



# Spanish Journal of Legal Medicine

## Revista Española de Medicina Legal

[www.elsevier.es/mlegal](http://www.elsevier.es/mlegal)



### REVIEW

## Update on the neurobiological, clinical and treatment aspects of gambling disorder ☆



Neus Solé-Morata<sup>a,b</sup>, Fernando Fernández-Aranda<sup>a,b,c,d</sup>, Isabel Baenas<sup>a,b,c</sup>,  
Mónica Gómez-Peña<sup>a,b</sup>, Laura Moragas<sup>a,b</sup>, Milagros Lizbeth Lara-Huallipe<sup>a</sup>,  
Bernat Mora-Maltas<sup>a</sup>, Anahí Gaspar<sup>a,b</sup>, Lucía Camacho-Barcia<sup>a,b,c</sup>, Ignacio Lucas<sup>a,b,c</sup>,  
Lucero Munguía<sup>a,b,c</sup>, Susana Jiménez-Murcia<sup>a,b,c,d,\*</sup>

<sup>a</sup> Departamento de Psiquiatría, Hospital Universitario de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

<sup>b</sup> Grupo de Psiconeurobiología de los Trastornos de la Conducta Alimentaria y Adicciones Comportamentales, Programa de Neurociencias, Instituto de Investigación Biomédica de Bellvitge (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain

<sup>c</sup> Ciber Fisiopatología Obesidad y Nutrición (CIBEROBn), Instituto Salud Carlos III, Madrid, Spain

<sup>d</sup> Departamento de Ciencias Clínicas, Escuela de Medicina, Universitat de Barcelona - UB, L'Hospitalet de Llobregat, Barcelona, Spain

Received 8 June 2022; accepted 17 July 2022

Available online 24 November 2023

### KEYWORDS

Gambling disorder;  
Addiction;  
Epidemiology;  
Risk factors;  
Neurobiology;  
Treatment

**Abstract** Gambling is an increasingly more common activity in our society, especially with the advent of new gambling modalities, such as online gambling. Although many people gamble without undergoing health problems, some individuals develop gambling disorder (GD). In recent years, the concern about this disorder has grown substantially among researchers and clinicians, and the number of studies exploring its etiopathogenesis and risk factors has increased significantly. Indeed, certain groups of individuals may have an elevated risk for GD; for example, being male, young, people with low socioeconomic, high impulsivity, and emotional instability. From a neurobiological perspective, GD has been associated with alterations in neurotransmitter systems involved in motivation and reward processing. Likewise, some studies have reported that hormonal factors may play an important role in the development and maintenance of GD. Taken together, all these findings have contributed to the improvement of preventive and treatment interventions of gambling disorder. However, further studies are needed to better understand the mechanisms involved in the development and maintenance of this disorder. The present review offers an update on the main clinical, neurobiological, and treatment aspects of gambling disorder.

© 2022 Asociación Nacional de Médicos Forenses. Published by Elsevier España, S.L.U. All rights reserved.

☆ Please cite this article as: Solé-Morata N, Fernández-Aranda F, Baenas I, Gómez-Peña M, Moragas L, Lara-Huallipe ML, et al. Actualización sobre los aspectos neurobiológicos, clínicos y de tratamiento sobre el juego patológico. Revista Española de Medicina Legal. 2023. <https://doi.org/10.1016/j.reml.2022.07.001>.

\* Corresponding author.

E-mail address: [sjimenez@bellvitgehospital.cat](mailto:sjimenez@bellvitgehospital.cat) (S. Jiménez-Murcia).

**PALABRAS CLAVE**

Trastorno de juego;  
Adicción;  
Epidemiología;  
Neurobiología;  
Factores de riesgo;  
Tratamiento

