familial subtype of depression) responded better to tricyclic antidepressants and electroconvulsive therapy (ECT) than those with negative family histories (a finding later supported by other researchers as well) (Winokur, 1976; Lundin et al., 2024). In the case of major depressive disorder, a positive family history of depression has also been found to predict treatment to sertraline in primary care patients (Archer et al., 2024). A similar finding of improved treatment response to selective serotonin reuptake inhibitors (SSRIs) was reported in adults with OCD who had a first-degree relative with OCD as compared to those without such a family history (Erzegovesi et al., 2001). Additionally, Garbutt and colleagues (2014) systematically reviewed 622 studies in an effort to understand variables that predicted treatment to naltrexone in alcohol use disorder. They found some evidence for a family history of alcohol problems, and a polymorphism of the μ-opioid receptor gene, with efficacy of naltrexone.

The purpose of this study was to investigate whether family history of gambling disorder affects the clinical presentation of gambling disorder, and its response to treatment. As such we sought to explore the potential value of a clinical subtype of gambling disorder linked to positive family history.

**Methods**

***Participants***

Data were aggregated from participants who attended clinical trials at the University of Chicago and the University of Minnesota, USA, led by one of the authors (JEG) (see Supplemental file). All diagnoses of gambling disorder were made by an experienced board-certified psychiatrist, using the criteria set forth by the 4th Edition of the Diagnostic and Statistical Manual (DSM-IV) (American Psychiatric Association, APA, 1994) and the diagnoses were later confirmed to be consistent with the current requirements for gambling disorder using the DSM-5 criteria (American Psychiatric Association, APA, 2013). Diagnosis was made using a validated instrument (Grant et al., 2004).

 The exclusionary criteria for these studies were: history of psychotic or bipolar disorder, any current (past 3 months) illicit drug use, or inability to provide informed consent. Data from ten published clinical trials (one involving psychotherapy, two using a nutraceutical, and seven using pharmacotherapy) were included (Kim et al., 2001; Kim & Grant, 2001; Kim et al., 2002; Grant et al. 2003; Grant & Potenza, 2006; Grant et al., 2007; Grant et al., 2008; Grant et al., 2010; Grant et al., 2013; Grant et al., 2014). Trials were from 8 weeks to 16 weeks in duration. The interventions included cognitive-behavioral therapy, N-acetyl cysteine, naltrexone, escitalopram, paroxetine, memantine, and tolcapone.

Our rationale for merging the data from these ten studies was that they all focus on interventions for gambling disorder, specifically pharmacotherapy. Despite the different interventions, they share common endpoints, such as gambling severity and treatment response. Combining these datasets increases statistical power and allows for a more comprehensive analysis of treatment effects and family history.

All study procedures were carried out in accordance with the Declaration of Helsinki. The Institutional Review Boards of the University of Minnesota and/or of the University of Chicago approved the procedures and the accompanying consent forms for each of the studies. For each of the studies, after all procedures were explained, all participants provided informed written consent. Each study was carried out in accordance with the latest version of the Declaration of Helsinki.

***Assessments***

Demographic variables, including age, gender, and highest level of education completed,

were recorded for all participants. Subjects received a psychiatric evaluation, which included the Mini International Neuropsychiatric Inventory (MINI) (Sheehan et al., 1998); the Structured Clinical Interview for Pathological Gambling (SCI-PG) (Grant et al., 2004) later adapted for DSM-5; Gambling Symptom Assessment Scale (GSAS) to measure overall self-reported symptom severity for the past week (Kim et al., 2009); Yale-Brown Obsessive-Compulsive Scale modified for Pathological Gambling (PG-YBOCS), a clinician-administered scale, to quantify symptom severity over the past seven days (Pallanti et al., 2005); Hamilton Depression Rating Scale (HAM-D) to measure severity of depressive symptoms (Hamilton, 1960); Hamilton Anxiety Rating Scale (HAM-A) to measure severity of anxiety symptoms (Hamilton, 1959); and the Sheehan Disability Scale (SDS) to measure overall disability / functioning (Sheehan, 1983).

