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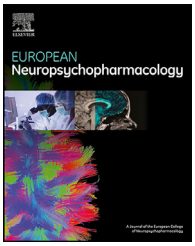

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Is there such a thing as gambling dual disorder? Preliminary evidence and clinical profiles

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Abstract
Patients with gambling disorder (GD) frequently present other mental disorders, such as substance use disorder (SUDs), attention deficit/hyperactivity disorder (ADHD), mood disorders, and impulse-control disorders. We propose that GD should not be conceptualized as a single nosological entity, but rather as a gambling dual disorder (GDD). This study aims to provide further evidence of the co-occurrence of GD and other mental disorders in routine clinical practice and to identify different clinical profiles of severity. This descriptive, cross-sectional, and observational study included 116 patients with GD who were undergoing treatment in a specialized center. The MULTICAGE-CAD 4 and South Oaks gambling screen questionnaires confirmed the presence of GD in 97.4% and 100% of the patients, respectively. Other addictive behaviors such as compulsive spending, Internet, video games, or SUD (59.5%, 27.6%, 11.2%, and 13.8%,

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respectively) were also identified. The most used substances were tobacco (42.2%) and alcohol (5.2%). Half of the patients suffered from ADHD, 30.2% showed moderate or severe depression, and 17.2% suffered from a social anxiety problem. The majority (76.7%) also presented a phenotype with high impulsiveness. The cluster analysis identified two different clinical profiles of severity in patients with GDD. One profile showed higher severity of other mental disorders (ADHD, depression, anxiety, SUD, or insomnia), impulsivity, general psychopathological burden, and disability. In conclusion, our study provides further evidence on the co-occurrence of GD and other mental disorders supporting the GDD existence, shows impulsiveness as a vulnerability factor for GD, and identifies two clinical severity profiles.
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1. Introduction

The concept of addiction, traditionally associated with the use of psychotropic substances, was officially extended in 2013 with the introduction of Gambling Disorder (GD) in the chapter of "substance-related and addictive disorders" of the 5th edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013; Petry et al., 2018). Previously, it was included among the impulse control disorders. The 11th revision of the International Classification of Diseases (ICD-11), developed by the World Health Organization (WHO), classified GD within the addictive disorder category, and characterized it as impaired control over gambling (frequency, intensity, or duration) and a continuation/escalation of the behavior despite the negative consequences (World Health Organization, 2022). In addition, ICD-11 (as well as the Section III of the DSM-5-TR) included gaming disorder (digital gaming or video gaming) as a mental disorder other than GD (World Health Organization, 2022). GD and gaming disorder often co-occur, and this dual diagnosis seemed to be related to the age at onset of the addiction problems (Ayala-Rojas et al., 2022). During the last decades, gambling availability, participation, and expenditure have notably increased (Abbot et al., 2020; Lind et al., 2021). A systematic review including data from general population studies revealed differences in the GD prevalence across countries worldwide varying from 0.1 to 5.8% and between 0.1% and 3.4% in European countries (Calado and Griffiths, 2016).

Dual disorder is a term used for patients with an addictive disorder and other mental disorders (Szerman and Martínez-Raga, 2015). Diverse studies have reported the frequent co-occurrence between GD and other mental disorders, including substance use disorders (SUDs), attention deficit/hyperactivity disorder (ADHD), mood disorders, or impulse-control disorders (Calado and Griffiths, 2016; Dowling et al, 2015; (Kessler et al., 2008); Potenza et al., 2019; Szerman et al., 2020). Indeed, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) revealed that 96% of individuals with GD have at least one other psychiatric disorder (Cowlishaw and Hakes, 2015) without taking into account personality disorders or personality traits. Similar findings were reported in a meta-analysis showing prevalence estimates for any lifetime DSM-IV Axis other psychiatric disorder in individuals seeking psychological or pharmacological treatment for problem gambling were as high as 75.5%, with a lifetime prevalence of 47.0% for any lifetime alcohol or substance use disorder (Dowling et al, 2015). Converesely, the lifetime prevalence of GD in patients with SUDs has been estimated of being 7.2% (varying from 4.1% to 10.3%) (Cowlishaw and Hakes, 2015). For this reason, we propose that GD should not be conceptualized as a single nosological entity but rather by the term gambling dual disorder (GDD) (Szerman et al., 2020). There is still a debate regarding the chronology of both disorder phenotypes (Maremmani et al., 2011). Whether GD is primary or secondary to the other mental disorders, this must be based on scientific evidence. From the neuroscience perspective, it is known that the brain presents changes long before mental disorders are diagnosed (Govidan et al., 2010). These brain changes can occur with subthreshold symptoms, which precede the onset of the disease (i.e. GD or ADHD symptoms) which should be kept in mind in longitudinal treatment.

Sensation-seeking and impulsivity are personality traits (endophenotypes) commonly presented in individuals with some type of addiction (Szerman et al., 2020). Impulsivity has been described as a behavioral endophenotype mediating the risk for addiction to stimulants and gambling (Ersche et al., 2010). Some individuals with high sensation-seeking traits but no familial vulnerability to addiction, are likely to use drugs or gamble but may have a relatively low risk of developing addiction (Ersche et al., 2013). Sensation seekers have some control over a compulsive behavior, unlike impulsive people. There is a growing interest in identifying transdiagnostic clinical characteristics that explain this frequent co-occurrence. GD has been associated with elevated impulsivity (Ioannidis et al., 2019), also observed in other categorical diagnoses that can occur together with GD (Hook et al., 2021).Although all forms of gambling are more common in people with GD compared to controls, certain forms of gambling activities, particularly those involving electronic gambling machines and internet gambling appear to be associated with a higher risk for developing a GD (King et al, 2015). Furthermore, researchers have tried to identify clinical distinctions between online and offline GD, but few differences have been established. Novel technologies have markedly facilitated the growth of remote gambling including internet, mobile phone, and interactive television gambling (Hubert and Griffiths, 2018). Due to its inherent properties (such as availability, accessibility, anonymity, or convenience), online gambling might

be more troubling than offline for vulnerable individuals (McCormack and Griffiths, 2013). Indeed, a German study demonstrated that replacing 10% of offline with online gambling resulted in an 8.8–12.6% increased risk of becoming a problem gambler (Effertz et al., 2018). Nevertheless, most online gamblers also gamble offline (Hing et al., 2017). Evidence indicates that dual disorders in individuals with any type of GD are the norm rather than the exception (Volkow, 2020).

The objective of this study is to provide further evidence on the co-occurrence of GD and other mental disorders in routine clinical practice, supporting the use of GDD term. Moreover, we aim to go one step further and identify clinical severity profiles in patients with GDD.

2. Materials and methods

2.1. Study design

This descriptive, cross-sectional and observational study included patients with GD who were already receiving treatment on the Madrid non-governmental organization Association for the Prevention and Assistance to the Gambling Problem (*Asociación para la Prevención y Ayuda al Ludópata*) between November 2020 and September 2021. Inclusion criteria were: adult ($\geq$ 18 years); a diagnosis of GD according to ICD-11; and signing the written informed consent. Exclusion criteria included: presence of concomitant diseases that might interfere with parameters evaluated in the study (such as organic or brain lesion, intellectual disability, dementia, etc.). All patients included in the study have signed the written informed consent. Procedures were in accordance with the Declaration of Helsinki and approved by the Ethics Research Committee of the Gregorio Marañón University Hospital of Madrid, Spain.

2.2. Endpoints and variables

The primary endpoint was to evaluate the clinical and psychopathological features that determine a dual disorder in patients who were under treatment for GD. For this, sociodemographic characteristics together with the presence of addictive disorders, including SUDs, ADHD, mood, anxiety, social phobia, insomnia, and personality traits disorders were analyzed. Due to the cross-sectional nature of the study, data were collected at the time of inclusion, without considering the treatment status of the patients.

