

# A Revision of the Relationship between Gambling Disorder, Attention Deficit Hyperactivity Disorder, and Parkinson's Disease

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## Abstract

*Purpose:* For the present review, publications in the field of gambling disorder that deal with its relationships with others, mainly attention deficit hyperactivity disorder (ADHD) and Parkinson's disease (PD) were consulted. *Methods:* The current revision includes a total of 63 references published between 1987 and 2017. It included human studies and revisions regarding the comorbidity of gambling disorder with ADHD or PD. The search terms included: gambling disorder, gambling disorder comorbidity, gambling disorder and ADHD, gambling disorder and PD, gambling disorder and impulsivity. The present review focused on the link among gambling disorder and ADHD or PD, because there were a large number of publications related to these disorders. For organization purpose the current work was split into two main parts: 1) Revision of previous scientific reviews about gambling disorder, and 2) Overview and conclusions of experimental work about gambling disorder. *Conclusions:* The principal conclusions of the current review are: 1) subjects with a gambling disorder have a higher incidence of ADHD (and also of attention deficit disorder [ADD]), 2) the presence of ADHD in subjects that suffer of gambling disorder implies more challenges for the health care system, and 3) PD treatments that increase the agonism of dopamine type of receptor are related to an elevated probability for developing a gambling problem or an impulse control disorder.

**Keywords:** ADHD, comorbidity, disorder, dopamine receptor, gambling PD.

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## Una revisión de la relación entre la ludopatía, el trastorno de déficit de atención e hiperactividad y la enfermedad de Parkinson

### Resumen

**Objetivo:** para la presente revisión, se consultaron publicaciones en el campo de la ludopatía que tratan de sus relaciones con otros trastornos, principalmente el trastorno por déficit de atención con hiperactividad (TDAH) y la enfermedad de Parkinson (EP). **Método:** la presente revisión tiene en cuenta 63 referencias publicadas entre 1987 y 2017 y tuvo en cuenta estudios en humanos y revisiones sobre la comorbilidad de la ludopatía con el TDAH o la EP. Los términos de la búsqueda incluyeron: ludopatía, comorbilidad de la ludopatía, ludopatía y TDAH, ludopatía y EP, ludopatía e impulsividad. Esta revisión se centró en el vínculo entre la ludopatía y el TDAH o la EP, puesto que existía un gran número de publicaciones relacionadas con estos trastornos. Para su organización, el presente trabajo se dividió en dos partes principales: 1) el análisis de revisiones científicas anteriores sobre la ludopatía y 2) el resumen y las conclusiones del trabajo experimental sobre la ludopatía. **Conclusiones:** las conclusiones principales de esta revisión son: 1) los sujetos con ludopatía tienen una mayor incidencia del TDAH (y también del trastorno de déficit de atención [TDA]), 2) la presencia del TDAH en sujetos que sufren de ludopatía implica más retos para el sistema de salud y 3) los tratamientos de la EP que aumentan el agonismo del receptor tipo dopamina están relacionados con una probabilidad elevada de desarrollar un problema de juego o un trastorno de control de impulsos.

**Palabras clave:** TDAH, comorbilidad, trastorno, receptor de dopamina, juego, EP.

## Uma revisão da relação entre a ludopatia, o transtorno de déficit de atenção e hiperatividade, e a doença de Parkinson

### Resumo

**Objetivo:** para esta revisão, foram consultadas publicações no campo da ludopatia que tratam de suas relações com outros transtornos, principalmente o transtorno por déficit de atenção e hiperatividade (TDAH) e a doença de Parkinson (DP). **Método:** esta revisão inclui um total de 63 referências publicadas entre 1987 e 2017, e considerou estudos em humanos e revisões sobre a comorbilidade da ludopatia com o TDAH ou a DP. Os termos de busca foram: ludopatia, comorbilidade da ludopatia, ludopatia e TDAH, ludopatia e DP, ludopatia e impulsividade. Além disso, esteve focada no vínculo entre a ludopatia e o TDAH ou a DP, visto que existia um grande número de publicações relacionadas com esses transtornos. Para sua organização, o presente trabalho foi dividido em duas partes principais: 1) a revisão de revisões científicas anteriores sobre a ludopatia e 2) o resumo e as conclusões do trabalho experimental sobre a ludopatia. **Conclusões:** as conclusões principais desta revisão são: 1) os sujeitos com ludopatia têm maior incidência do TDAH (e também do transtorno de déficit de atenção [TDA]); 2) a presença do TDAH em sujeitos que sofrem de ludopatia implica mais desafios para o sistema de saúde e 3) os tratamentos da DP que aumentam o agonismo do receptor tipo dopamina estão relacionados com uma probabilidade elevada de desenvolver um problema de jogo ou um transtorno de controle de impulsos.

**Palavras-chave:** TDAH, comorbilidade, transtorno, receptor de dopamina, jogo, DP.

## Introduction

### Methodological procedure of the review

The current revision includes a total of 63 references (published between 1987 and 2017) obtained from a publication exploration of PubMed (January 1987 – January 2017). It comprised mostly, clinical investigations and revisions regarding the comorbidity of gambling disorder with Parkinson's disease (PD) or attention deficit hyperactivity disorder (ADHD). The word search included: gambling disorder, gambling disorder comorbidity, gambling disorder and impulsivity, gambling disorder and PD, gambling disorder and ADHD.