We undertook the family history method where the proband is asked about psychiatric problems in their relatives, despite its methodological limitations (Andreasen et al., 1977; Kendler et al., 1991). Participants were asked about the presence of gambling disorder in all first-degree relatives. Gambling disorder in relatives was defined as the chronic engagement in gambling resulting in either noticeable social and occupational dysfunction or the need for a twelve-step program or formal treatment. All information about relatives came from the proband. No direct evaluations of the first-degree relatives were performed.

***Data Analysis***

Differences in demographic and clinical variables between the groups (those with vs without a family history of gambling disorder) were characterized using analysis of variance (ANOVA) for continuous normally distributed measures; Mann-Whitney U tests for continuous non-normally distributed measures; and likelihood ratio chi-square tests for categorical data. Statistical significance was defined as p<0.05.

In order to identify the influence of a positive family history of gambling disorder on treatment outcome, we examined differences in the change on the Gambling Symptom Assessment Scale (G-SAS) (Kim et al., 2009) in people who had received active treatment (i.e. the intervention groups rather than those who received placebo). Least squares regression was then used to explore potential effects of confounds. We also examined the influence of family history on G-SAS change in people who had received placebo.

**Results**

Of the 455 adults with gambling disorder, 223 (49.0%) reported a positive family history of gambling disorder in one or more first-degree family members. Comparisons between the two groups on the variables of interest are summarized in **Table 1**. For demographic variables, family history of gambling disorder was significantly associated with female gender.

**Table 1. Demographic characteristics of those with versus without a family history of gambling disorder.**

|  |  |  |
| --- | --- | --- |
|    | **Family history of gambling disorder** |      |
| **No (n=232)** | **Yes (n=223)** |
| Mean/n | Std Dev/% | Mean/n | Std Dev/% | Statisticaltest | P |
| **Age, years** | 47.7 | 11.7 | 47.6 | 10.4 | 25217 | 0.759 |
| **Sex** | Female | 107 | 46.3% | 137 | 61.4% | LR 10.471 | **0.001\*\*** |
| Male | 124 | 53.7% | 86 | 38.6% |
| **Relationship/Marital Status** | Single | 74 | 32.2% | 62 | 27.9% | LR 7.754 | 0.051 |
| Married | 91 | 39.6% | 109 | 49.1% |
| Divorced | 54 | 23.5% | 48 | 21.6% |
| Other | 11 | 4.7% | 3 | 1.4% |
| **Racial-ethnic group** | Caucasian | 176 | 90.3% | 186 | 90.3% | LR 0.000 | 0.991 |
| Other | 19 | 9.7% | 20 | 9.7% |
| **Education level** | 3.05 | 1.02 | 3.09 | 0.98 | 23600 | 0.691 |
| **Number of current comorbidities (mainstream mental disorders)** | 0 | 85 | 52.1% | 89 | 54.3% | LR 1.319 | 0.517 |
| 1 | 62 | 39.0% | 54 | 32.9% |
| >1 | 16 | 9.9% | 21 | 12.8% |
| **Tobacco use** | No | 114 | 50.4% | 98 | 43.9% | LR 1.332 | 0.248 |
| Yes | 117 | 50.6% | 125 | 56.1% |

Statistical tests are analysis of variance (Mann-Whitney U test was used for non-parametric comparisons, with ‘U’ reported under statistical test) except where indicated LR = Likelihood ratio chi-square test. Education level is a score reflecting the highest level of education obtained to date, ranging from 0 (did not complete initial basic schooling) through to 5 (higher degree completed). Note that total cell sizes per group may differ due to missing data for some variables. \* p<0.05, \*\* p<0.01.

For gambling clinical variables (**Table 2**), family history of gambling disorder was significantly associated with earlier age of first gambling, longer duration of untreated illness, and greater likelihood of having legal problems secondary to gambling.