Disease severity was assessed with the clinical global impression (CGI) scale (Busner and Targum, 2007). Addictive behaviors were evaluated using the Spanish version of the MULTICAGE-CAD 4 questionnaire (Pedrero-Pérez et al., 2007) and South Oaks gambling screen (SOGS) questionnaire (Lesieur and Blume, 1987).

The MULTICAGE-CAD 4 comprises 32 items (8 scales, each with 4 items) with dichotomous responses which psychometric properties are validated (Pedrero-Pérez et al., 2007).

The SOGS is a 20-item questionnaire based on DSM-III criteria for GD. The total score ranges from 0 to 20, and a score $\geq$5 is indicative of the probable existence of GD (Echeburúa et al., 1994; Lesieur and Blume, 1987).

The SUDs were measured by using the Spanish version of the severity of dependence scale (SDS), where each item is rated on a 0–4 Likert scale (Iraurgi Castillo et al., 2010).

The presence of ADHD was evaluated with the Adult Self-Report Scale version 1.1 (ASRS-v.1.1) and the Conners' Adult ADHD Rating Scale (CAARS). The ASRS v.1.1 is an instrument consisting of the eighteen DSM-IV-TR criteria (Kessler et al., 2007; Pedrero-Pérez and Puerta-García, 2007). Part A, with six items have been reported to be most predictive of a possible ADHD in adults and commonly used as a screener. Items are scored by a 5-option scale (never, rarely, sometimes, frequently, and very frequently).

The CAARS scale is used to assess the presence and severity of ADHD symptoms in adult individuals with ADHD (Richarte et al., 2017).

The Symbol Digit Modalities Test (SDMT) is a tool for detecting cognitive and attention impairment by measuring the information processing speed (Smith, 2002). The test shows a symbol digit key on the top of the page, pairing nine symbols with a number from 1 to 9. Below, rows including these symbols randomly depicted, are presented. The participants were asked to match each symbol with the corresponding number, according to the symbol digit key. A total of 110 items were presented. The maximum score was 110 calculated by the total number of substitutions in a 90-second interval.

Mood disorders were evaluated with the second version of Beck's Depression Inventory (BDI-II) (Beck et al., 1996, Sanz et al., 2003). The BDI-II is a 21-item instrument designed to evaluate the severity of existing symptoms of depression. For each item, subjects choose one of the four alternatives (from least to most severe) that better described their condition during the previous two weeks. The score of each item ranges from 0 to 3. According to the total score, subjects were classified as minimal (0-9), mild (10-16), moderate (17-29), or severe depression (30-63).

Anxiety-related disorders were evaluated with the State-Trait Anxiety Inventory (STAI) and the Social Phobia Inventory (SPIN). The STAI evaluates anxiety as a state (transitory) and as a trait (stable condition) (Ortuño-Sierra et al., 2016; Spielberger and Vagg, 1984). A total of 40 items are divided into two subscales (state and trait), and each item is rated on a 0–3 Likert scale. The total score for each subscale ranges from 0 to 60, and is transformed into centiles according to sex and age.

The 17-item SPIN test measures behavioral, physiological, and cognitive symptoms associated with social phobia (Baños et al., 2007; Connor et al., 2000). Items measure avoidance, fear, and physiological discomfort in social situations by using a Likert scale (0-4). Total scores vary from 0 to 68, and higher scores are indicative of greater levels of social anxiety. The first four items are analyzed on a 10-point visual analogue scale (from 0, "no disability", to 10, "maximum disability").

Insomnia Severity Index (ISI) is a 7-item instrument used to evaluate the nature, severity, and impact of insomnia on a Likert scale (Sierra et al., 2008). Subjects were classified as "no insomnia" (0-7 points), "insomnia under the threshold" (8-14), "moderate clinical insomnia" (15-21), and "severe clinical insomnia" (22-28).

Temperament and Character Inventory Revised (TCI-R) (Gutiérrez-Zotes et al., 2004) and Barrat Impulsiveness Scale (BIS) were used for evaluating personality disorders and related traits (Martínez-Loredo et al., 2015). The TCI-R test is a 30-item self-administrated questionnaire divided into three subscales (cognitive, motor, and unplanned impulsivity), designed to measure four temperaments (novelty seeking, harm avoidance, reward dependence, and persistence) and three characters (self-directedness, cooperativeness, and self-transcendence) (Gutiérrez-Zotes et al., 2004).

Brief Symptom Inventory (BSI) is a psychopathological screening instrument that determines, on a Likert scale, the intensity degree of feeling annoyed or affected by the description of each item during the last few weeks (Derogatis and Melisartos, 1983; Martínez-Loredo et al., 2015). In its Spanish adaptation, the BSI comprises a single dimension that assesses general discomfort or distress, with excellent reliability (Martínez-Loredo et al., 2015).

The disability in daily life caused by social phobia was evaluated using the Sheehan Disability inventory (SDI) (Bobes et al., 1999; Sheehan and Sheehan, 2008).

All variables were analyzed globally and considering offline or online GD. The preferred type of gambling addiction (online, offline, or unspecific) was based on ICD-11 criteria (World Health Organization, 6C50 Gambling Disorder; World Health Organization, 6C51 Gaming Disorder).

2.3. Clustering and statistical analysis

To identify different clinical profiles of severity in patients with GD, a cluster analysis for dummy variables was performed (including sociodemographic characteristics of the patients, all questionnaires, and evaluated variables). To perform the analysis, all variables were considered together with the total scores derived from the different questionnaires and those were categorized into dummy variables. Thus, variables were dichotomized into 0 or 1, representing the absence or presence of a category, respectively.

Continuous variables are expressed as mean, SD, or range (minimum-maximum values), while categorical ones are as absolute and relative frequencies. Comparisons in variables regarding the type of gambling addiction (offline versus online) and the cluster (1 versus 2) were carried out using the chi-square or Fisher Exact test, for categorical variables, and the T-test or Mann-Whitney test, for continuous ones, when appropriate. Statistical significance was established with $p \leq 0.05$. Statistical analysis was performed with SAS 14.0 software.

3. Results

3.1. Study population

A total of 116 patients from specific GD-treating centers were included in our study. All fulfilled the criteria for GD defined in ICD-11 and were receiving treatment at the time of inclusion. None of the patients was excluded from the analysis based on the study-defined exclusion criteria. Sociodemographic and clinical characteristics of patients are shown in Table 1. Patients were predominantly males (89.7%), with a mean age of 39.2 years (standard deviation, SD: 11.5), and 12.9% had at least one medical comorbidity, especially type 2 diabetes mellitus/dyslipidemia (4.3%). The majority of patients were equally divided into predominantly online (41.7% of patients) or predominantly offline (41.7%) gamblers. Further 17.2% of the patients reported an unspecified gambling disorder. Ten patients (8.6%) also experienced video game addiction (VGA) according to ICD-11 criteria.

3.2. Clinical and psychopathological features of patients

Regarding to the disease severity evaluated by the CGI scale, 43.9% of the patients were considered moderately to severely ill (Table 2). Various addictive behaviors were identified with the MULTICAGE-CAD 4 questionnaire, i.e. compulsive spending (59.5%), alcohol use (32.4%), internet addiction (27.6%), VGA (11.2%), SUDs (13.8%), sex addiction (6.1%), and eating disorders (4.3%; Table 2). Concerning GD, the MULTICAGE-CAD 4 questionnaire did not ascertain the presence of GD in three of those patients (2.6%). However, all patients presented GD when evaluated with the SOGS questionnaire. The mean SOGS score was 11.7 (range: 6-18), and casino/gambling halls were the most frequent gambling activities (78.4%), followed by lotteries and pools (74.1%; Table 2). Regarding the maximum money spent in one day on gambling, 64.7% of the patients had spent more than 500€ at some time. Related to SUDs, the most commonly used substances were tobacco (42.2%) and alcohol (5.2%), and only one patient showed active GD (0.9%; Supplementary Figure 1). According to the 5-ítem SDS scale, the highest addiction severity was shown by GD (mean: 7.8, range: 0-14; calculated for all patients), followed by tobacco (mean: 6.8, range: 0-14), cocaine (mean: 4.0, range: 0-15), cannabis (mean: 3.0, range: 0-7), alcohol (mean: 2.5, range: 0-14), and caffeine (mean: 1.7, range: 0-4).