The current review focuses on the associations among gambling disorder, PD and ADHD, since there were a large number of publications linked to these disorders, and this was considered enough for conducting an independent review.

### Description of gambling disorder: characteristics and comorbidities

The game conduct may be defined as putting something important in hazard, and relying on the expectancy of gaining benefit or profit (Potenza, Kosten, & Rounsaville, 2001). Gambling disorder is characterized by playing conducts that seriously disrupt the labor conditions, finances, and interpersonal relationships (NORC, 1999). The gambling disorder has a life incidence of roughly 0.4% to 4.2% (Lorains, Cowlshaw, & Thomas, 2011). Also, gambling disorder was classified in the 4<sup>th</sup> edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM) IV-TR* (APA, 2000) and in the 10<sup>th</sup> edition of the *International Classification of Diseases (ICD; WHO, 2003)* as a disease of impulse control. However, the DSM-5 regrouped gambling disorder in a different class, within the addictions category (behavioral addictions; APA, 2013).

Different investigations have explored linkages among mental diseases and gambling disorder across varied ethnic clusters (Barry, Stefanovics, Desai, & Potenza, 2011a; 2011b). Particularly, an investigation (Barry et al., 2011b) utilized a cluster of 31,830 adult fellows (13% Hispanic and 87% white), and concluded that diverse gravity grades of playing disease were associated to the commonality of mental diseases (axes I and II) in Latinos and whites. Moreover, it was discovered that Hispanic fellows had more

probability of developing a gambling-linked disease than white ones. Besides, this investigation found a firm interrelation amid moderate gambling disorders and a broad diversity of axis I (eagerness, humor and drug intake related diseases) and axis II's diseases (specially group B) in Latin fellows, compared to the white cluster (Barry et al., 2011b).

Other work analyzed a cluster consisting (n = 32,316) of white and African - American population to evaluate discrepancies in the relationships between gambling disorder gravity and mental diseases (Barry et al., 2011a). This work stated that black people had a higher probability of developing a gambling disease and found a firmer association between gambling disorder and substance consume problems, humor diseases, and (low gravity) mania (Barry et al., 2011a). Generally, both works stressed the relevance considering ethnicity in psychic health safeguard and therapy for gambling disorders (Barry et al., 2011a; 2011b).

Other set of studies have highlighted the strong relationship between gambling disorder and PD. For instance, a study contrasted a group of PD patients with and without active impulse control disorder symptoms and concluded that dopamine augmentation is a possible causative for the appearance of impulse control disorder in PD patients (Claassen et al., 2011). Also, another investigation contrasted a group of fellows with comorbid gambling disorder and PD, against a group of fellows with gambling disorder and without PD (Jiménez-Murcia et al., 2012), it found that both groups differ in terms of aging factors, onset of gambling disorder, alcohol consumption and other factors. Another research compared a group of fellows with gambling disorder and matched controls based on a series of psychological tests; the main difference was that gamblers showed variances (deficits) in blocks 3, 4 and 5 of the Iowa Gambling Task (slow learning and augmented detrimental options) (Kertzman, Lidogoster, Aizer, Kotler, & Dannon, 2011).

Another investigation contrasted electroencephalographic responses of three clusters of subjects (PD patients with impulse control disorder, PD patients without impulse control disorder, and controls) and concluded that impulse control disorder in PD patients was linked to a weaker control of fronto-central theta power by recompense valence, and to a greater fronto-central theta power after high and unanticipated outcomes. It also concluded that impulse control disorder in PD patients was linked to

the reversal of the hazard effect on beta oscillations (Carriere et al., 2016).

On the other hand, another recent study compared PD patients (with and without gambling disorder) based on the personality profile of the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) and found that PD subjects with gambling disorder displayed higher values on the validity scales and some content scales (Brusa et al., 2016). Finally, a current revision work (Heiden, Heinz, & Romanczuk-Seiferth, 2017) confirmed the higher comorbidity of gambling disorder in PD patients compared to the general population. Some of the factors that explained this comorbidity were dopamine agonist medication, age (younger), higher scores in novelty seeking and impulsivity scales, history of substance abuse disorder (alcohol), genetic mutations, increased functional activation in the mesolimbic reward system, increased dopamine release in the mesolimbic reward system and distorted learning processes (Heiden et al., 2017).

Other studies have confirmed the association between gambling disorder and ADHD. For instance, a study in Australia (Waluk, Youssef, & Dowling, 2016) reported that 24.9% of gamblers have also ADHD diagnosis. Also, another investigation in a group of gamblers analyzed them by means of different instruments (related to gambling habits and other socio-demographic variables; Romo et al., 2016) and concluded that the existence of ADHD results in an augmented level of cognitive distortions. Also, another study in a cluster of fellows with gambling disorder reported that 25.2% of them displayed ADHD (full syndrome; Retz, Ringling, Retz-Junginger, Vogelgesang, & Rosler, 2016), and concluded that ADHD patients had a higher probability of displaying gambling disorders.

On the other hand, a French study contrasted gamblers and control fellows based on different instruments (the South Oaks Gambling Screen, the Adult ADHD Self-Report Scale, and others; Fatseas et al., 2016), and reported that 20.7% of the gamblers screened positive for lifetime ADHD. The authors concluded that ADHD was associated to more severe gambling and broader psychiatric comorbidities (Fatseas et al., 2016).