**Table 2. Gambling clinical characteristics for those with versus without a family history of gambling disorder.**

|  |  |  |
| --- | --- | --- |
|     | **Family history of gambling disorder** |      |
| **No (n=232)** | **Yes (n=223)** |
| Mean/n | Std Dev/% | Mean/n | Std Dev/% | Statisticaltest | P |
| **Dollars lost to gambling in the past year** | 26046 | 37462 | 24651 | 25835 | 16510 | 0.556 |
| **GSAS** | 33.9 | 10.7 | 36.1 | 12.9 | 20073 | 0.295 |
| **PG-YBOCS** | 21.3 | 5.6 | 20.7 | 4.9 | 8986 | 0.342 |
| **Age when first started to gamble, years** | 30.9 | 14.5 | 27.1 | 13.5 | 15664 | **0.011\*** |
| **Duration of Untreated Illness, years** | 8.8 | 7.5 | 11.4 | 8.5 | 20040 | **<0.001\*\*** |
| **Legal problems linked to gambling** | No | 135 | 64.0% | 107 | 49.5% | LR 9.106 | **0.003\*\*** |
| Yes | 76 | 36.0% | 109 | 50.5% |
| **Previous Gambling Treatment** | No | 85 | 57.4% | 94 | 52.8% | LR 0.698 | 0.403 |
| Yes | 63 | 42.6% | 84 | 47.2% |

Statistical tests are analysis of variance (Mann-Whitney U test was used for non-parametric comparisons, with ‘U’ reported under statistical test) except where indicted LR = Likelihood ratio chi square test. GSAS = Gambling Symptom Assessment Scale; PG-YBOCS = Yale-Brown Obsessive-Compulsive Scale Modified for Pathological Gambling. Note that total cell sizes per group may differ due to missing data for some variables. \* p<0.05, \*\* p<0.01.

For other clinical variables (**Table 3**), family history of gambling disorder was significantly associated with a positive family history of alcohol use disorders.

**Table 3. Other clinical characteristics in those with versus without a family history of gambling disorder.**

|  |  |  |
| --- | --- | --- |
|    | **Family history of gambling disorder** |      |
| **No (n=232)** | **Yes (n=223)** |
| Mean / n | Std Dev / % | Mean / n | Std Dev / % | Statisticaltest | p |
| **HAMA** | 7.8 | 4.6 | 7.1 | 4.6 | 17242 | 0.094 |
| **HAMD** | 7.4 | 4.0 | 7.0 | 4.2 | 17857 | 0.262 |
| **Sheehan Disability Scale** | 14.8 | 6.6 | 14.3 | 6.9 | 7506 | 0.463 |
| **Family history of alcohol use disorder (1' relative)** | No | 136 | 58.6% | 83 | 37.4% | LR 20.647 | **<0.001\*\*** |
| Yes | 96 | 41.4% | 139 | 62.6% |

Statistical tests are analysis of variance (Mann-Whitney U test was used for non-parametric comparisons, with ‘U’ value reported under statistical test) except where indicated LR = Likelihood ratio chi square test. HAMA = Hamilton Anxiety Rating Scale; HAMD = Hamilton Depression Rating Scale. Note that total cell sizes per group may differ due to missing data for some variables. \* p<0.05, \*\* p<0.01.

We also compared GSAS change between those with and without a family history of gambling (restricted to people who were assigned to active treatment in the double-blind clinical trials, n=351). There was a significantly greater symptom improvement (reduction in GSAS) in those with a family history versus those without (mean improvement in GSAS family history positive 16.8 [SD 14.0] versus family history negative 13.1 [11.7]; F=3.953, p=0.048). This effect of family history on GSAS in those who had received active treatment remained statistically significant (F=4.895, p=0.029) in a least squares regression model controlling for potential confounders of sex, age at first gambling / DUI, legal problems, and family history of alcohol use disorder; effects of these potential confounders were non-significant (each p>0.50).