**Actualización sobre los aspectos neurobiológicos, clínicos y de tratamiento sobre el juego patológico**

**Resumen** El juego es una actividad cada vez más común en nuestra sociedad, especialmente con la aparición de nuevas modalidades de juego, que lo hacen más fácilmente accesible. A pesar de que para la mayoría de individuos jugar es solo un entretenimiento, algunas personas pueden desarrollar un trastorno de juego (TJ). En los últimos años, el interés por dicho trastorno ha ido aumentando tanto en la comunidad clínica como científica, y el número de estudios sobre etiopatogenia y factores de riesgo ha crecido significativamente. Entre los distintos factores asociados a un mayor riesgo de desarrollar un TJ destacan la edad, el sexo masculino, tener un nivel socioeconómico bajo, niveles altos de impulsividad y baja regulación emocional. A nivel neurobiológico, se han descrito anomalías en los sistemas de neurotransmisión que regulan las conductas de recompensa. Asimismo, algunos estudios han demostrado la implicación de factores hormonales y en el desarrollo y mantenimiento del TJ. Todo esto ha contribuido notablemente en la mejora de las acciones de prevención y tratamiento. No obstante, aún quedan muchas cuestiones por resolver y es necesario seguir avanzando en la exploración de este trastorno. La presente revisión ofrece una actualización sobre los aspectos clínicos, neurobiológicos y de tratamiento del trastorno de juego.

© 2022 Asociación Nacional de Médicos Forenses. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

**Introduction**

Betting involves risking a certain amount of money in the hope of obtaining a larger sum. The most usual forms of gambling include slot machines, the lottery, and online gambling, especially poker and sport betting.<sup>1</sup> Although this is a highly popular form of entertainment and leisure, it is not free of risk and some players may develop an addictive disorder with dramatic consequences. The latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) uses the term *gambling disorder* (GD), which replaces the term *pathological gambling*, to refer to a pattern of persistent and recurrent gambling which causes deterioration and discomfort in the subject. Furthermore, although it was initially classified as an impulse control disorder, the latest version of the DSM includes it in the same category as substance abuse disorders (SADs). This reclassification is due to multiple empirical indications which show that SAD and GD are highly similar at the clinical and neurobiological levels, as well as in terms of their response to treatment.

The figures corresponding to the prevalence of GD vary very widely from country to country, depending above all on their current legislation or cultural context. Worldwide, the prevalence of this disorder is estimated to stand at from 0.1% to 5.8%,<sup>2</sup> while in the specific case of Spain, 4.4% of citizens describe gambling behaviour with an element of risk.<sup>3</sup> It should also be underlined that the development of new and far more accessible forms of gambling, such as online gambling, as well as aggressive advertising and marketing, are also affecting the epidemiology of this disorder.<sup>4</sup>

A range of factors have been identified over the last decades which may increase the probability of developing problems in association with gambling. For example, at a

sociodemographic level, being male, starting at an early age, excessive alcohol and tobacco consumption and having a low educational and socioeconomic level, among other factors, have all been associated with a higher risk of developing GD.<sup>5</sup> In the same way, certain personality traits are also considered to be risk factors. For example, these include a strong tendency to avoid harm (or neuroticism), together with low levels of self-management, difficulties in decision-making and planning, as well as high levels of impulsiveness and sensation-seeking.<sup>6</sup>

In aetiological terms, GD should be considered to be the end result of a complex interaction of genetic, environmental, psychological, and neurobiological factors. Of the different theoretical models that have been proposed, the most outstanding and the one that best explains the heterogeneous nature of GD is the so-called pathways or subtypes model. This suggests that 3 different groups exist of individuals who are predisposed to suffer gambling problems: those who are behaviourally conditioned, those who are emotionally vulnerable and antisocial impulsive individuals.<sup>7</sup> This model supplies a theoretical framework to explain the aetiology of the disorder, and to understand the complex interactions between the variables involved in the pathogenesis of GD. This framework is indispensable for progress in developing prevention strategies and specific forms of treatment. Having said that, this review has the purpose of offering an update on the clinical and neurobiological aspects of GD, as well as its treatment.

**Clinical symptoms**

The most important clinical characteristics of patients with GD include tolerance (the increasing need to make larger bets and to bet more often), the abstinence syndrome (nervousness and irritability when gambling behaviour is

interrupted), as well as repeated failed attempts to cease gambling behaviour. Patients with GD have also often been described as tending to gamble again after having lost money (to recover their losses) and to lie to hide the importance of what they spend on gambling, as well as to endanger their professional, personal, or family relationships. They may also come to depend economically on others to relieve a desperate financial situation caused by their gambling.<sup>8</sup>

At a psychological level, patients with GD have high levels of impulsiveness and sensation-seeking and damage-avoidance, as well as low levels of self-control (difficulty in guiding behaviour to achieve specific objectives, as well as a lack of ambition and self-confidence).<sup>9</sup> What is more, the presence of problems in emotional control and high levels of impulsiveness have been linked to more severe disorders and a poorer response to treatment.<sup>10</sup> It has also been suggested that deficits observed, the control of impulses may underlie higher cognitive processes, such as decision-making or working memory.<sup>11</sup>