## Revision of previous scientific reviews about gambling disorder

It is important to acknowledge that scientific reviews about gambling disease have varied in content. For example, some reviews have depicted the comorbidity of gambling disease with other diseases (Lorains

et al., 2011), the association between impetuosity and gambling disorder (Dannon, Shoenfeld, Rosenberg, Kertzman, & Kotler, 2010), neurobiological aspects of gambling disorder (Goudriaan, Oosterlaan, de Beurs, & Van den Brink, 2004), the link between ADHD and hazardous gambling conduct (Groen, Gaastra, Lewis-Evans, & Tucha, 2013), and the interrelation between the gambling disorder and PD (Santangelo, Barone, Trojano, & Vitale, 2013). In the next section, these and other recent revisions will be addressed.

## Gambling disorder and ADHD

A recent meta-regression analysis based on 37 studies compared risky decisions in a group of subjects with ADHD ( $n=1.175$ ) and a control group ( $n=1.222$ ; Dekkers, Popma, Agelink van Rentergem, Bexkens, & Huizenga, 2016). The analysis found that the cluster with ADHD displayed augmented hazard decision making compared to the control cluster. Moreover, this finding suggested that ADHD was linked to augmentation of hazard decision making in lab scenery, which tended to be more marked if ADHD was combined with a disruptive behavior disorder (Dekkers et al., 2016). This study was relevant because gambling disorder (like other impulse control disorders or addictions) can be characterized by risky decisions. On the other hand, a broader German review also pointed out the relationship between gambling disorder and other psychiatric disorders (including ADHD); authors proposed that the probability of displaying gambling disorder augments if there is comorbidity of other psychiatric disorders (like ADHD, personality disorder, anxiety disorder, substance use disorders or mood disorder; Gisela Buchner, & Wodarz, 2011). Other revision work also informed about the comorbidity of gambling disorder with ADHD and other disorders (affective and substance use disorders) (Sood, Pallanti, & Hollander, 2003).

Another recent review explored the connection between ADHD and adventurous performance in gambling tasks (Groen et al., 2013; this review by Groen and collaborators does not include subjects with gambling disorder, it is described in the present paper because it deals with risky performance in gambling tasks that can be found in subjects with gambling disorder). This revision reported that around 50% of the investigations in kids and teens suffering ADHD (7/14) discovered proofs that they run higher hazards of gaming tasks when contrasted to normal controls. However, adults with ADHD showed a difference because only a minority showed aberrant

risky behavior. This review work concluded that children and adolescents with ADHD have a higher hazardous performance in gambling activities compared to older subjects suffering ADHD; also, investigators suggested that these differences could be due to developmental variations in recompense (and, or punishment) susceptibility, or publication bias for positive results in kids and teens (Groen et al., 2013).

Furthermore, Groen et al. (2013) also suggested that comorbidity of oppositional defiant and behavior types of ailments is a risk factor in subjects with ADHD for an increase in hazardous conduct in gambling tasks. Despite this review focused mainly on gambling tasks (rather than real gambling disorder or marked gambling behavior), it is useful to mention because its findings suggest that ADHD and other comorbidities (oppositional defiant and behavior type of ailments) during infancy or adolescence could elevate the likelihood of suffering gambling disorder in the future.

### **Gambling disorder and PD**

A recent review reported that the incidence of gambling disorder in PD treated patients is around 2 to 7 %, which is superior than the general population rate (Santangelo et al., 2013). Moreover, according to that revision, different factors were associated with a gambling disorder in PD patients, including masculine gender, young age, younger age at PD beginning, individual or parental history of drug consumption or impulse control disorder, impulsive personality, and medication with dopamine agonists rather than levodopa medication. Also, it suggested that PD's treatment induced down regulation of fronto-striatal connections and an increment of striatum connections, which could be combined and generate impulsive conduct (Santangelo et al., 2013). Furthermore, according to the authors' revision, an impairment of frontal-subcortical loop in patients with comorbid PD and gambling disorder was confirmed by disrupted executive controlling skills based on neuropsychological testing (Santangelo et al., 2013).

Moreover, different imaging and psychological researches about the brain have established a correlation between the gambling disorder, irregularities in the prefrontal brain and the subcortico-cortical net connecting to the frontal brain (Goudriaan et al., 2004; Goldstein & Volkow, 2002; Jentsch & Taylor, 1999), based on the Santangelo's revision (Santangelo et al., 2013). Finally, few investigations have examined the cognitive traits of gambling disorder in PD sufferers (Santangelo et al., 2013); for instance, an

investigation informed that PD sufferers with a gambling disorder displayed more disruption of frontal lobe function compared to PD patients without gambling disorder (Santangelo et al., 2009).

Another recent review work (Pirritano et al., 2014) also pointed out the comorbidity of gambling disorder and PD in human patients. Pirritano stated that the gambling disorder is a complication that stems from dopamine agonist therapy; also, the management of gambling disorder in PD patients could be demanding. Moreover, according to Pirritano and collaborators' review, the treatment in these cases was based on the sufferer and family's scholarship, alteration of dopamine substitution treatment, and in some instances, psychoactive medication supply. Finally, the paper explained the pathogenesis of how dopaminergic treatment could induce gambling disorders (Pirritano et al., 2014).