GSAS change did not differ significantly as a function of family history in people who had received placebo (n=176), across the studies (mean improvement in GSAS family history positive 12.0 [SD 11.7] versus family history negative 12.4 [14.8]; F=0.0274, p=0.8668). This indicated that the earlier findings were specific to active treatment conditions.

**Discussion**

This study examined demographic and clinical associations with family history of gambling disorder in a large sample of adults with well characterized gambling disorder. The study found that a familial subtype of gambling disorder is common and has a number of important clinical associations.

For the demographic measures, family history of gambling disorder was associated with a higher likelihood of female gender. There are of course several reasons why this association may be present. Based on evidence so far, it seems unlikely that gambling (and gambling disorder) has a stronger genetic link in women than in men (e.g. Slutske & Richmond-Rakerd, 2014; Xuan et al., 2017). As such, it would appear unlikely that the link between female gender and family history of gambling disorder, observed in our study, reflects differences in gender-related genetic propensity for gambling. Earlier literature found that females were more likely to gamble due to depression (Grant & Kim, 2001). The finding of a familial link in females, which was not examined in the earlier literature focusing on gender differences (Potenza et al.,2001; Ladd & Petry, 2002; Grant & Kim, 2002) may enlarge our understanding of the role of depression as well. One could hypothesize that growing up in a family with a gambling parent, and as these data further show, a family member with alcoholism as well (see Table 3), that a person may struggle with mood symptoms and gamble as a means of escape from these family dynamics. Research indicates that gambling disorder and alcohol use disorder do tend to co-aggregate within families (e.g. Black et al., 2006). This is further in keeping with possible associations between family environment and childhood trauma that may be especially important for the development of gambling disorder in women (Estevez, 2023). Relatedly, type-2 gambling, per Blaszczynski’s model, may be more common in women and reflect a role for mood/anxiety and perhaps prior trauma (Nower et al., 2022). The data in this study do not show higher depression scores in the familial group but this could be due to the fact that we only examined depressive symptoms over the week prior to inclusion in the study. These familial findings do suggest that further examination may be called for in the area of gender in gambling disorder to further clarify what processes may account for this association.

 For the clinical measures, family history of gambling disorder was associated with earlier age of onset of gambling. This has been found in other psychiatric disorders as well (i.e. earlier onset of alcoholism linked to familial alcoholism (Cook & Winokur, 1985; Bogenschutz et al., 2009; Pilatti et al., 2014); earlier onset of OCD linked to positive family history (Swedo et al., 1992; Sharma et al., 2015; Brakoulias et al., 2016). In terms of common environmental mediators that may contribute to the link between earlier onset and family history, a likely explanation is that observing one’s parents gambling could lead to ‘modelling’ whereby offspring are more likely to gamble (e.g. Dowling et al., 2020). Perhaps earlier interventions would be useful in families predisposed to gambling disorder to prevent years of untreated illness. We observed that family history was also linked to higher levels of legal problems due to gambling – this did not appear to reflect current severity of gambling disorder since severity was not associated significantly with family history status. Potentially this link with legal problems could reflect the longer duration of untreated illness, i.e. a greater time period over which to accrue legal problems due to gambling. Of note is that we defined legal problems in a broad sense that included not only e.g. violence but also aspects such as writing bad checks and embezzlement.

 Perhaps most importantly, the familial version of gambling disorder responded better to treatment interventions in general than the non-familial version. This was specific to the active interventions, as no such effect was seen when considering those who had received placebo. Prior work in other conditions, including alcohol use disorder, suggests that family history may be linked to treatment seeking/engagement through life (Milne et al., 2009). In the context of psychological treatments for gambling disorder, several studies report better outcomes in females than in men (Merkouris et al., 2016), and so gender may account for this finding herein (i.e. female gender linked to family history linked to better treatment response). Reassuringly for patients, these findings militate against the notion that family history of gambling means a person’s symptoms will not respond to treatment or is somehow ‘hard wired’ and permanent.