The description of ADHD, mood, anxiety, social phobia, insomnia, and abnormal personality traits in patients is shown in Table 3. Based on the ASRS-v.1.1, 50.0% of the patients screened positive for ADHD. Most patients had a minimal depression (52.6%), while 30.2% experienced moderate or severe depression. According to the BIS scale, 76.7% of the patients had an impulsivity personality trait, with a mean score of 48.0 (SD: 17.2). Cognitive, motor and unplanned impulsivity were shown by 78.4%, 69.8% and 75.9% of the patients, respectively. Regarding the SDI questionnaire, scores were 14.2 (SD: 9.6) and 10.0 (SD: 7.6) for total and global disability. No significant differences were found regarding offline or online GD except for slot machine use (in the SOGS) which was higher in preferentially offline gamblers, and the number of answered questions and correct answers (in the SDMT) which were higher in preferentially online gamblers (Supplementary Tables 1 and 2).

3.3. Clusters comprising clinical profiles of patients with GD

Another main objective of the study was the identification of different clinical severity profiles in patients with GD. To meet such an aim, a cluster analysis for dummy variables was performed. A total of 115 patients with 3,232 variables were analyzed. One patient was excluded from the cluster analysis due to a missing variable. After the analysis, two main clusters were identified. Fifteen patients were not included in any group due to the distance from other patients. Analyzing the two important cluster groups, significant differences were found between them regarding eating disorders and internet addiction (in the MULTICAGE-CAD 4; $p = 0.031$ and $p = 0.035$, respectively), presence of ADHD (in the ASRS v.1.1; $p = 0.001$ and CAARS' all dimensions, $p \leq 0.010$), depression (in the BDI-II; $p = 0.001$), anxiety (according to STAI, $p = 0.001$), insomnia (ISI, $p = 0.001$), novelty seeking and exploratory excitability (in the TCI-R; $p = 0.029$ and $p = 0.003$), impulsiveness (in the BIS, $p \leq 0.019$), general psychopathology (in the BSI's all dimensions, $p = 0.001$), and total and global disability (in the SDI; $p = 0.014$ and $p = 0.025$; Table 4).

4. Discussion

Epidemiological and clinical studies support the high prevalence of co-occurring addictive and other mental disorders, commonly known as dual disorders (Calado and Griffiths, 2016; (Kessler et al., 2008); Potenza et al., 2019;

Table 1 Sociodemographic and clinical characteristics of patients.

	Patients (N=116)
Age, mean years (SD)	39.2 (11.5)
Gender, n (%)	
Male	104 (89.7)
Female	12 (10.3)
Marital Status, n (%)	
Never been married	48 (41.4)
Married	33 (28.4)
Separated	4 (3.4)
Divorced	7 (6.0)
Living with romantic partner	24 (20.7)
Dominant hand, n (%)	
Right-handed	107 (92.2)
Left-handed	9 (7.8)
Educational level, n (%)	
No studies	0 (0.0)
Primary education	14 (12.1)
Secondary education	46 (39.7)
University studies	40 (34.5)
Other	16 (13.8)
Employment status, n (%)	
Employed	82 (70.7)
Self-employed	8 (6.9)
Student	6 (5.2)
Retired	4 (3.4)
Unemployed (by health reasons)	4 (3.4)
Unemployed (by other reasons)	12 (10.3)
Medical Comorbidities, n (%)	15 (12.9%)
Type 2 diabetes mellitus/ dyslipidemia	5 (4.3)
Obesity (BMI >30 Kg/m^2)	1 (0.9)
Others	11 (9.5)
Type of gambling addiction, n (%)	
Predominantly online	48 (41.4)
Predominantly offline	48 (41.4)
Unspecific	20 (17.2)
Video game addiction, n (%)	10 (8.6)
Time under treatment, mean months (SD)	20.5 (30.3)
Psychopharmacological treatment, n (%)	6 (5.2)
Non-pharmacological therapy (psychotherapy), n (%)	116 (100.0)
Individual and group psychotherapy	100 (86.2)
Only group psychotherapy	16 (13.8)

BMI, body mass index; SD, standard deviation.

Szerman et al., 2020, Szerman et al.,2022). Previously, we had proposed that it would be clinically more useful to refer to GD as GDD (Szerman et al., 2020). The use of this term would help make clinicians more aware of the need to look for other mental disorders, mental symptoms, or pathological personality traits in patients consulting for GD. The present study confirms the co-occurrence of other mental disorders, specifically ADHD, mood disorders, anxiety, SUDs, social phobia, and insomnia. At the same time, most GD patients with these different categorical diagnoses also presented a phenotype with high impulsiveness.

Categorical diagnoses of mental disorders such as schizophrenia (Granero et al., 2021) or bipolar disorder (Jones et al., 2015) are found in higher prevalence among pathological gamblers than in the general population. Here, ADHD, which is not commonly included in epidemiological studies (Petry et al., 2005), showed the highest prevalence by categorical diagnosis. Individuals with a history of ADHD have elevated rates of GD and more severe gambling problems (Breyer et al., 2009; Fatseas et al., 2016; Gall-Bronnec et al., 2011). Likewise, the prevalence of ADHD in adult problematic gamblers has been estimated around 10-20% (Dowling et al, 2015). Subjects with childhood ADHD symptoms that persisted into young adulthood (aged 18-24) showed greater gambling problem severity than those with no ADHD or with non-persistent ADHD (Breyer et al., 2009). The co-occurrence of both disorders is also linked to a poor prognosis (Breyer et al., 2009; Fatseas et al., 2016). More-

Table 2 Description of disease severity and addictive behaviors in patients.

	Patients (N=116)
Clinical global impression Scale	
Disease severity, n (%)	
Not evaluated	3 (2.6)
Normal/not ill	7 (6.0)
Borderline mentally ill/not at all ill	23 (19.8)
Mildly ill	32 (27.6)
Moderately ill	28 (24.1)
Markedly ill	20 (17.2)
Severely ill	3 (2.6)
MULTICAGE-CAD 4 questionnaire	
Alcohol use/ alcohol dependence, n (%)	
Non-existence of the problem	90 (77.6)
Existence of the problem	26 (32.4)
Probable existence	9 (7.8)
Very probable existence	14 (12.1)
Sure existence	3 (2.6)
Gambling disorder, n (%)	
Non-existence of the problem	3 (2.6)
Existence of the problem	113 (97.4)
Probable existence	22 (19.0)
Very probable existence	35 (30.2)
Sure existence	56 (48.3)
Substance use, n (%)	
Non-existence of the problem	100 (86.2)
Existence of the problem	16 (13.8)
Probable existence	4 (3.4)
Very probable existence	7 (6.0)
Sure existence	5 (4.3)
Eating disorder, n (%)	
Non-existence of the problem	111 (95.7)
Existence of the problem	5 (4.3)
Probable existence	3 (2.6)
Very probable existence	1 (0.9)
Sure existence	1 (0.9)
Internet addiction, n (%)	
Non-existence of the problem	84 (72.4)
Existence of the problem	32 (27.6)
Probable existence	17 (14.7)
Very probable existence	10 (8.6)
Sure existence	5 (4.3)
Video game addiction, n (%)	
Non-existence of the problem	103 (88.8)
Existence of the problem	13 (11.2)
Probable existence	6 (5.2)
Very probable existence	2 (1.7)
Sure existence	5 (4.3)
Compulsive spending, n (%)	
Non-existence of the problem	47 (40.5)
Existence of the problem	69 (59.5)
Probable existence	24 (20.7)
Very probable existence	28 (24.1)
Sure existence	17 (14.7)
Sex addiction, n (%)	
Non-existence of the problem	109 (94.0)

(*continued on next page*)

Table 2 (*continued*)