On the other hand, another review explored which specific subtype of dopamine receptor agonist was mainly related to induction of impulse control disturbance (for instance: gambling disorder, uncontrollable shopping or hyper-sexuality) in PD patients (Seeman, 2015). It concluded that type 3 dopamine receptors (D3) rather than type 2 dopamine receptors (D2) were the most relevant, with pramipexole keeping the highest link with, or incidence of, impulse control disturbance (Seeman, 2015).

A current revision (Calandrella & Antonini, 2011) stated that gambling disorder and other related ailments were more prevalent in PD subjects taking dopamine medication, having an early age of PD onset, carrying specific personality traits, and displaying specific brain activity patterns (Calandrella & Antonini, 2011). On the other hand, other revisions confirmed that the incidence of gambling disorder in PD sufferers was higher than that found in the general population. Some of the factors that explained this tendency were dopamine agonist medication, age (younger), marked novelty seeking and impulsivity, background of alcohol use disorder, diverse genetic mutations (N-methyl D-aspartate receptor subtype 2B, dopamine receptor D3, and serotonin-transporter-linked polymorphic region), augmented functional activation in the mesolimbic reward system, augmented dopamine release in the mesolimbic reward system, and distorted learning processes (Heiden et al., 2017). Other revision (meta-analysis) confirmed that patients with PD following dopamine medication denoted disruption in the Iowa Gambling Task performance compared to controls (Evens, Hoefler, Biber, & Lueken, 2016).

## Comorbidity of gambling disorder with other disorders (besides ADHD and PD)

A significant portion of the work (including review) about comorbidity of gambling and other disorders relates to ADHD and PD (the main focus of this review); however, other comorbidities are described briefly in this subsection.

A review reported that subjects diagnosed with gambling disorder (or problem gambling) have elevated proportions of other parallel ailments (Lorains et al., 2011). Specifically, a meta-analysis technique was employed on eleven eligible studies, and it was found that the top average frequency was for nicotine use disorder (around 60%), continued by substance use problem (around 57%), humor disturbance (around 38%), and anxiety ailments (around 37%) (Lorains et al., 2011). Another related study suggested that gambling disorder runs in families, and co-aggregates with substance misuse (Black, Monahan, Temkit, & Shaw, 2006). This study also concluded that gambling disorder co-aggregates with antisocial personality disorder and recommended to perform additional research on the heritability of gambling disorders (Black et al., 2006).

A review analyzed the association between gambling disorder and the degree of impulsivity by means of different neurocognitive tests (Dannon et al., 2010). This review found a lower degree of impulsivity in subjects with a gambling disorder, based on different neuropsychological tests (Stop Signal, Stroop Test, Matching Familiar Figures, Wisconsin Card Sorting Test, Iowa Gambling Task, Tower of London Test, and Continuous Performance Test). This review concluded that differences in neurocognitive performance between subjects with gambling disorder and normal subjects can be explained by addictive behavioral traits instead of impulsive conduct (Dannon et al., 2010).

## Overview and conclusions of experimental work about gambling disorder

### Overview of the experimental work about the link between gambling disorder and ADHD

Two studies by Carlton and collaborators were the first to report about the relationship between gambling disorder and ADD. Specifically, one study showed that alcoholics and subjects with gambling

disorder had a higher level of attention deficit disorder-related behaviors (as children) compared to control groups (Carlton & Manowitz, 1992). The second study by Carlton compared a group of subjects with a gambling disorder ( $n=14$ ) and controls ( $n=16$ ) by means of questionnaires concerning their childhood conducts (Carlton et al., 1987). The study concluded that there was a firm relationship between gambling disorder and infancy conducts associated with ADD. However, because of the reduced size of the sample of this study (14 and 16 subjects), its findings should be considered with precautions.

An investigation compared the incidence of ADHD in medication-requesting problem gamblers and the common population (Waluk et al., 2016). A total of 214 major subjects (27% women, 72% men and 1% non-specified) who were seeking cures for their gambling disorders were analyzed. Around 25% of the cure-searching problem gamblers obtained an ADHD diagnosis, and this was considerably superior to the 14% incidence in the community sample. Besides, ADHD denoted a considerably positive correlation with gambling severity, movement impetuosity, and group B personality ailments; however, ADHD was not linked to liquor and substance use disorder, sexual genre or age. This study proposed that a substantial percentage of alleviation-searching problem gamblers reported ADHD, and that their health profile was entangled by the existence of elevated impulsivity and group B personality disease. The authors considered the necessity for clinicians to promote detection, evaluation and treatment arrangements for comorbid ADHD to improve the efficiency of therapy (Waluk et al., 2016).

A study by Chamberlain and collaborators (2015) evaluated the relationship between ADHD and gambling disorder. A total of 126 non-therapy asking young adults with gambling disorder were enlisted and clustered, based on the existence or absence of actual ADHD (Chamberlain, Derbyshire, Leppink, & Grant, 2015). The subjects were evaluated by means of mental health evaluation tools, surveys, and computer based neuropsychological exams. The study found that likely current ADHD was detected in approximately 20% of the evaluated subjects, and it was linked to an early age of gambling behavior beginning, higher impulsivity (Barratt scales), higher caffeine consumption, inferior response inhibition (Task of Stop Signal), and disrupted judgment-execution (Cambridge Gamble Test). Moreover, problem gamblers with different levels of ADHD did not vary

on demographic traits, the percentage of other mental health illness, depression index, tobacco or alcohol intake, and body mass scores. No meaningful cluster variations were found in the speed of general response, executive process (planning) and memory (working). The main conclusions were that ADHD is frequent in young adults with problematic gaming conducts, and it is linked to higher impulsivity along with elevated caffeine consumption (Chamberlain et al., 2015).