There are several limitations to this study. Participants included in the study were seeking treatment for gambling disorder. Thus, these findings may not generalize to other people with gambling disorder who do not seek treatment. Second, we did not differentiate between parental and sibling family history of gambling disorder. We used a well-established method to establish family history but we did not interview family members directly. Due to the cross-sectional nature of the data, the study can only show association – not causality. Longitudinal research in this area would be valuable. We did not report socioeconomic status though we note that education level did not differ as a function of family history of gambling disorder.

In conclusion, despite family history constituting an important aspect of the clinical presentation of mental disorders, surprisingly little research has explored how it may impact the clinical presentation of gambling disorder and its response to treatment. This study, in a treatment-seeking sample of people with gambling disorder, found that family history of gambling disorder had a number of important clinical associations – notably with female gender, earlier age of gambling onset (plus longer typical duration of untreated illness), legal problems due to gambling, family history of alcohol use disorder, and greater response to treatment interventions. Future work should further explore the nature of these associations using a longitudinal approach.

**References**

Andreasen, N.C., Endicott, J., Spitzer, R.L., Winokur, G. (1977). The family history method

using diagnostic criteria. Reliability and validity. Archives of General Psychiatry, 34(10), 1229–

1235. doi:10.1001/archpsyc.1977.01770220111013

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental

Disorders: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA.

Archer C, Kessler D, Lewis G, Araya R, Duffy L, Gilbody S, Lewis G, Kendrick T, Peters TJ,

Wiles N. What predicts response to sertraline for people with depression in primary

care? a secondary data analysis of moderators in the PANDA trial. PLoS One. 2024 May

9;19(5):e0300366. doi: 10.1371/journal.pone.0300366. PMID: 38722970; PMCID:

PMC11081306.

Black DW, Monahan PO, Temkit M, Shaw M. A family study of pathological gambling.

Psychiatry Res. 2006 Mar 30;141(3):295-303. doi: 10.1016/j.psychres.2005.12.005. Epub 2006

Feb 24. PMID: 16499975.

Bogenschutz MP, Scott Tonigan J, Pettinati HM. Effects of alcoholism typology on response to

naltrexone in the COMBINE study. Alcohol Clin Exp Res. 2009 Jan;33(1):10-8. doi:

10.1111/j.1530-0277.2008.00804.x. Epub 2008 Sep 30. PMID: 18828797; PMCID:

PMC2626136.

Brakoulias V, Starcevic V, Martin A, Berle D, Milicevic D, Viswasam K. The familiality of

specific symptoms of obsessive-compulsive disorder. Psychiatry Res. 2016 May 30;239:315-9.

doi: 10.1016/j.psychres.2016.03.047. Epub 2016 Mar 30. PMID: 27058157.

Conlin WE, Hoffman M, Steinley D, Vergés A, Sher KJ. Predictors of symptom course in

alcohol use disorder. Alcohol Clin Exp Res (Hoboken). 2023 Dec;47(12):2288-2300. doi:

10.1111/acer.15201. Epub 2023 Oct 25. PMID: 38151783; PMCID: PMC10935605.

Cook BL, Winokur G. A family study of familial positive vs. familial negative alcoholics. J

Nerv Ment Dis. 1985 Mar;173(3):175-8. doi: 10.1097/00005053-198503000-00007. PMID:

3973579.

Dowling NA, Francis KL, Dixon R, Merkouris SS, Thomas SA, Frydenberg E, Jackson AC. “It

Runs in Your Blood": Reflections from Treatment Seeking Gamblers on Their Family History of

Gambling. J Gambl Stud. 2021 Jun;37(2):689-710. doi: 10.1007/s10899-020-09959-w. PMID:

32671673.

Drake AI, Butters N, Shear PK, Smith TL, Bondi M, Irwin M, Schuckit MA. Cognitive recovery

with abstinence and its relationship to family history for alcoholism. J Stud Alcohol. 1995

Jan;56(1):104-9. doi: 10.15288/jsa.1995.56.104. PMID: 7752625.

Erzegovesi S, Cavallini MC, Cavedini P, Diaferia G, Locatelli M, Bellodi L. Clinical

predictors of drug response in obsessive-compulsive disorder. J Clin Psychopharmacol.