	Patients (N=116)
Existence of the problem	7 (6.1)
Probable existence	6 (5.2)
Very probable existence	1 (0.9)
South Oaks Gambling Screen questionnaire	
Money games, n (%)	
Casino/gaming halls	91 (78.4)
Lotteries and pools	86 (74.1)
Card games	72 (62.1)
Slot machines	68 (58.6)
Bingo	62 (53.4)
Skills	45 (38.8)
Stock exchange	42 (36.2)
Horses	40 (34.5)
Sports betting	36 (31.0)
Maximum one-day expense, n (%)	
<10€	2 (1.7%)
10-50€	0 (0.0%)
50-100€	3 (2.6%)
100-500€	36 (31.0%)
>500€	75 (64.7%)
Total score, mean (range)	11.7 (6-18)
Gambling disorder according to the questionnaire, n (%)	116 (100.0)

over, specific personality traits and mental symptoms have been described in GD patients with ADHD. They tend to experience higher emotional instability and interpersonal sensitivity, are more prone to stress, have lower self-esteem and self-discipline, and find it more difficult to be assertive (Davtian et al., 2012; Huțul and Karner- Huțuleac, 2022). Also, pathological gamblers with a childhood ADHD history have shown a significantly lower capacity to delay gratification and higher impulsivity scores (Fatseas et al., 2016; Rodríguez-Jiménez et al., 2006).

Furthermore, the prevalence of SUDs is greater in individuals with GD, compared to the general population (Dowling et al, 2015; Rodríguez-Monguio et al., 2017). Tobacco is the substance most frequently associated with GD (Jiménez-Murcia et al., 2021), which is also confirmed in our study, although with a lower prevalence (62.4% and 42.2%, respectively). This may be associated with the involvement of the cholinergic/nicotinic system in patients with ADHD and high impulsivity (Potter et al., 2014). There is also evidence of the correlation between GD and anxiety or depression, in line with our results. Huțul et al. (2022) have reported that anxiety and depression predict a gambling variance of 31.5% and 26.3%, respectively.

A significant correlation between impulsivity and several psychiatric disorders has been identified, proposing impulsivity as a transdiagnostic endophenotype for psychopathology (Sanchez-Roige et al., 2019). According to our results, most GD patients also had an impulsivity problem independent of the categorical diagnosis (i. e. ADHD, depression, or anxiety) in all subscales (cognitive, motor, and unplanned). High impulsivity has been previously associated with GD (González-Bueso et al., 2018; Rodríguez-Jiménez et al. 2006). Severe gambling symptoms, earlier age of GD onset, a larger number of suicide attempts, higher frequency of co-occurring psychiatric disorders, and a greater family history of psychiatric illness, were observed in those patients.

A recent systematic review pointed to increased impulsivity across a range of cognitive domains in GD (Ioannidis et al., 2019). Conversely, sensation seeking is a less relevant trait, as GD patients can maintain more control over their behavior, unlike impulsive people (Ersche et al., 2013). Black et al. (2015) found that patients with GD had significantly higher scores in measures of impulsiveness and novelty seeking. Their first-degree relatives also scored higher on impulsiveness, but not novelty seeking (Black et al., 2015). The fact that high impulsivity and impulse control disorders were found in family members of GD patients suggests that symptoms related to impulsivity may be regarded as vulnerability markers. This highlights the need to incorporate the "drug of choice model" and precision psychiatry (Szerman and Peris, 2018). This concept considers that people may be more susceptible to a particular class of drugs (i.e. compulsive gambling behavior) based on personality traits or other individual differences (Morrow and Flagel, 2016). It is well known that psychoactive substances do not have the same effect in all individuals (Ward et al., 2022; Wardle et al., 2015). According to this hypothesis, in our study, it could be inferred that compulsive gambling could act as an effort of self-medication for these people with ADHD and high impulsivity (Fatseas et al., 2016).

Like other psychiatric disorders, GD is characterized by differences between the sexes regarding prevalence, treatment response, or symptoms (Szerman et al., 2020). In the literature, the prevalence of GD is higher among men

Table 3 Description of attention deficit/hyperactivity disorder, mood, anxiety, social fear, insomnia, and personality trait disorders in patients.

	Results
Adult self-reported scale 1.1	
ASRS total score, mean (range)	25.6 (0-57)
ASRS cut-off, mean (range)	4.4 (0-17)
Presence of ADHD, n (%)	58 (50.0)
Conners' adult ADHD rating scale, mean (SD)	
Attentional/memory problems	46.5 (10.3)
Hyperactivity/ Agitation	45.4 (9.5)
Impulsivity/ Emotional lability	45.9 (11.2)
Self-concept problems	48.8 (10.34)
Inattention symptoms	46.9 (12.9)
Hyperactivity-impulsivity symptoms	45.5 (11.2)
ADHD general symptoms	45.9 (12.7)
ADHD index	46.5 (9.9)
Symbol digit modalities test, mean (SD) *	
Number of questions	51.1 (10.7)
Number of correct answers	49.9 (11.3)
Percentage of correct answers	97.3 (10.2)
Beck's depression inventory II, mean score (SD)	12.6 (10.9)
Classification of depression, n (%)	
Minimal	61 (52.6)
Mild	20 (17.2)
Moderate	22 (19.0)
Severe	13 (11.2)
State-trait anxiety inventory, mean score (SD)	
Anxiety, state	20.5 (11.3)
Anxiety, trait	20.4 (11.4)
Social phobia inventory, mean score (SD)	12.7 (12.0)
Insomnia severity index, mean score (SD)	8.0 (6.0)
Severity of the Insomnia severity, n (%)	
No insomnia	63 (54.6)
Insomnia lower than the threshold	36 (31.0)
Moderate clinical insomnia	14 (12.1)
Severe clinical insomnia	3 (2.6)
Temperament and character inventory revised, mean (SD) **	
Novelty search	34.4 (14.0)
Harm Avoidance	35.4 (13.9)
Reward Dependence	39.7 (13.1)
Persistence	35.0 (12.4)
Self-direction	40.6 (13.3)
Cooperativity	49.5 (10.6)
Self-transcendence	38.9 (14.0)
Exploratory Excitability	55.2 (11.3)
Barrat impulsiveness scale, mean score (SD)	48.0 (17.2)
General problem of impulsivity, n (%)	89 (76.7)
Cognitive impulsivity subscale, n (%)	91 (78.4)
Mean score (SD)	14.3 (5.4)
Motor impulsivity subscale, n (%)	81 (69.8)
Mean score (SD)	13.7 (7.5)
Unplanned impulsivity subscale, n (%)	88 (75.9)
Mean score (SD)	20.0 (7.4)
Brief symptoms inventory, mean score (SD)	
Somatization	0.4 (0.6)
Obsession/Compulsion	0.7 (0.6)
Interpersonal sensitivity	0.7 (0.7)
Depression	0.7 (0.7)
Anxiety	0.5 (0.6)
Hostility	0.4 (0.6)
Phobic anxiety	0.3 (0.5)
Paranoid ideation	0.5 (0.6)
Psychoticism	0.6 (0.7)
Distress index of positive symptoms	0.6 (0.5)
Total index of positive symptoms	20.2 (14.3)
Global index of severity	1.3 (0.4)
Sheehan disability inventory, mean score (SD)	
Total disability	14.2 (9.6)
Global disability	10.0 (7.6)

(*continued on next page*)

Table 3 (*continued*)

ADHD, attention deficit hyperactivity disorder; SD, standard deviation.
The analysis referred to n=116 except for: the *symbol digit modalities test (n=105) and the **temperament and character inventory revised (n =104) where patients who did not answer at least 15 questions were eliminated as it was considered an error in the application of the test.

(Di Nicola et al., 2017; Jacobs, 2004; Wong et al., 2013). In our study, the percentage of males was even higher than in other published data studies (89.7%). Furthermore, both sexes experience GD in different ways (Fattore et al., 2014; Szerman et al., 2020). In contrast to men, GD in women is frequently associated with stressful life situations or depressive states (American Psychiatric Association, 2013).