On the other hand, a work by an Aymami group analyzed the relationship between ADHD and gambling disorder in a group of 354 consecutive patients (Aymami et al., 2015). The subjects were evaluated by means of a wide range of tests related to gambling conduct, abnormal psychology and personality traits. It was found that women and men players did not vary significantly in their mean punctuations on the ADHD measurement. Moreover, it was found that higher ADHD scores were linked to a young age (18-35 years old), marked seriousness of gambling disorder, and a broader mental health dysfunction.

Conversely, the evaluation of personality traits did show that elevated constancy and independence were inversely linked to ADHD rates; furthermore, in women, a direct interrelation was discovered between ADHD rates and the incidences of damage prevention and personal transcendence. It was concluded that the existence of ADHD signs in women and men subjects with playing disorders could serve as a pointer of the seriousness of gambling, broad mental dysfunction, and abnormal personality characteristics (Aymami et al., 2015).

Another investigation explored the relationship between gambling, ADHD and console play disorder in a group of young students (Romo et al., 2014). For this purpose, students from (n = 720, 62 % men and 38 % women) French higher education institutions were evaluated by means of questionnaires, including the Canadian Problem Gambling Index, UPPS (urgency, premeditation, perseverance, sensation seeking) Wender Utah Rating Scale, Impulsive Behavior Scale, Rosenberg scales, Adult ADHD Self-Report Scale, and socio-demographic information. It was reported that around 13 % of the participants displayed signs of ADHD during infancy, and around 40 % of them displayed signs of ADHD in the adult stage of development. The study found a relationship between ADHD and gambling disorder; also, ADHD was linked to impulsivity, school problems, and gambling disorder. Furthermore, the relationship between gambling

disorder and ADHD was more frequent in some age clusters like teenagers and might be linked to personal self-esteem, which seems to potentially impair the recovery (Romo et al., 2014).

Another investigation studied the association between impulsivity, gambling-linked cognitions and behaviors, in mature subjects with or without ADHD disorder (Dai, Harrow, Song, Rucklidge, & Grace, 2013). A group of subjects with ADHD and controls (respective samples of 31 and 29 subjects) were compared by means of instruments that evaluate mental health illness, gambling surveys, imitated playing delay, and likelihood discounting exercises. The study reported that the ADHD cluster was most probably to fulfill the gambling disorder's criteria, and it was more impetuous than the control cluster. Furthermore, ADHD signs were interrelated with gambling-associated cognitions and conduct. The study confirmed a link between gambling and adult ADHD, and it suggested that the appearances of impetuosity, linked to hazardous tendency might be a vulnerability variable for gambling disorder in this group (Dai et al., 2013).

On the other hand, an investigation by Davtian and collaborators analyzed the influence of personality in gambling disorder under the presence or absence of ADHD disorder (Davtian, Reid, & Fong, 2012). Specifically, it contrasted subjects with gambling disorder with and without ADHD (samples of 52 and 43 subjects respectively). The subjects were compared by means of the NEO (Neuroticism - Extraversion - Openness to experience) personality inventory (revised), the National Opinion Research Center DSM Screen for Gambling Problems (NODS), Mini International Neuropsychiatric Interview, and the Adult ADHD Self-Report Scale. Despite that both groups showed impairments like higher impetuosity, depressed mood, lack of personal esteem, and lack of personal discipline, these aspects of personality were firmer in subjects displaying gambling disorder with ADHD. In general, the study found a marked tendency in gamblers with problems of ADHD to display a higher degree of affective unsteadiness, social relationship touchiness, and stress vulnerability. However, both clusters were similar in terms of impetuosity. The research concluded that the presence of adult ADHD in gamblers might predispose for more difficulties and challenges to appear, compared to the absence of ADHD (Davtian et al., 2012).

Conversely, a study by Rodríguez and collaborators contrasted diverse impetuosity and focused

attention variables in three different groups: subjects with gambling disorder and with infancy ADHD background; subjects with gambling disorder and without that background; and control subjects (respective samples of 16, 39 and 40 subjects; Rodríguez-Jiménez et al., 2006). The different psychometric tools used were the Barratt Impulsivity Scale, the Stop Signal Test, the Low Rate Responding Task (differential reinforcement), and the Continuous Performance Test.

An ADHD's incidence of 29.1 % was found in the sample of subjects with gambling disorder. Moreover, this work found that the subjects with gambling disorder and ADHD did show a significant lower capacity to delay gratification compared to the other two groups (gamblers without ADHD and control). Furthermore, the subjects with gambling disorder and ADHD displayed less inhibitory control compared to disordered gamblers without ADHD. Finally, subjects with gambling disorder and ADHD showed higher level of impulsivity compared to the other groups (gamblers without ADHD and control). On the other hand, no differences among groups were found in terms of sustained attention.