2001 Oct;21(5):488-92. doi: 10.1097/00004714-200110000-00006. PMID: 11593074.

Estévez A, Macía L, Ontalvilla A, Aurrekoetxea M. Exploring the psychosocial characteristics of

women with gambling disorder through a qualitative study. Front Psychol. 2023 Dec

20;14:1294149. doi: 10.3389/fpsyg.2023.1294149. PMID: 38173857; PMCID: PMC10761503.

Garbutt JC, Greenblatt AM, West SL, Morgan LC, Kampov-Polevoy A, Jordan HS, Bobashev

GV. Clinical and biological moderators of response to naltrexone in alcohol dependence: a

systematic review of the evidence. Addiction. 2014 Aug;109(8):1274-84. doi:

10.1111/add.12557. Epub 2014 May 23. PMID: 24661324.

Gooding NB, Kim HS, Williams RJ, Williams JN. Individual differences and predictors of

general awareness in problem gambling. Addict Behav. 2023 Jan;136:107505. doi:

10.1016/j.addbeh.2022.107505. Epub 2022 Sep 24. PMID: 36183686.

Grant JE, Kim SW. Demographic and clinical features of 131 adult pathological gamblers.

J Clin Psychiatry. 2001 Dec;62(12):957-62. doi: 10.4088/jcp.v62n1207. PMID: 11780876.

Grant JE, Kim SW. Gender differences in pathological gamblers seeking medication

treatment. Compr Psychiatry. 2002 Jan-Feb;43(1):56-62. doi: 10.1053/comp.2002.29857.

PMID: 11788920.

Grant JE, Kim SW, Potenza MN, Blanco C, Ibanez A, Stevens L, Hektner JM, Zaninelli R.

Paroxetine treatment of pathological gambling: a multi-centre randomized controlled trial. Int

Clin Psychopharmacol. 2003 Jul;18(4):243-9. doi: 10.1097/00004850-200307000-00007. PMID:

12817159.

Grant, J.E., Steinberg, M.A., Kim, S.W., Rounsaville, B.J., Potenza. M.N. (2004). Preliminary

validity and reliability testing of a structured clinical interview for pathological gambling.

Psychiatry Research, 128(1), 79–88. DOI: 10.1016/j.psychres.2004.05.006

Grant JE, Potenza MN. Escitalopram treatment of pathological gambling with co-occurring anxiety: an open-label pilot study with double-blind discontinuation. Int Clin Psychopharmacol. 2006 Jul;21(4):203-9. doi: 10.1097/00004850-200607000-00002. PMID: 16687991.

Grant JE, Kim SW, Odlaug BL. N-acetyl cysteine, a glutamate-modulating agent, in the treatment of pathological gambling: a pilot study. Biol Psychiatry. 2007 Sep 15;62(6):652-7. doi: 10.1016/j.biopsych.2006.11.021. Epub 2007 Apr 18. PMID: 17445781.

Grant JE, Kim SW, Hartman BK. A double-blind, placebo-controlled study of the opiate antagonist naltrexone in the treatment of pathological gambling urges. J Clin Psychiatry. 2008 May;69(5):783-9. doi: 10.4088/jcp.v69n0511. PMID: 18384246.

Grant JE, Chamberlain SR, Odlaug BL, Potenza MN, Kim SW. Memantine shows promise in reducing gambling severity and cognitive inflexibility in pathological gambling: a pilot study. Psychopharmacology (Berl). 2010 Dec;212(4):603-12. doi: 10.1007/s00213-010-1994-5. Epub 2010 Aug 19. PMID: 20721537; PMCID: PMC3465841.

Grant JE, Odlaug BL, Chamberlain SR, Hampshire A, Schreiber LR, Kim SW. A proof of concept study of tolcapone for pathological gambling: relationships with COMT genotype and brain activation. Eur Neuropsychopharmacol. 2013 Nov;23(11):1587-96. doi: 10.1016/j.euroneuro.2013.07.008. Epub 2013 Aug 6. PMID: 23953269.