Researchers have tried to identify differentiating factors between online and offline gamblers (Effertz et al., 2018; Hubert and Griffiths, 2018; Ioannidis et al., 2019; McCormack and Griffiths, 2013). Novel technologies facilitate the growth of online gambling which also may be more conducive to the development of addictive behavior in vulnerable subjects. However, our results do not show relevant differences in the presence of other mental disorders concerning the predominant type of GD. The result may have been limited by the classification of the patients who were not exclusively divided into online and offline gamblers.

An additional goal of our study was to identify two clinical severity profiles of patients with GD in order to optimize their clinical management. One profile of patients with GD (cluster 1) was characterized by the greater presence of ADHD, depression, anxiety, insomnia, impulsivity, higher general psychopathology burden, and disability. This pattern could be considered "more severe" as associated with the predominance of other severe mental disorders (GDD). The second profile of patients with GD (cluster 2) presented with the same mental disorders and general psychopathology burden, but with a significantly lower severity or clinical impact. This pattern could be considered "less severe" or "mild/moderate" compared with cluster 1. Elevated decision-making impulsivity was also demonstrated in

Table 4 Clinical characteristics of patients comprised of different clusters.

	Cluster 1 (n=18)	Cluster 2 (n=82)	*p*
Sociodemographic, n (%)			
Age, median years (range)	39.5 (21.0-63.0)	37.0 (21.0-62.0)	0.362
Gender, male	17 (94.4)	76 (92.7)	0.791
Marital Status, never been married	9 (50.0)	30 (36.6)	0.308
Dominant hand, right-handed	17 (94.4)	77 (93.9)	0.930
Educational level, university studies	7 (38.9)	28 (34.1)	0.728
Employment status, employed	14 (77.8)	62 (75.6)	0.546
Diagnosis, n (%)			
Type of gambling addiction, offline	7 (38.9)	35 (42.7)	0.918
Clinical global impression test			
Severity (ill)	17 (94.4)	70 (85.4)	0.300
Global improvement (improved)	14 (77.8)	75 (91.5)	0.093
Addictive disorders, n (%)			
MULTICAGE-CAD 4 questionnaire			
Alcohol use/dependence	6 (33.3)	13 (15.8)	0.087
Gambling disorder	18 (100.0)	79 (96.3)	1.000
Substance use	2 (11.1)	8 (9.8)	0.862
Eating disorders	2 (11.1)	0 (0.0)	0.031
Internet addiction	8 (44.4)	17 (20.7)	0.035
Video game addiction	0 (0.0)	11 (13.4)	0.206
Compulsive spending	11 (61.1)	45 (54.9)	0.630
Sex addiction	1 (5.6)	3 (3.7)	0.710
South Oaks gambling screen questionnaire			
Money games	18 (100.0)	82 (100.0)	-
Current use of substances			
Tobacco	8 (44.4)	31 (37.8)	0.601
Alcohol	2 (11.1)	3 (3.7)	0.219
Caffeine	0 (0.0)	4 (4.9)	1.000
Cannabis	0 (0.0)	1 (1.2)	1.000
Cocaine	0 (0.0)	0 (0.0)	-
ADHD, n (%)			
Adult self-reported scale, presence of ADHD	15 (83.3)	28 (34.1)	0.001
Conners' adult ADHD rating scale, median (range)			
Attentional/memory problems	49.0 (38.0-64.0)	42.0 (32.0-73.0)	0.009
Hyperactivity/ Agitation	47.5 (37.0-57.0)	40.0 (33.0-70.0)	0.008
Impulsivity/ Emotional lability	52.5 (39.0-66.0)	40.0 (30.0-61.0)	0.001
Self-concept problems	51.5 (39.0-69.0)	44.0 (33.0-72.0)	0.002
Inattention symptoms	51.5 (39.0-65.0)	41.0 (28.0-72.0)	0.001
Hyperactivity-impulsivity symptoms	49.0 (32.0-61.0)	39.0 (32.0-71.0)	0.010
ADHD general symptoms	50.5 (37.0-64.0)	40.0 (27.0-66.0)	0.001
ADHD index	50.5 (39.0-69.0)	41.5 (31.0-63.0)	0.001
Symbol digit modalities test			
Number of questions	44.5 (0.0-66.0)	52.5 (0.0-78.0)	0.078
Percentage of correct answers	98.9 (0.0-100.0)	100.0 (0.0-100.0)	0.347
Mood disorder, n (%)			
Beck's depression inventory, depression	14 (77.8)	25 (30.5)	0.001
Anxiety disorder, median (range)			
State-trait anxiety inventory			
Anxiety, state	32.0 (28.0-41.0)	15.0 (3.0-41.0)	0.001
Anxiety, trait	28.5 (24.0-38.0)	15.0 (0.0-37.0)	0.001
Social phobia inventory, n (%)	3 (16.7)	7 (8.5)	0.297
Sleep disorder, n (%)			
Insomnia severity index	5 (27.8)	4 (4.9)	0.001
Personality traits disorders, median (range)			
Temperament and character inventory revised			
Novelty seeking	40.6 (0.0-50.0)	28.1 (0.0-65.6)	0.029
Harm Avoidance	37.5 (0.0-68.7)	31.3 (0.0-59.3)	0.103

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Table 4 (*continued*)

	Cluster 1 (n=18)	Cluster 2 (n=82)	*p*
Reward Dependence	45.3 (0.0-56.2)	34.4 (0.0-68.7)	0.088
Persistence	39.1 (0.0-53.1)	31.3 (0.0-59.3)	0.072
Self-direction	40.6 (0.0-68.7)	37.5 (0.0-75.0)	0.512
Cooperativity	50.0 (0.0-71.8)	46.9 (0.0-75.0)	0.515
Self-transcendence	32.8 (0.0-56.2)	34.4 (0.0-75.0)	0.960
Exploratory excitability	50.0 (0.0-58.3)	58.3 (0.0-83.3)	0.003
Barrat impulsiveness scale, n (%)			
General problem of impulsivity	18 (100.0)	55 (67.1)	0.004
Cognitive impulsivity subscale	18 (100.0)	57 (69.5)	0.007
Motor impulsivity subscale	18 (100.0)	48 (58.5)	0.001
Unplanned impulsivity subscale	17 (94.4)	55 (67.1)	0.019
General psychopathology, brief symptom inventory median (range)			
Somatization	0.4 (0.0-1.9)	0.0 (0.0-2.1)	0.001
Obsession/Compulsion	1.1 (0.3-1.8)	0.3 (0.0-2.5)	0.001
Interpersonal sensitivity	1.0 (0.3-1.8)	0.3 (0.0-2.3)	0.001
Depression	0.9 (0.5-2.2)	0.3 (0.0-2.8)	0.001
Anxiety	1.0 (0.5-1.7)	0.2 (0.0-2.8)	0.001
Hostility	0.7 (0.0-1.6)	0.0 (0.0-2.2)	0.001
Phobic anxiety	0.6 (0.0-1.8)	0.0 (0.0-1.8)	0.001
Paranoid ideation	1.0 (0.2-1.6)	0.2 (0.0-1.4)	0.001
Psychoticism	1.0 (0.4-2.4)	0.2 (0.0-3.0)	0.001
Distress index of positive symptoms	1.3 (1.0-1.8)	1.1 (0.0-2.6)	0.001
Total index of positive symptoms	36.0 (22.0-44.0)	11.0 (0.0-47.0)	0.001
Global index of severity	0.9 (0.5-1.3)	0.3 (0.0-2.3)	0.001
Disability, median (range)			
Sheehan disability inventory			
Total disability	16.7 (2.8-32.4)	8.9 (0.0-37.9)	0.014
Global disability	11.5 (0.0-24.0)	6.0 (0.0-27.0)	0.025

ADHD, attention deficit hyperactivity disorder.

both profiles, traits that are not routinely explored in this phenotype of a gambling problem. Therefore, impulsiveness should be considered a vulnerability factor for GDD.