On the other hand, patients with GD usually suffer cognitive distortions that perpetuate their decision-making deficit.<sup>12</sup> The most common such distortions are: superstitions, such as thinking that a certain garment brings luck; or the gambler's fallacy that consists of believing that chance events in the past affect those in the future; the illusion that certain events can be controlled; as well as perceiving losses to be almost gains. A recent study of more than 500 patients over the age of 18 years and associated with public centres or gamblers' associations around the country showed that cognitive distortions, in men as well as in women, are one of the factors most closely linked to the severity of the disorder.<sup>13</sup>

Different clinical characteristics have been described for men and women. Although GD is a more prevalent disorder among men, women have been observed to be more likely to hide it. This is probably because they are subject to more social stigma linked to gambling, so that the figures may be under-reported.<sup>14</sup> The data also show that women tend to participate more in games that do not involve strategy (such as slot machines that give prizes or bingo) and that they use gambling to regulate negative emotional states.<sup>15</sup> Furthermore, the disorder has been observed to progress differently over time in women, in a phenomenon known as the telescope effect.<sup>16</sup> Thus, while men usually debut with problematic gambling at an earlier age and take longer to develop it, women usually start to gamble later in life but develop the disorder over a far shorter period of time.

Regarding comorbidities, 96% of patients with GD have been estimated to also have another psychiatric disorder, among which mood disorders and substance abuse stand out.<sup>1</sup> Although they are less common, comorbidities have also been observed with attention deficit and hyperactivity disorder (ADHD). The results of a recent study of the relationship between ADHD and GD indicated that the presence of symptoms characteristic of ADHD was linked to more severe GD.<sup>17</sup> Likewise, a certain degree of comorbidity has also been described with other behavioural addictions such as the problematic use of videogames or compulsive shopping.<sup>18</sup> Moreover, individuals with GD are at higher risk of committing suicidal acts than is the case for the general population.<sup>8</sup>

Finally, numerous studies have shown that there is an association between GD and committing illegal acts.<sup>19,20</sup> In fact, GD used to be classified within the impulse control disorders, together with pyromania, kleptomania, and intermittent explosive disorder.<sup>21</sup> The DSM-IV also included a diagnostic criterion based on the commission of illegal acts,<sup>22</sup> although this was eliminated from the DSM-5. In spite of this, the figures indicate that this symptom should be taken into account when evaluating the severity of the disorder. In a recent study, 23.26% of the patients with GD stated that they had committed at least 1 illegal act,<sup>21</sup> and these figures are even higher (36.0%) when only a young adult population is considered.<sup>23</sup>

Respecting the hypotheses proposed to explain this behaviour, some authors have suggested that committing crimes may be a direct result of gambling; either to finance it, or to pay the resulting debts.<sup>19</sup> On the other hand, accumulated evidence suggests that illegal acts associated with GD are linked to greater severity of the same, with an earlier starting age for gambling and a longer-lasting disorder.<sup>21,24</sup> The majority of gamblers who commit illegal acts have been found to be men, with higher levels of psychopathology, impulsiveness, and sensation-seeking, as well as a reduced tendency to avoid harm and persistency, understanding the latter to be perseverance in spite of frustration or fatigue.<sup>24</sup> Lastly, in reference to volition, in patients with GD, gambling causes highly intense emotions over short periods of time: excitement, agitation, hope, and disgust. It is therefore understandable that the sentences of some patients with legal problems may be mitigated due to the allegation of impaired judgement or a loss of control.<sup>20</sup>

## The neurobiological substratum of GD

Several regions of the brain and signalling routes have been identified in the last 2 decades that are involved in the aetiopathogenesis of GD. One of the ranges of theoretical models suggested stands out. This model consists of the "interaction between person–affect–cognition–execution",<sup>25</sup> and it combines the accumulated evidence for the neurobiological processes which underlie addictive behaviours, offering a comprehensive theoretical framework that makes it possible to comprehend the development and continuation of addictive disorders. From this viewpoint, GD is associated with a dysfunction within the regions of the brain that are associated with decision-making, reward processing, and impulsiveness.<sup>26</sup> More specifically, neuroimaging studies have linked the presence of alterations within the prefrontal cortex with problems in making decisions. Furthermore, the tonsils and hippocampus have been linked to the regulation of stress and emotional learning.<sup>1</sup>

At neurotransmitter level, the accumulated evidence points to the central role of dopamine in the development and continuation of addictive behaviours.<sup>26</sup> More concretely, the dopaminergic system would be directly linked to motivation and reward processing. It has therefore been suggested that the presence of a gratifying stimulus triggers the liberation of dopamine in the ventral tegmental area (VTA) and the nucleus accumbens (NAcc), thereby generating positive feedback. Nevertheless, although the role of

dopamine has been extensively analysed in substance addictions, many questions still exist about its role in GD.