Grant JE, Odlaug BL, Chamberlain SR, Potenza MN, Schreiber LR, Donahue CB, Kim SW. A randomized, placebo-controlled trial of N-acetylcysteine plus imaginal desensitization for nicotine-dependent pathological gamblers. J Clin Psychiatry. 2014 Jan;75(1):39-45. doi: 10.4088/JCP.13m08411. PMID: 24345329.

Hamilton M. 1959. The assessment of anxiety states by rating. Br J Med Psychol 1959; 32:50-55.

Hamilton M. 1960. A rating scale for depression. J Neurol Neurosurg Psych 1960;23:56-62.

Hashimoto N, Habu H, Takao S, Sakamoto S, Okahisa Y, Matsuo K, Takaki M, Kishi Y,

Yamada N. Clinical moderators of response to nalmefene in a randomized-controlled trial for

alcohol dependence: An exploratory analysis. Drug Alcohol Depend. 2022 Apr 1;233:109365.

doi: 10.1016/j.drugalcdep.2022.109365. Epub 2022 Feb 18. PMID: 35228081.

Hodgins DC, Stea JN, Grant JE. Gambling disorders. Lancet. 2011 Nov 26;378(9806):1874-84.

DOI: 10.1016/S0140-6736(10)62185-X

Kendler KS, Silberg JL, Neale MC, Kessler RC, Heath AC, Eaves LJ. The family history

method: whose psychiatric history is measured? Am J Psychiatry. 1991 Nov;148(11):1501-4.

doi: 10.1176/ajp.148.11.1501. PMID: 1928463.

Kim SW, Grant JE. An open naltrexone treatment study in pathological gambling disorder. Int

Clin Psychopharmacol. 2001 Sep;16(5):285-9. doi: 10.1097/00004850-200109000-00006.

PMID: 11552772.

Kim SW, Grant JE, Adson DE, Shin YC. Double-blind naltrexone and placebo comparison study

in the treatment of pathological gambling. Biol Psychiatry. 2001 Jun 1;49(11):914-21. doi:

10.1016/s0006-3223(01)01079-4. PMID: 11377409.

Kim SW, Grant JE, Adson DE, Shin YC, Zaninelli R. A double-blind placebo-controlled study

of the efficacy and safety of paroxetine in the treatment of pathological gambling. J Clin

Psychiatry. 2002 Jun;63(6):501-7. doi: 10.4088/jcp.v63n0606. PMID: 12088161.

Kim SW, Grant JE, Potenza MN, Blanco C, Hollander E. The Gambling Symptom

Assessment Scale (G-SAS): a reliability and validity study. Psychiatry Res. 2009 Mar

31;166(1):76-84. doi: 10.1016/j.psychres.2007.11.008. Epub 2009 Feb 5. PMID: 19200607;

PMCID: PMC3641525.

Ladd GT, Petry NM. Gender differences among pathological gamblers seeking treatment. Exp Clin Psychopharmacol. 2002 Aug;10(3):302-9. doi: 10.1037//1064-1297.10.3.302. PMID: 12233991.

Lundin RM, Falcao VP, Kannangara S, Eakin CW, Abdar M, O'Neill J, Khosravi A, Eyre H, Nahavandi S, Loo C, Berk M. Machine Learning in Electroconvulsive Therapy: A Systematic Review. J ECT. 2024 Jun 10. doi: 10.1097/YCT.0000000000001009. Epub ahead of print. PMID: 38857315.

Merkouris SS, Thomas SA, Browning CJ, Dowling NA. Predictors of outcomes of psychological treatments for disordered gambling: A systematic review. Clin Psychol Rev. 2016 Aug;48:7-31. doi: 10.1016/j.cpr.2016.06.004. Epub 2016 Jun 23. PMID: 27372437.