Given the observed differences between patients and the associated severity, is important to create specialized and validated tools able to identify potential profiles of patients with higher severity of dual disorders. Early identification of the more severe/vulnerable patients with GD will allow us to focus on their vulnerabilities and, thereby provide a more effective therapeutic approach. Open questions about whether the “more severe” pattern represents a longer-term evolution or whether it constitutes different phenotypes, need to be addressed in especially designed studies. A recently published review about GD in the UK remarked on the key research priorities and the urgent need for funding (Bowden-Jones et al., 2022). In this work, was pointed out the need to select and refine the most suitable pragmatic measurement tools, identify predictors of vulnerability, and improve understanding of the neurobiological basis of GD including impulsivity. In this way, our study aims to cover some of the needs in the research and therapeutic approach to gambling.

Limitations of our study should also be considered. First, there are limitations derived from the cross-sectional nature of the study, restricting the analysis to a fixed point of time. Moreover, the study includes only patients with GD who were under treatment at the time of the consultation, without considering their treatment state. In this respect, it is noteworthy that only one patient confirmed in the interview an active gambling behavior. Although this may seem confusing, the sample comes from specialized GD-treating centers, so it is foreseeable that they were in remission. Also, all mental disorders and symptoms that can co-occur with GD were not included, and neither a standard interview (i. e. MINI) was performed to assess psychiatric comorbidities. Doubtless, it would have been interesting to include other categorial diagnoses, however, it will open a window for future investigation. Another limitation of the study was the relatively low sample size. Although a larger cohort of patients would strengthen our present results and conclusions, they are in accordance with the literature (Breyer et al., 2009; Davtian et al., 2012; Dowling et al., 2015; Gall-Bronnec et al., 2011; González-Bueso et al., 2018; Rash et al., 2016; Rodríguez-Jiménez et al., 2006; Rodríguez-Monguio et al., 2017; Sheehan and Sheehan, 2008; Wardle et al., 2015).

On the other hand, all the patients included in the study have a GD diagnosis based on the ICD-11 diagnostic cri-

teria then confirmed by SOGS questionnaire (Lesieur and Blume, 1987). However, MULTICAGE-CAD 4 cannot ascertain the presence of GD in three of the patients. Moreover, VGA was diagnosed in fewer patients by the clinicians than when MULTICAGE-CAD 4 was used (8,6% vs. 11.2%). These discrepancies may be due to a limitation of the tool explained by the reclassification of GD and VGA as behavioral addictions (Potenza et al., 2019) after the validation of the MULTICAGE-CAD 4 questionnaire (Pedrero-Pérez et al., 2007). Nonetheless, this result shows the importance of relying on objective evaluations as the validated scales and questionnaires during the clinical evaluation. Moreover, it points out the need to design new reliable tools or adequate the existing ones to the novel findings in GD, including dual disorder. Finally, the low level of psychopharmacological treatment may be considered a patient selection bias, derived from including patients in healthcare centers with no psychiatrists or physicians.

In conclusion, our present study provides further evidence that GD is associated with other mental disorders and, in a transdiagnostic way, most of them had marked traits of impulsiveness. This high impulsivity could indicate a specific phenotype of the different mental disorders that occur in people with GD, and appears to be a marker of vulnerability to severe forms of GD. Our results support that dual disorders are a rule and not an exception, allowing us to introduce the concept of "gambling dual disorder". These findings have long-term clinical significance for patient management, highlighting the complex nature of seemingly unrelated manifestations that are contributing to the condition of the individual. This could shift the focus to a more personalized approach to treating the person and not just the GD (Szerman et al., 2022). Two different clinical severity profiles in terms of psychopathological burden, but both with increased impulsivity have been identified in adult patients with GDD. Further prospective, long-term studies, including other categorical diagnoses, are required to confirm these results.

Author Contributions

All authors had full access to the data and contributed to data interpretation and to the drafting, critical review, and revision of the manuscript.

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Data availability statement

The data presented in this study are available on request from the corresponding author.

Declaration of Competing Interest

NS declares that he has received honoraria/expenses from Janssen, Takeda, Lundbeck, Exeltis, and Rovi. He also has participated as consulting/advisory board for Lundbeck. IBV has received research grants from Lundbeck, Otsuka, and Exeltis, and educational grants from Janssen, Lundbeck, and Exeltis. PV declares that he has received honoraria/expenses from Gilead, Abbvie, Lundbeck, and Exeltis. BM declares no conflicts of interest. JMR has been a consultant to or has received honoraria or grants from Adamed, Janssen Cilag, Lundbeck, Otsuka, Pfizer, Rovi, Servier, and Takeda. FF declares that has received honoraria and grnats from Janssen Cilag, Lundbeck, and Servier. CA has been a consultant to or has received honoraria or grants from Acadia, Angelini, Biogen, Boehringer, Gedeon Richter, Janssen Cilag, Lundbeck, Medscape, Minerva, Otsuka, Pfizer, Roche, Sage, Servier, Shire, Schering Plough, Sumitomo Dainippon Pharma, Sunovion and Takeda.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.euroneuro.2022.11.010.

References

Abbott, M.W., 2020. The changing epidemiology of gambling disorder and gambling-related harm: public health implications. Public Health 184, 41–45.

Association, American Psychiatric, 2013. Diagnostic and statistical manual of mental disorders, 5th. APA, Washington, DC.

Ayala-Rojas, R.E., Granero, R., Mora-Maltas, B., Rivas, S., Fernández-Aranda, F., Gómez-Peña, M., Moragas, L., Baenas, I., Solé-Morata, N., Menchón, J.M., Jiménez-Murcia, S., 2022. Factors related to the dual condition of gambling and gaming disorders: A path analysis model. J. Psychiatr. Res. 145, 148–158.

Baños, R.M., Botella, C., Quero, S., Medina, P., 2007. The social phobia and anxiety inventory: psychometric properties in a Spanish sample. Psychol. Rep. 100 (2), 441–450.

Beck, A.T., Steer, R.A., Brown, G.K., 1996. BDI-II. Beck depression inventory-second edition. The Psychological Corporation, San Antonio.

Black, D.W., Coryell, W.H., Crowe, R.R., Shaw, M., McCormick, B., Allen, J., 2015. Personality disorders, impulsiveness, and novelty seeking in persons with DSM-IV pathological gambling and their first-degree relatives. J. Gambl. Stud. 31, 1201–1214.

Bobes, J., Badía, X., Luque, A., García, M., González, M.P., Dal-Ré, R., 1999. Validation of the Spanish version of the Liebowitz social anxiety scale, social anxiety and distress scale and Sheehan disability inventory for the evaluation of social phobia. Med. Clin. (Barc) 112 (14), 530–538.

Bowden-Jones, H., Hook, R.W., Grant, J.E., Ioannidis, K., Corazza, O., Fineberg, N.A., Singer, B.F., Roberts, A., Bethlehem, R., Dymond, S., Romero-Garcia, R., Robbins, T.W., Cortese, S., Thomas, S.A., Sahakian, B.J., Dowling, N.A., Chamberlain, S.R., 2022. Gambling disorder in the UK: key research priorities and the urgent need for independent research funding. Lancet Psychiatry 9 (4), 321–329.

Breyer, J.L., Botzet, A.M., Winters, K.C., Stinchfield, R.D., August, G., Realmuto, G., 2009. Young adult gambling behaviors and their relationship with the persistence of ADHD. J. Gambl. Stud. 25, 227–238.

Busner, J., Targum, S.D., 2007. The clinical global impressions scale: applying a research tool in clinical practice. Psychiatry (Edgmont) 4 (7), 28–37.

Calado, F., Griffiths, M.D., 2016. Problem gambling worldwide: An update and systematic review of empirical research (2000-2015). J. Behav. Addict. 5 (4), 592–613.

Connor, K.M., Davidson, J.R., Churchill, L.E., Sherwood, A., Foa, E., Weisler, R.H., 2000. Psychometric properties of the Social Phobia Inventory (SPIN). New self-rating scale. Br. J. Psychiatry 176, 379–386.