Apart from dopamine, other neurotransmitters have also been linked to the aetiopathogenesis of GD. For example, serotonin has been associated with the commencement or cessation of the behaviour, while opiates have been linked to the processes of abstinence and pleasure, while glutamate seems to be involved in compulsive behaviour and cognitive inflexibility.<sup>27</sup> It has also been suggested that complex interactions between neurotransmitter systems and neuronal networks would participate in a different way in the stages of addictive processes. For example, while dopamine seems to be involved in the earliest phases of the disorder, changes in brain structure associated with serotonin and opiates are associated with the later phases of GD.<sup>26</sup>

Several studies have recently shown several hormonal factors to be involved in behaviours associated with reward and gratification. For example, a link has been described between addictions to substances and alterations in the secretion of certain hormones within the hypothalamic–pituitary–adrenal (HPA) axis, as well as melanocortin and orexin.<sup>28</sup> Ghrelin, a hormone associated with ingestion, has also been said to perhaps play a relevant role in the reward mechanisms involved in alcohol consumption.<sup>29</sup> In a similar way, LEAP2, a factor discovered very recently which is involved in the ghrelin system, may also be linked to addictive processes.<sup>30</sup> Likewise, new circulating proteins have recently been described whose levels are altered in addictive disorders. These proteins include prolactin, insulin, brain-derived neurotrophic factor (BDNF), or tumour necrosis factor (TNF- $\alpha$ ).<sup>31</sup> Despite all of these highly interesting findings, the specific role of all of these molecules in GD has yet to be properly elucidated.

Finally, although the accumulated evidence indicates that genetic factors account for 50% of the risk of suffering GD, very few genes closely associated with addictive disorders have actually been identified.<sup>1</sup> In fact, the first and only large-scale specific genome analysis (GWAS) of GD did not detect any genetic variant that was significantly linked to a higher risk of suffering this disorder.<sup>32</sup> A study of candidate genes recently confirmed that certain genetic variants in genes that code for different neurotrophic factors (NTF) may be associated with a higher risk of having this disorder.<sup>33</sup> It is also necessary to consider additional mechanisms that may explain how these genetic factors contribute to the aetiology of this disorder. These factors include epigenetic alterations which alter the expression of certain genes and are influenced by environmental factors. Definitively, in spite of all of the said findings, much still has to be done to understand the neurobiology of GD.

## Evidence-based treatments

Epidemiological studies suggest that approximately 15% of the individuals who have problems with gambling receive professional help. The reasons for such a low figure include the limited availability of services or the lack of insurance coverage in many countries.<sup>1</sup> The stigma associated with this disorder has also been considered to be a major barrier against seeking help or asking for treatment. Moreover, for women, as occurs with alcohol, because gambling behaviour

is less accepted for them, the shame associated with starting treatment for a GD is even greater.<sup>34</sup>

Different types of intervention have been described in recent years for the treatment of GD. At a psychological level, the therapies which have had the greatest impact are cognitive and cognitive-behavioural therapies (CBT).<sup>35</sup> On the one hand, cognitive therapies centre on modifying the cognitive distortions intrinsic to the disorder, such as magical thinking and other concepts associated with chance.<sup>36</sup> On the other hand, cognitive-behavioural therapy combines these cognitive components with behavioural interventions, with the aim of identifying the external factors that trigger gambling behaviour and strengthening alternative forms of behaviour to combat them.<sup>37</sup> Some studies have recently shown the usefulness of including motivational therapy in CBT protocols, centring on improving how individuals with GD participate in treatment and overcoming the possible ambivalence they may experience.<sup>37–39</sup>