In general, this study concluded that there was a potential special involvement of the prefrontal brain area (cortex) in gambling disorder dynamics, and this could be more evident in the group with an infancy background of ADHD (Rodríguez-Jiménez et al., 2006). Finally, a research work by Specker and collaborators also compared the incidence of ADD and impulse control disorders in subjects with gambling disorder or controls (Specker, Carlson, Christenson, & Marcotte, 1995). This work found that an impulse control disorder was found in around a third of the subjects with gambling disorder, contrasted to a 3% of the control group. Furthermore, uncontrollable shopping and uncontrollable sexual conduct were also remarkably higher in subjects with gambling disorder. This study found a strong correlation between subjects with gambling disorder, attention disorders and/or disorders related to self control. ADD was found in about 20% of the subjects with a gambling disorder (Specker et al., 1995).

Conversely, another group of investigations indicated the remarkable association between gambling disorder and ADHD. For instance, a study in Australia explored in a group of gamblers seeking treatment, the relationship between ADHD and gambling disorder (n=214; Waluk et al., 2016). They found that 24.9% of the participants displayed confirmation for ADHD diagnosis, this is remarkably

higher than the frequency of the community (14%; Waluk et al., 2016). This finding warned about considering the higher probability of ADHD in gambling disorder patients, and the complications related to the comorbidity of both diagnosis during the screening and treatment stages (Waluk et al., 2016).

Moreover, another investigation in a group of gamblers (n=628; 18 to 65 years) who gambled at least one time in the previous year, evaluated them by means of different instruments (gambling habits, the Wender Utah Rating Scale – Child, the South Oaks Gambling Screen, the Gambling Attitudes and Beliefs Survey - 23, the Adult ADHD Self-report Scale, and socio-demographic characteristics) (Romo et al., 2016). The study concluded that the existence of ADHD resulted in an elevated degree of cognitive distortions and recommended the instauration of cognitive work during treatment and prevention of gambling disorder (Romo et al., 2016).

Another study explored the association between gambling disorder and ADHD (n=163) in a group of subjects with gambling disorder. A 25.2% displayed full syndrome of ADHD based on the DSM-5 (Retz et al., 2016). The authors concluded that ADHD patients had a higher probability of displaying gambling disorders, and that the existence of comorbidity of both disorders made the treatment more challenging (Retz et al., 2016).

On the other hand, a French study (n=599) compared gamblers (from gambling clinics and gambling places) with control subjects, based on different instruments (the South Oaks Gambling Screen, the Adult ADHD Self-Report Scale, the Mini International Neuropsychiatric Interview, the Temperament and Character Inventory, the Wender-Utah Rating Scale-Child, and questionnaires related to gambling habits and cognitions; Fatseas et al., 2016). The investigation found that around a fifth of the gamblers (20.7%) screened positive for lifetime ADHD. The investigation also found that ADHD was linked to a more marked gambling severity, and more psychiatric comorbidities (Fatseas et al., 2016).

Another study compared non-medicated ADHD patients (with or without gambling disorder) with a control group (paired by sex and age variables), based on electroencephalogram (EEG) responses, and the stimulus-locked event-related potentials (ERP) during tasks in the Iowa Gambling Task (simplified version; Abouzari, Oberg, & Tata, 2016). The study found that ADHD problem gamblers displayed subjacent shortages in reward learning (not found in ADHD patients

without gambling; Abouzari et al., 2016). Moreover, another investigation studied a group of young people (male and female) from a community sample, and the results were contrasted with subjects that had ADHD - lifetime diagnosis (n=46), non-diagnosed fellows with high-ADHD-symptoms (n=83), and non-diagnosed fellows with low ADHD-symptom group (n=84; Davis, Cohen, Davids, & Rabindranath, 2015). The study concluded that the management of ADHD with stimulant prescription had no effect (increase or decrease) in the probability of displaying substance use disorders (Davis et al., 2015).

On the other hand, an investigation in adolescents (n=1,130 aged 12 to 19) found that those with ADHD diagnosis displayed higher probabilities for engaging in gambling activities or developing gambling problems, compared to adolescents with non-ADHD diagnosis (Faregh & Derevensky, 2011).

Furthermore, adolescents with diagnosis of ADHD were twice as likely to develop gambling problems compared to adolescents with ADD (mainly inattentive traits; Faregh & Derevensky, 2011). Also, another study (n=84) evaluated subjects with gambling disorder or in risk of gambling disorder based on different variables (gambling, socio-demographic and clinical; Grall-Bronnec et al., 2011) and found that more than a fourth of the participants reported a background of ADHD. Moreover, this subgroup of fellows denoted more noticeable gambling problems, more evident cognitions related to gambling, an augmented proneness to suicide, and a higher incidence of psychiatric comorbidities (Grall-Bronnec et al., 2011). Finally, a research compared adolescents with ADHD diagnosis (n=142; diagnosed before age 12) to a community population, based on the incidence of early addictive behaviors (Ostojic, Charach, Henderson, McAuley, & Crosbie, 2014). This study concluded that youth with a background of childhood - ADHD diagnosis might not be at greater risk for substance abuse onset in early adolescence; but considered that a tendency to begin early with gambling behaviors should be investigated in this group (Ostojic et al., 2014).