Cowlishaw, S., Hakes, J.K., 2015. Pathological and problem gambling in substance use treatment: Results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Am. J. Addictions 24 (5), 467–474.

Davtian, M., Reid, R.C., Fong, TW., 2012. Investigating facets of personality in adult pathological gamblers with ADHD. Neuropsychiatry (London) 2, 163–174.

Derogatis, L.R., Melisaratos, N., 1983. The brief symptom inventory: an introductory report. Psychol. Med. 13 (3), 595–605.

Di Nicola, M., Ferri, V.R., Moccia, L., Panaccione, I., Strangio, A.M., Tedeschi, D., Grandinetti, P., Callea, A., De-Giorgio, F., Martinotti, G, Janiri, L., 2017. Gender differences and psychopathological features associated with addictive behaviors in adolescents. Front. Psychiatry 8, 256.

Dowling, N.A., Cowlishaw, S., Jackson, A.C., Merkouris, S.S., Francis, K.L., Christensen, D.R., 2015. Prevalence of psychiatric comorbidity in treatment-seeking problem gamblers: A systematic review and meta-analysis. Aust. N. Z. J. Psychiatry 49 (6), 519–539.

Echeburúa-Odriozola, E., Báez-Gallo, C., Fernández-Montalvo, J., Páez-Rovira, D., 1994. In: Cuestionario de juego patológico de South Oaks (SOGS): validación española, 20. Análisis y Modificación de la conducta, p. 74.

Effertz, T., Bischof, A., Rumpf, H.J., Meyer, C., John, U., 2018. The effect of online gambling on gambling problems and resulting economic health costs in Germany. Eur. J. Health Econ. 19 (7), 967–978.

Ersche, K.D., Jones, P.S., Williams, G.B., Smith, D.G., Bullmore, E.T., Robbins, T.W., 2013. Distinctive personality traits and neural correlates associated with stimulant drug use versus familial risk of stimulant dependence. Biol. Psychiatry 74 (2), 137–144.

Ersche, K.D., Turton, A.J., Pradhan, S., Bullmore, E.T., Robbins, T.W., 2010. Drug addiction endophenotypes: impulsive versus sensation-seeking personality traits. Biol. Psychiatry 68 (8), 770–773.

Fatseas, M., Alexandre, J.M., Vénisse, J.L., Romo, L., Valleur, M., Magalon, D., Chéreau-Boudet, I., Luquiens, A., Guilleux, A., Jeu, Groupe, Challet-Bouju, G., Grall-Bronnec, M., 2016. Gambling behaviors and psychopathology related to Attention-Deficit/Hyperactivity Disorder (ADHD) in problem and non-problem adult gamblers. Psychiatry Res. 239, 232–238.

Fattore, L., Melis, M., Fadda, P., Fratta, W., 2014. Sex differences in addictive disorders. Front. Neuroendocrinol. 35 (3), 272–284.

González-Bueso, V., Santamaría, J.J., Fernández, D., Merino, L., Montero, E., Ribas, J., 2018. Association between internet gaming disorder or pathological video-game use and comorbid psychopathology: A comprehensive review. Int. J. Environ. Res. Public Health 15, 668.

Govindan, R.M., Behen, M.E., Helder, E., Makki, M.I., Chugani, H.T., 2010. Altered water diffusivity in cortical association tracts in children with early deprivation identified with Tract-Based Spatial Statistics (TBSS). Cereb. Cortex 20 (3), 561–569.

Grall-Bronnec, M., Wainstein, L., Augy, J., Bouju, G., Feuillet, F., Vénisse, J.L., Sébille-Rivain, V., 2011. Attention deficit hyperactivity disorder among pathological and at-risk gamblers seeking treatment: a hidden disorder. Eur. Addict. Res. 17 (5), 231–240.

Granero, R., Fernández-Aranda, F., Pino-Gutierrez, A.D., Etxandi, M., Baenas, I., Gómez-Peña, M., Moragas, L., Valenciano-Mendoza, E., Mora-Maltas, B., Valero-Solís, S., Codina, E., Guillén-Guzmán, E., Lara-Huallipe, M., Caravaca, E., Mestre-Bach, G., Menchón, J.M., Jiménez-Murcia, S., 2021. The prevalence and features of schizophrenia among individuals with gambling disorder. J. Psychiatr. Res. 136, 374–383.

Gutiérrez-Zotes, J.A., Bayón, C., Montserrat, C., Valero, J., Labad, A., Cloninger, C.R., Fernández-Aranda, F., 2004. Inventario del Temperamento y el Carácter-Revisado (TCI-R). Baremación y datos normativos en una muestra de población general [Temperament and Character Inventory Revised (TCI-R). Standardization and normative data in a general population sample]. Actas Esp. Psiquiatr. 32 (1), 8–15.

Hing, N., Russell, A.M., Browne, M., 2017. Risk factors for gambling problems on online electronic gaming machines, race betting and sports betting. Front. Psychol. 8, 779.

Hook, R.W., Grant, J.E., Ioannidis, K., Tiego, J., Yücel, M., Wilkinson, P., Chamberlain, S.R., 2021. Trans-diagnostic measurement of impulsivity and compulsivity: A review of self-report tools. Neurosci. Biobehav. Rev. 120, 455–469.

Hubert, P., Griffiths, M.D., 2018. A comparison of online versus offline gambling harm in portuguese pathological gamblers: an empirical study. Int. J. Ment. Health Addict. 16, 1219–1237.

Huțul, T.D., Karner-Huțuleac, A., 2022. The level of gambling prediction using depression and anxiety in the romanian population. J. Gambl. Stud. 38 (2), 653–662.

Ioannidis, K., Hook, R., Wickham, K., Grant, J.E., Chamberlain, S.R., 2019. Impulsivity in Gambling Disorder and problem gambling: a meta-analysis. Neuropsychopharmacology 44 (8), 1354–1361.

Iraurgi Castillo, I., González Saiz, F., Lozano Rojas, O., Landabaso Vázquez, M.A., Jiménez Lerma, J.M., 2010. Estimation of cut-off for the Severity of Dependence Scale (SDS) for opiate dependence by ROC analysis. Actas Esp. Psiquiatr. 38 (5), 270–277.

Jacobs, D.F., 2004. Youth gambling in North America: Long-term trends and future prospects. In: Derevensky, JL, Gupta, R (Eds.), Gambling problems in youth: Theoretical and applied perspectives. Klewer Academic/Plenum Publishers, New York, NY.

Jiménez-Murcia, S., Giménez, M., Granero, R., Masuet-Aumatell, C., Ramón, J.M., Agüero, F., Morchón, S., Moragas, L., Baenas, I., Del Pino-Gutierrez, A., Codina, E., Valenciano-Mendoza, E., Mora-Maltas, B., Valero-Solís, S., Etxandi, M., Guillen-Guzmán, E., Menchón, J.M., Fernández-Aranda, F., 2021. Gambling disorder seeking treatment patients and tobacco use in relation to clinical profiles. Addict. Behav. 114, 106723.

Jones, L., Metcalf, A., Gordon-Smith, K., Forty, L., Perry, A., Lloyd, J., Geddes, J.R., Goodwin, G.M., Jones, I., Craddock, N., Rogers, R.D., 2015. Gambling problems in bipolar disorder in the UK: prevalence and distribution. The Br. j. psychiatry: j. mental sci. 207 (4), 328–333.

Kessler, R.C., Adler, L.A., Gruber, M.J., Sarawate, C.A., Spencer, T., Van Brunt, D.L., 2007. Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. Int. J. Methods Psychiatr. Res. 16 (2), 52–65.

Kessler, R.C., Hwang, I., LaBrie, R., Petukhova, M., Sampson, N.A., Winters, K.C., Shaffer, H.J., 2008. DSM-IV pathological gambling in the national comorbidity survey replication. Psychol. Med. 38 (9), 1351–1360.