At a pharmacological level, different types of drugs are used to alleviate the symptoms of the disorder. These drugs include antidepressants, mood stabilisers, and opiate antagonists.<sup>39</sup> The use of these drugs is based on the similarities observed with other mental disorders, chiefly bipolar disorders, SAD, and obsessive-compulsive disorder. From a neurobiological viewpoint, the drugs that have been studied act by targeting serotonergic, dopaminergic, opiate, or glutamatergic neurotransmitters. On the one hand, antidepressants and particularly selective serotonin reuptake inhibitors (SSRI), have been shown to be significantly superior to placebos in the treatment of GD. On the other hand, a recent review of the use of opiate antagonists in behavioural addictions concluded that naltrexone and nalmefene were the only evidence-based pharmacological treatments for the treatment of GD.<sup>38</sup> The other drugs studied either gave negative results in comparison to a placebo or offered inconclusive evidence. Finally, although there is no clear hierarchy in the drugs that should be used to treat GD, several studies agree that each one of the drugs mentioned is more or less effective depending on the comorbidities of the patients. For example, opiate antagonists seem to be more effective in patients who are addicted to alcohol.

Due to the complex nature of this disorder and the limitations of CBT, an increasing number of authors agree on the need to include other therapeutic tools in the treatment of GD.<sup>40</sup> The heterogeneous nature of the disorder also has to be taken into account when selecting the most appropriate treatment. Therefore, based on the subtype or pathways model mentioned above, it is indispensable to have a range of therapeutic tools that can be adapted to fit each patient, according to precision medicine or therapy.<sup>39</sup> Additionally, there are also telephonic interventions and online CBT programmes. Interventions of this type have certain advantages over face-to-face therapies, including their flexibility, anonymity, and confidentiality. This type of approach has given satisfactory results in terms of reducing the severity of problems, as well as lowering the levels of anxiety and depression while improving quality of life, at the end of treatment as well as after 36 months.<sup>41</sup>

On the other hand, several studies suggest that it is beneficial to include third-generation therapy elements in the treatment of GD.<sup>39</sup> For example, mindfulness, understood as a meditation-based technique which aims of

improve awareness of the current moment without judging it, has had a significant impact on how addictions are managed. Thus, this technique has given positive results in addictions to substances as well as in GD, reducing the severity of the disorder and abstinence, as well as reducing the emotional and psychological discomfort associated with addiction.<sup>42</sup> Similarly, the use of virtual reality and *serious* video games has also been studied, to simulate emotional contexts where patients are able to apply the therapeutic tools they acquired through cognitive-behavioural therapies.

Finally, including significant individuals who function as co-therapists is becoming increasingly important in clinical practice as a highly effective tool to improve the efficacy of treatment.<sup>39</sup> Although little empirical evidence has been accumulated to date, the results of a recent study show that the patients accompanied by a significant individual suffered fewer relapses and adhered better to treatment.<sup>43</sup>

Cognitive-behavioural therapy has been shown to be the most effective, while pharmacological therapy has been found to be useful in reducing associated symptoms, although it is less effective over the long-term.<sup>39</sup> Nevertheless, controversy exists over which CBT programme is the most effective, how long this method remains effective or the way in which it should be applied. Furthermore, the fact that the concept of a response to treatment has yet to be correctly defined should also be taken into account, meaning that this concept has been evaluated inconsistently.<sup>44</sup> The aspects associated with the response to treatment that have been studied the most are relapse and abandonment. Although no agreement exists regarding why relapse occurs, some factors which predict relapse have been described, including cognitive distortions, high exposure to gambling, and socioeconomic problems.<sup>45</sup> Likewise, the probability of treatment abandonment would be associated with being young and having a low social and educational level.<sup>6</sup> On the contrary, distraction techniques that prevent thinking about the need to gamble, vigilance, motivation to change, and a supportive social network would all be factors that protect against relapse.<sup>46</sup>

On the other hand, rates of abandonment have been linked to a young population, less severity, drug use, and a family history of GD, among other factors. The presence of comorbid disorders also seems to hinder adherence to treatment. On the contrary, factors such as a low level of sensation-seeking or greater awareness of the consequences of gambling have been associated with better adherence.<sup>47</sup> Finally, we should point out that no consensus has been reached on how to define recovery from this disorder.<sup>44</sup> The authors of a recently published systematic review concluded that the recovery construct is multidimensional, so that therefore, apart from a reduction in symptoms, other aspects associated with patient mental, physical, and social well-being should also be taken into account when evaluating the efficacy of treatments.<sup>48</sup>