### **Conclusions of the experimental work about the association between gambling disorder and ADHD**

When analyzing the previously described reports, one may point out the following tendencies:

- 1) In general, different authors agree that subjects with gambling disorder have a high incidence of ADD or ADHD. Specifically, different works in the field have reported incidences of ADHD that ranges from 20 to 29%: Fatseas et al. (2016) report 20.7%; Waluk et al., (2016) find 25%; Retz et al. (2016) mention 25.2%; Grall-Bronnec et al. (2011) state >25%; Chamberlain et al. (2015) indicate 21%; and Rodríguez-Jiménez et al. (2006) notify 29.1%. Also, an ADD incidence of 20% in subjects with gambling disorder (Specker et al., 1995) has been reported. Moreover, older studies by Carlton and collaborators also reported that subjects with gambling disorder have a higher level of ADD as children compared to controls (Carlton & Manowitz, 1992; Carlton et al., 1987).
- 2) On the other hand, some studies supported the tendency that fellows with ADHD display a higher incidence of gambling disorder compared to non ADHD subjects. Specifically, 46.2% of ADHD subjects displayed gambling problems (lifetime prevalence) compared to non ADHD subjects (Dai et al., 2013); also, adolescents with ADHD tend to have higher incidence of gambling or gambling problems compared to adolescents without ADHD (Faregh & Derevensky, 2011).
- 3) Based on different studies, the main differences between subjects with comorbid gambling disorder and ADHD, and their counterparts without ADHD, is that the first ones have a marked tendency of: more severe gambling, more psychiatric comorbidities (Fatseas et al., 2016), earlier age of gambling conducts onset, higher impetuosity, higher caffeine consumption, poorer response restraint, impaired decision-making (Chamberlain et al., 2015), lower self-esteem, depressed mood, upper impulsivity, poorer personal control, greater levels of emotional instability, interpersonal sensitivity, stress proneness (Davtian et al., 2012), and augmented cognitive distortions (Romo et al., 2016). Moreover ADHD subjects with gambling problems have limitations in reward learning (Abouzari et al., 2016).
- 4) Relating to treatment, the presence of ADHD in a subject with gambling disorder implies more challenges for screening, assessment and treatment, according to different authors. For instance, the presence of adult ADHD in gamblers might predispose to more difficulties and challenges compared to the absence of ADHD (Davtian et al., 2012). Moreover, some authors recommend clinicians to

elaborate, monitor, evaluate, and undergo caring procedures for comorbid ADHD, to improve therapy efficacy (Romo et al., 2016; Waluk et al., 2016). Finally, Aymami and his research group suggest that the presence of ADHD in subjects with gambling disorder may be an index of playing severity, general abnormal mental health, and abnormal personality traits (Aymami et al., 2015).

- 5) Even in the normal population, with like subjects in general (Aymami et al., 2015) and young students (Romo et al., 2014), research supports the relationship between ADHD and gambling disorder.

### **Overview of the experimental work about the relationship between gambling disorder and PD**

There are various experimental publications that have recalled the relationship between gambling disorder and PD.

An investigation by Pontieri and his research group explored the relationship between gambling disorder and PD (Pontieri et al., 2015). Specifically, this investigation tried to define the relationship between gambling disorder and specific neuropsychiatric or cognitive domains. This work evaluated PD patients ( $n = 155$ ) without dementia or cognitive impairments that were studied by different instruments (including neuropsychological tests). Inmates were separated into three clusters: the first, those with a gambling disorder; the second, those with impulse control disorders not otherwise specified (ICD-NOS), and the third one, those who lack impulse control disorders. No dissimilarity was found between the clusters in any cognitive measure. However, subjects with gambling disorder and those with ICD-NOS displayed longer disease duration, and large dosages of anti-PD drugs compared to those who lacked impulse control disorders. Moreover, subjects with a gambling disorder did show more severity of anxious and depressive symptoms compared to the two other groups. Finally, subjects with gambling disorder and ICD-NOS patients displayed more severe psychotic symptoms than the group of those who lacked impulse control disorders (Pontieri et al., 2015).

Other research by Vitale and collaborators contrasted the cognitive profiles of PD patients affected by different types of impulse control disorders: gambling disorder ( $n = 14$ ), hyper-sexuality ( $n = 13$ ), compulsive eating ( $n = 12$ ), and multiple impulse control

disorders ( $n = 10$ ; Vitale et al., 2011). These groups were contrasted against a control group of PD patients (matched in age and education), but without impulse control disorder ( $n = 14$ ). All the subjects were evaluated based on demographic aspects, clinical features, neuropsychiatric and neuropsychological functioning. No differences were reported among the clusters.

The four groups of PD patients with impulse control disorders displayed more dysfunction on assignments related to spatial organization, and set shifting tests compared to controls. Comparisons among the PD sufferers with impulse control disorders showed that those with hyper-sexuality displayed more dysfunction in the Stroop Test contrasted to those with gambling problems. Furthermore, those with a gambling ailment showed lower impairment on verbal learning and memory test compared to the other impulse control disorder groups (hyper-sexuality, compulsive eating, and multiple disorders).

This study concluded that impulse control disorders were linked to dysfunction in cognitive functioning, but there were differences in the severity of the dysfunction. The severity increased according to the following tendency: gambling disorder < compulsive eating < hyper-sexuality and multiple control disorders. Finally, according to Vitale et al. (2011), hyper-sexuality is linked to prefrontal dysfunction and memory problems, whereas gambling disorder appears to be linked solely to alteration of the frontal lobe. Nevertheless, because the relative small sample of this investigation (samples from 10 to 14 subjects per group), findings should be considered with discretion.