Milne BJ, Caspi A, Harrington H, Poulton R, Rutter M, Moffitt TE. Predictive value of family history on severity of illness: the case for depression, anxiety, alcohol dependence, and drug dependence. Arch Gen Psychiatry. 2009 Jul;66(7):738-47. doi: 10.1001/archgenpsychiatry.2009.55. PMID: 19581565; PMCID: PMC3752832.

Nower L, Blaszczynski A, Anthony WL. Clarifying gambling subtypes: the revised pathways model of problem gambling. Addiction. 2022 Jul;117(7):2000-2008. doi: 10.1111/add.15745. Epub 2021 Nov 30. PMID: 34792223; PMCID: PMC9299878.

Pallanti S, DeCaria CM, Grant JE, Urpe M, Hollander E. Reliability and Validity of the Pathological Gambling Adaptation of the Yale-Brown Obsessive-Compulsive Scale (PG-YBOCS). *J Gambl Stud* 2005; 21 (4): 431–443.

Pilatti A, Caneto F, Garimaldi JA, Vera Bdel V, Pautassi RM. Contribution of time of drinking onset and family history of alcohol problems in alcohol and drug use behaviors in Argentinean college students. Alcohol Alcohol. 2014 Mar-Apr;49(2):128-37. doi: 10.1093/alcalc/agt176. Epub 2013 Dec 8. PMID: 24322673.

Potenza MN, Steinberg MA, McLaughlin SD, Wu R, Rounsaville BJ, O'Malley SS. Gender-

related differences in the characteristics of problem gamblers using a gambling helpline.

Am J Psychiatry. 2001 Sep;158(9):1500-5. doi: 10.1176/appi.ajp.158.9.1500. PMID:

11532738.

Potenza MN, Balodis IM, Derevensky J, Grant JE, Petry NM, Verdejo-Garcia A, Yip SW.

Gambling disorder. Nat Rev Dis Primers. 2019 Jul 25;5(1):51. doi: 10.1038/s41572-019-0099-7.

PMID: 31346179.

Sharma E, Sundar AS, Thennarasu K, Reddy YC. Is late-onset OCD a distinct phenotype?

Findings from a comparative analysis of "age at onset" groups. CNS Spectr. 2015 Oct;20(5):508-

14. doi: 10.1017/S1092852914000777. Epub 2015 Jul 20. PMID: 26189938.

Sharman S, Clark L, Roberts A, Michalczuk R, Cocks R, Bowden-Jones H. Heterogeneity in

Disordered Gambling: Decision-Making and Impulsivity in Gamblers Grouped by

Preferred Form. Front Psychiatry. 2019 Aug 19;10:588. doi: 10.3389/fpsyt.2019.00588.

PMID: 31481905; PMCID: PMC6709538.

Sheehan DV. The Anxiety Disease. New York, NY: Scribner, 1983.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E. (1988). The

Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a

structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical

Psychiatry, 59, Suppl 20:22-33.

Slutske WS, Richmond-Rakerd LS. A closer look at the evidence for sex differences in the

genetic and environmental influences on gambling in the national longitudinal study of

adolescent health: from disordered to ordered gambling. Addiction. 2014 Jan;109(1):120-7. doi:

10.1111/add.12345. Epub 2013 Oct 22. PMID: 24033632; PMCID: PMC3946982.

Swedo SE, Leonard HL, Rapoport JL. Childhood-onset obsessive compulsive disorder.

Psychiatr Clin North Am. 1992 Dec;15(4):767-75. PMID: 1461794.

Winokur G. Familial (genetic) subtypes of pure depressive disease. Am J Psychiatry. 1979

Jul;136(7):911-3. doi: 10.1176/ajp.136.7.911. PMID: 453352.

Xuan YH, Li S, Tao R, Chen J, Rao LL, Wang XT, Zheng R. Genetic and Environmental

Influences on Gambling: A Meta-Analysis of Twin Studies. Front Psychol. 2017 Dec 5;8:2121.

doi: 10.3389/fpsyg.2017.02121. PMID: 29259572; PMCID: PMC5723410.