Lastly, the emergence of new forms of internet-based gambling, as well as the increasing popularity and social acceptance of gambling behaviour, are increasingly worrying experts, who agree on the need for gambling prevention policies. Different studies have shown that some types of gambling are more closely associated with the development of a disorder than others. For example, individuals who

gamble in casinos (online or physically present) are at higher risk of developing problems with gambling than those who play the lottery, especially for large prizes. Nevertheless, the results obtained by several recent studies show certain contradictions about the relative importance of the type of gambling in connection with the development of problematic gambling. Thus, while some studies show that certain forms of gambling are riskier than others, other authors have found that participation is the most important factor, i.e., the number of games in which a single individual participates. A recent study remarks that although both aspects would be closely involved in the development of a disorder, further studies are required that take different sociodemographic factors into account for the development of specific preventive strategies for the population.<sup>49</sup>

## Conclusions

Thus definitively, GD is a disease that increasingly studied, and its prevalence worldwide is worrying the population more and more. Because of this, and in spite of its recent recognition as a disorder, numerous studies have centred on understanding its aetiopathogenic mechanisms. There can be no doubt that all of these factors have contributed to improving its prevention and treatment. However, further studies are needed to improve comprehension of the neurobiological mechanisms involved in this disorder, as well as its main risk factors.

## Declaration of Competing Interest

Fernando Fernández-Aranda has received consultancy fees from Novo Nordisk and editorial fees as a Wiley EIC. The other authors have no conflict of interests to declare.

## Acknowledgements

This work was undertaken with the support of the Ministerio de Ciencia, Innovación y Universidades (RTI2018-101837-B-100), the Instituto Salud Carlos III (ISCIII), the Ministerio de Sanidad, Servicios Sociales e Igualdad (FIS PI20/00132, FIS PI17/01167), The Government Delegation for the National Plan for Drugs (2019I47 and 2021I031), CIBER Fisiología Obesidad y Nutrición (CIBERObn) del ISCIII. This work was also supported by the ISCIII CM21/00172 (cofinanced by the European Social Fund. ESF investing in your future). We would like to thank the CERCA Programme of the *Generalitat de Catalunya* for its institutional support, as well as the European Regional Development Fund (ERDF) "A Way of Making Europe".

## References

1. Potenza MN, Balodis IM, Devereensky J, Grant JE, Petry NM, Verdejo-Garcia A, et al. Gambling disorder. *Nat Rev Dis Prim.* 2019 Dec 25;5(1):51.
2. Calado F, Griffiths MD. Problem gambling worldwide: an update and systematic review of empirical research (2000–2015). *J Behav Addict.* 2016 Dec;5(4):592–613.