King, D.L., Gainsbury, S.M., Delfabbro, P.H., Hing, N., Abarbanelm, B., 2015. Distinguishing between gaming and gambling activities in addiction research. J. Behav. Addict. 4 (4), 215–220.

Lesieur, H.R., Blume, S.B., 1987. The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. Am. J. Psychiatry 144 (9), 1184–1188.

Lind, K., Marionneau, V., Järvinen-Tassopoulos, J., Salonen, A.H., 2021. Socio-Demographics, Gambling Participation, Gambling Settings, and Addictive Behaviors Associated with Gambling Modes: A Population-Based Study. J. Gambl. Stud. doi:10.1007/s10899-021-10074-7.

Maremmani, A.G., Dell'Osso, L., Pacini, M., Popovic, D., Rovai, L., Torrens, M., Perugi, G., Maremmani, I., 2011. Dual diagnosis and chronology of illness in treatment-seeking Italian patients dependent on heroin. J. Addict. Dis. 30 (2), 123–135.

Martínez-Loredo, V., Fernández-Hermida, J.R., Fernández-Artamendi, S., Carballo, J.L., García-Rodríguez, O., 2015. Spanish adaptation and validation of the Barratt Impulsiveness Scale for early adolescents (BIS-11-A). Int. J. Clin. Health Psychol. 15 (3), 274–282.

McCormack, A., Griffiths, M.D., 2013. A Scoping Study of the Structural and Situational Characteristics of Internet Gambling. IJCBPL 3 (1), 29–49.

Morrow, J.D., Flagel, S.B., 2016. Neuroscience of resilience and vulnerability for addiction medicine: From genes to behavior. Prog. Brain Res. 223, 3–18.

Ortuño-Sierra, J., García-Velasco, L., Inchausti, F., Debbané, M., Fonseca-Pedrero, E., 2016. New approaches on the study of the psychometric properties of the STAI. Actas Esp. Psiquiatr. 44 (3), 83–92.

Pedrero Pérez, E.J., Puerta García, C., 2007. ASRS v.1.1., a tool for attention-deficit/hyperactivity disorder screening in adults treated for addictive behaviors: psychometric properties and estimated prevalence. Adicciones 19 (4), 393–407.

Pedrero-Pérez, E.J., Rodríguez-Monje, M.T., Gallardo-Alonso, F., Fernández-Girón, M., Pérez-López, M., Chicharro-Romero, J., 2007. Validation of a tool for screening of impulse control disorders and addiction: MULTICAGE CAD-4. Trastornos Adictivos 9, 269–278.

Petry, N.M., Stinson, F.S., Grant, B.F., 2005. Comorbidity of DSM-IV pathological gambling and other psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J. Clin. Psychiatry 66 (5), 564–574.

Petry, N.M., Zajac, K., Ginley, M.K., 2018. Behavioral addictions as mental disorders: to be or not to be? Annu. Rev. Clin. Psychol. 14, 399–423.

Potenza, M.N., Balodis, I.M., Derevensky, J., Grant, J.E., Petry, N.M., Verdejo-Garcia, A., Yip, S.W., 2019. Gambling disorder. Nat. Rev. Dis. Primers 5 (1), 51.

Potter, A.S., Schaubhut, G., Shipman, M., 2014. Targeting the nicotinic cholinergic system to treat attention-deficit/hyperactivity disorder: rationale and progress to date. CNS Drugs 28 (12), 1103–1113.

Rash, C.J., Weinstock, J., Van Patten, R., 2016. A review of gambling disorder and substance use disorders. Subst. Abuse Rehabil. 7, 3–13.

Richarte, V., Corrales, M., Pozuelo, M., Serra-Pla, J., Ibáñez, P., Calvo, E., Corominas, M., Bosch, R., Casas, M., Ramos-Quiroga, J.A., 2017. Spanish validation of the adult Attention Deficit/Hyperactivity Disorder Rating Scale (ADHD-RS): relevance of clinical subtypes. Validación al español de la ADHD Rating Scale (ADHD-RS) en adultos: relevancia de los subtipos clínicos. Rev. Psiquiatr. Salud. Ment. 10 (4), 185–191.

Rodríguez-Jiménez, R., Avila, C., Jiménez-Arriero, M.A., Ponce, G., Monasor, R., Jiménez, M., Aragüés, M., Hoenicka, J., Rubio, G., Palomo, T., 2006. Impulsivity and sustained attention in pathological gamblers: influence of childhood ADHD history. J. Gambl. Stud. 22, 451–461.

Rodríguez-Monguio, R., Errea, M., Volberg, R., 2017. Comorbid pathological gambling, mental health, and substance use disorders: health-care services provision by clinician specialty. J. Behav. Addict. 6, 406–415.

Sanchez-Roige, S, Fontanillas, P, Elson, SL, Gray, JC, de Wit, H, MacKillop, J, Palmer, AA., 2019. Genome-wide association studies of impulsive personality traits (bis-11 and upps-p) and drug experimentation in up to 22,861 adult research participants identify loci in the CACNA1I and CADM2 genes. J. Neurosci. 39 (13), 2562–2572.

Sanz, J., Perdigón, A.L., Vázquez, C., 2003. The spanish adaptation of Beck's Depression Inventory-II (BDI-II): 2. Psychometric properties in the general population. Clínica y Salud 14 (3), 249–280.

Sheehan, K.H., Sheehan, D.V., 2008. Assessing treatment effects in clinical trials with the discan metric of the sheehan disability scale. Int. Clin. Psychopharmacol. 23 (2), 70–83.

Sierra, J.C., Guillén-Serrano, V., Santos-Iglesias, P., 2008. Insomnia Severity Index: algunos indicadores acerca de su fiabilidad y validez en una muestra de personas mayores [Insomnia Severity Index: some indicators about its reliability and validity on an older adults sample]. Rev. Neurol. 47 (11), 566–570.

Smith, A., 2002. Symbol and digit modalities test. TEA Ediciones SA, Eds.

Spielberger, C.D., Vagg, P.R., 1984. Psychometric properties of the STAI: a reply to Ramanaiah, Franzen, and Schill. J. Pers. Assess 48, 95–97.

Szerman, N., Ferre, F., Basurte-Villamor, I., Vega, P., Mesias, B., Marín-Navarrete, R., Arango, C., 2020. Gambling dual disorder: a dual disorder and. Front. Psychiatry 11, 589155.

Szerman, N., Martinez-Raga, J., 2015. Dual disorders: two different mental disorders? Adv. Dual Diagn. 8, 61–64.

Szerman, N., Peris, L., 2018. Precision psychiatry and dual disorders. J. Dual Diagn. 14, 237–246.

Szerman, N., Torrens, M., Maldonado, R., Balhara, Y., Salom, C., Maremmani, I., Sher, L., Didia-Attas, J., Chen, J., Baler, R.World Association on Dual Disorders (WADD), 2022. Addictive and other mental disorders: a call for a standardized definition of dual disorders. Transl Psychiatry 12 (1), 446.

Volkow, N.D., 2020. Personalizing the treatment of substance use disorders. Am. J. Psychiatry 177, 113–116.

Ward, H.B., Beermann, A., Nawaz, U., Halko, M.A., Janes, A.C., Moran, L.V., Brady Jr., R.O., 2022. Evidence for schizophrenia-specific pathophysiology of nicotine dependence. Front. Psychiatry 13, 804055.

Wardle, M.C., Marcus, B.A., de Wit, H., 2015. A preliminary investigation of individual differences in subjective responses to D-amphetamine, alcohol, and delta-9-tetrahydrocannabinol using a within-subjects randomized trial. PLoS One 10, e0140501.

Wong, G., Zane, N., Saw, A., Chan, A.K., 2013. Examining gender differences for gambling engagement and gambling problems among emerging adults. J. Gambl. Stud. 29, 171–189.

World Health Organization. 6C50 Gambling disorder. Accessed 17/01/2022. Available from: https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/1041487064.

World Health Organization. 6C51 Gaming disorder. Accessed 17/01/2022. Available from: https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who.int%2ficd%2fentity%2f499894965