3. DGOJ. Dirección General de Ordenación del Juego. Memoria Anual 2015. Madrid: Ministerio de Hacienda y Administraciones Públicas; 2015.
4. Abbott MWW. The changing epidemiology of gambling disorder and gambling-related harm: public health implications. *Public Health*. 2020 Jul;184:41–5.
5. Dowling NA, Merkouris SS, Greenwood CJ, Oldenhof E, Toumbourou JW, Youssef GJ. Early risk and protective factors for problem gambling: a systematic review and meta-analysis of longitudinal studies. *Clin Psychol Rev*. 2017 Feb;51:109–24.
6. Jiménez-Murcia S, Granero R, Fernández-Aranda F, Arcelus J, Aymamí MN, Gómez-Peña M, et al. Predictors of outcome among pathological gamblers receiving cognitive behavioral group therapy. *Eur Addict Res*. 2015;21(4):169–78.
7. Blaszczynski A, Nower L. A pathways model of problem and pathological gambling. *Addiction*. 2002 May;97(5):487–99.
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric association (APA); 2013.
9. Zilberman N, Yadid G, Efrati Y, Neumark Y, Rassovsky Y. Personality profiles of substance and behavioral addictions. *Addict Behav*. 2018;82(March):174–81.
10. Vintró-Alcaraz C, Mestre-Bach G, Granero R, Gómez-Peña M, Moragas L, Fernández-Aranda F, et al. Do emotion regulation and impulsivity differ according to gambling preferences in clinical samples of gamblers? *Addict Behav*. 2022 Mar;126:107176.
11. Mallorquí-Bagué N, Tolosa-Sola I, Fernández-Aranda F, Granero R, Fagundo ABAB, Lozano-Madrid M, et al. Cognitive deficits in executive functions and decision-making impairments cluster gambling disorder sub-types. *J Gambl Stud*. 2018 Mar 20;34(1):209–23.
12. Granero R, Fernández-Aranda F, Valero-Solís S, Pino-Gutiérrez A del, Mestre-Bach G, Baenas I, et al. The influence of chronological age on cognitive biases and impulsivity levels in male patients with gambling disorder. *J Behav Addict*. 2020 Jun;9(2):383–400.
13. Jiménez-Murcia S, Granero R, Giménez M, del Pino-Gutiérrez A, Mestre-Bach G, Mena-Moreno T, et al. Moderator effect of sex in the clustering of treatment-seeking patients with gambling problems. *Neuropsychiatrie*. 2020 Sep 3;34(3):116–29.
14. Kaufman A, Jones Nielsen JD, Bowden-Jones H. Barriers to treatment for female problem gamblers: a UK perspective. *J Gambl Stud*. 2017 Sep 22;33(3):975–91.
15. Hing N, Russell AMT, Vitartas P, Lamont M. Demographic, behavioural and normative risk factors for gambling problems amongst sports bettors. *J Gambl Stud*. 2016 Jun;32(2):625–41.
16. Grant JE, Odlaug BL, Mooney ME. Telescoping phenomenon in pathological gambling: association with gender and comorbidities. *J Nerv Ment Dis*. 2012;200(11):996–8.
17. Mestre-Bach G, Steward T, Potenza MN, Granero R, Fernández-Aranda F, Mena-Moreno T, et al. The role of ADHD symptomatology and emotion dysregulation in gambling disorder. *J Atten Disord*. 2021 Jul 30;25(9):1230–9.
18. Ford M, Håkansson A. Problem gambling, associations with comorbid health conditions, substance use, and behavioural addictions: opportunities for pathways to treatment. Rodda S, editor. *PLoS One*. 2020 Jan 10;15(1):e0227644.
19. Adolphe A, Khatib L, van Golde C, Gainsbury SM, Blaszczynski A. Crime and gambling disorders: a systematic review. *J Gambl Stud*. 2019;35(2):395–414.
20. Blum AW, Grant JE. Behavioral addictions and criminal responsibility. *J Am Acad Psychiatry Law*. 2017;45(4):464–71.
21. Jiménez-Murcia S, Granero R, Fernández-Aranda F, Sauvaget A, Fransson A, Hakansson A, et al. A comparison of DSM-IV-TR and DSM-5 diagnostic criteria for gambling disorder in a large clinical sample. *Front Psychol*. 2019 Apr 26;10.
22. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 2000.
23. Mestre-Bach G, Granero R, Vintró-Alcaraz C, Juvé-Segura G, Marimon-Escudero M, Rivas-Pérez S, et al. Youth and gambling disorder: what about criminal behavior? *Addict Behav*. 2021 Feb;113:106684.
24. Gorsane MA, Reynaud M, Vénisse JL, Legauffre C, Valleur M, Magalon D, et al. Gambling disorder-related illegal acts: regression model of associated factors. *J Behav Addict*. 2017;6(1):64–73.
25. Brand M, Wegmann E, Stark R, Müller A, Wölfling K, Robbins TW, et al. The Interaction of Person-Affect-Cognition-Execution (I-PACE) model for addictive behaviors: update, generalization to addictive behaviors beyond internet-use disorders, and specification of the process character of addictive. *Neurosci Biobehav Rev*. 2019;104(May):1–10.
26. Antons S, Brand M, Potenza MN. Neurobiology of cue-reactivity, craving, and inhibitory control in non-substance addictive behaviors. *J Neurol Sci*. 2020;415:116952.
27. Pettorruso M, Zoratto F, Miuli A, De Risio L, Santorelli M, Pierotti A, et al. Exploring dopaminergic transmission in gambling addiction: a systematic translational review. *Neurosci Biobehav Rev*. 2020;119:481–511.
28. Vinson GP, Brennan CH. Addiction and the adrenal cortex. *Endocr Connect*. 2013 Sep;2(3):R114.
29. Ralevski E, Horvath TL, Shanabrough M, Hayden R, Newcomb J, Petrakis I. Ghrelin is suppressed by intravenous alcohol and is related to stimulant and sedative effects of alcohol. *Alcohol Alcohol*. 2017 Jul;52(4):431–8.
30. Ge X, Yang H, Bednarek MA, Galon-Tilleman H, Chen P, Chen M, et al. LEAP2 is an endogenous antagonist of the ghrelin receptor. *Cell Metab*. 2018 Feb;27(2):461–469.e6.
31. Choi S-WW, Shin Y-CC, Mok JY, Kim D-JJ, Choi J-SS, Suk-Hyun Hwang S. Serum BDNF levels in patients with gambling disorder are associated with the severity of gambling disorder and Iowa Gambling Task indices. *J Behav Addict*. 2016 Mar;5(1):135–9.
32. Lang M, Leménager T, Streit F, Fauth-Bühler M, Frank J, Juraeva D, et al. Genome-wide association study of pathological gambling. *Eur Psychiatry*. 2016 Aug 23;36:38–46.
33. Solé-Morata N, Baenas I, Etxandi M, Granero R. The role of neurotrophin genes involved in the vulnerability to gambling disorder. *Sci Rep*. 2022:1–11.
34. Dąbrowska K, Wieczorek Ł. Perceived social stigmatisation of gambling disorders and coping with stigma. *Nord Stud Alcohol Drugs*. 2020 Jun 1;37(3):279–97.
35. Baño M, Mestre-Bach G, Granero R, Fernández-Aranda F, Gómez-Peña M, Moragas L, et al. Women and gambling disorder: Assessing dropouts and relapses in cognitive behavioral group therapy. *Addict Behav*. 2021;123.
36. Ledgerwood DM, Dyszniku F, McCarthy JE, Ostojic-Aitkens D, Forfitt J, Rumble SC. Gambling-related cognitive distortions in residential treatment for gambling disorder. *J Gambl Stud*. 2020 Jun 27;36(2):669–83.
37. Jiménez-Murcia S, Granero R, Fernández-Aranda F, Aymamí N, Gómez-Peña M, Mestre-Bach G, et al. Developmental trajectories of gambling severity after cognitive-behavioral therapy. *Eur Psychiatry*. 2019 Aug 1;60:28–40.
38. Di Nicola M, De Crescenzo F, D'Alò GL, Remondi C, Panaccione I, Moccia L, et al. Pharmacological and psychosocial treatment of adults with gambling disorder: a meta-review. *J Addict Med*. 2020;14(4):e15–23.
39. Menchón JM, Mestre-Bach G, Steward T, Fernández-Aranda F, Jiménez-Murcia S. An overview of gambling disorder: from treatment approaches to risk factors. *F1000Research*. 2018;7:434.

40. Tolchard B. Cognitive-behavior therapy for problem gambling: a critique of current treatments and proposed new unified approach. *J Ment Heal*. 2017 May 4;26(3):283–90.
41. Chebli J-L, Blaszczyński A, Gainsbury SM. Internet-based interventions for addictive behaviours: a systematic review. *J Gambl Stud*. 2016 Dec 22;32(4):1279–304.
42. McIntosh CC, Crino RD, O'Neill K. Treating problem gambling samples with cognitive behavioural therapy and mindfulness-based interventions: a clinical trial. *J Gambl Stud*. 2016 Dec 4;32(4):1305–25.
43. Jiménez-Murcia S, Tremblay J, Stinchfield R, Granero R, Fernández-Aranda F, Mestre-Bach G, et al. The involvement of a concerned significant other in gambling disorder treatment outcome. *J Gambl Stud*. 2017 Sep 17;33(3):937–53.
44. Granero R, Valero-Solis S, Fernández-Aranda F, Gómez-Peña M, Moragas L, Mena-Moreno T, et al. Response trajectories of gambling severity after cognitive behavioral therapy in young-adult pathological gamblers. *J Behav Addict*. 2020;9(1):140–52.
45. Ginley MK, Rash CJ, Petry NM. Psychological interventions in gambling disorder. *Gambling Disorder*. Cham: Springer International Publishing; 2019. p. 181–94.
46. Ronzitti S, Soldini E, Smith N, Clerici M, Bowden-Jones H. Gambling disorder: exploring pre-treatment and in-treatment dropout predictors. A UK study. *J Gambl Stud*. 2017 Dec 22;33(4):1277–92.
47. Ronzitti S, Soldini E, Smith N, Bayston A, Clerici M, Bowden-Jones H. Are treatment outcomes determined by type of gambling? A UK study. *J Gambl Stud*. 2018 Sep 30;34(3):987–97.
48. Pickering D, Keen B, Entwistle G, Blaszczyński A. Measuring treatment outcomes in gambling disorders: a systematic review. *Addiction*. 2018 Mar;113(3):411–26.
49. Mazar A, Zorn M, Becker N, Volberg RA. Gambling formats, involvement, and problem gambling: which types of gambling are more risky? *BMC Public Health*. 2020 Dec 18;20(1):711.