Another experimental work contrasted clinical and cognitive aspects of PD patients with current gambling disorder ( $n = 21$ ) against PD controls without any impulse control disorder ( $n = 42$ ) (Siri et al., 2010). The subjects were evaluated by means of neuropsychological testing (memory, learning, language, frontal lobe's executive functioning, attention, and visual-spatial skills), neuropsychiatric instruments, and a gambling disorder scale (South Oaks Gambling Screen). The study found that PD patients with a gambling disorder tend to be younger and male. Furthermore, in terms of test performance, PD patients outperformed the control group in the next tests: Rey Auditory Verbal Learning Test, verbal phonemic fluencies, verbal semantic fluencies, and attentive matrices. No differences were found between both groups in the other cognitive tests. The study concluded that the executive functions of PD patients

with a gambling disorder were preserved (Siri et al., 2010).

On the other hand, another investigation contrasted two groups of patients: the first one ( $n=21$ ) consisted of patients with idiopathic PD and a gambling disorder (after receiving medications), and the second one ( $n=42$ ) were subjects with idiopathic PD lacking uncontrollable conducts (Voon et al., 2007). The study reported that factors like novelty search, individual or family background of alcohol consume ailments, and an earlier age of PD onset, precisely forecasted gambling disorder (around 84% based on a logistic regression design); furthermore, it concluded that these factors also increased the probability of gambling disorder in PD patients receiving treatment with dopamine agonists (Voon et al., 2007).

As already pointed previously by Santangelo in a recent review (Santangelo et al., 2013), opposed results among the studies (above described) of Vitale et al. (2011), Voon et al. (2007), and Siri et al. (2010) were found. Specifically, Vitale's study found that PD patients with gambling disorder display disruption in frontal functioning and memory tasks (but a lower one compared to other single or combined impulse control disorders). Nevertheless, Siri et al., and Voon et al., studies reported absence of frontal dysfunction in PD patients with gambling disorder.

Another study by Santangelo's research group (Santangelo et al., 2009) contrasted non demented PD patients affected by gambling disorder ( $n=15$ ) against non demented PD patients without gambling disorder ( $n=15$ ). The groups were compared based on clinical, neuropsychiatric features, and several cognitive domains (principally executive functions). No differences were found between both groups regarding clinical and neuropsychiatric aspects. However, the cluster of PD patients with a gambling disorder performed significantly worse compared to the other group, based on cognitive tests that assessed visual long term memory (spatial) and functions of the frontal brain area.

Moreover, Santangelo et al., (2009) concluded that there was an association between gambling disorder and frontal lobe ailments in PD sufferers; also, inferior punctuations on the Frontal Assessment Battery were related to a higher probability of gambling disorder in PD patients. Nonetheless, since the size of the sample was relatively small (15 subjects per group), findings should be considered with caution.

A study by Riba and collaborators suggested that dopamine based medication for PD might explain

gambling disorder tendencies in some PD patients (Riba, Kramer, Heldmann, Richter, & Munte, 2008). This study employed a double blind design with a placebo condition; moreover, it included a cluster of normal health subjects. The investigation found that administration of D3 receptor agonist pramipexole induced a preference for hazardous selections in lottery exercises. Furthermore, this study found a reduced activity level in the midbrain and rostral basal ganglia after facing unexpected elevated profits. Moreover, because these neural structures were a fundamental part of the brain's reward system, it proposed that gambling disorder in PD patients was a consequence of the elevated recompense necessity to overcome the decreased reaction in this system (Riba et al., 2008).

A study performed by Micheli's research group evaluated PD patients ( $n=6$ ) receiving piribedil (a dopamine agonist) and displaying gambling disorder and impulse control disorders (compulsive eating, hyper-sexuality, compulsive shopping; Micheli, Giugni, Espinosa, Calvo, & Raina, 2015). It concluded that piribedil should be considered in the differential diagnosis of gambling disorder in patients with PD. However, because the reduced sample size of the study (6 subjects), findings should be considered with discretion.

An investigation by Castrioto and collaborators contrasted, in a cluster of PD sufferers and age matched controls, the effect of subthalamic nucleus excitation on the decision-making processes (related to impulsivity) with the Iowa Gambling Test. It found that stimulation at deeper levels of the brain induces a marked decrease of dopaminergic treatment, and hence the associated improvement of therapy-induced impairment in judgment process (Castrioto et al., 2015).

A study by Gaboriau and collaborators explored the causality of aripiprazole on gambling disorder using an algorithm in a sample of eight subjects with PD disease (Gaboriau et al., 2014). It found that the likelihood that gambling disorder was caused by aripiprazole was evident in 87.5% of the cases, and doubtful in 12.5% of the cases. Based on the results, it considered that the effect of aripiprazole on gambling disorder incidence is explained by its partial dopamine agonism. Nevertheless, because the small sample of this investigation (8 subjects), these findings should be considered with discretion.

A work by Pérez-Lloret and collaborators evaluated the incidence of impulse monitoring diseases and

pharmacological variables associated with a group of sufferers with ( $n=203$ ) and without PD ( $n=52$ , post-stroke patients) in a sample of French patients (Pérez-Lloret et al., 2012). The disorders related to impulse control explored in the study were: gambling disorder, uncontrollable sexual behavior, compulsive shopping and uncontrollable eating. 25 % of PD sufferers showed at least one type of disorder related to control of impulse, and none (0 %) of the patients without PD had those disorders. Gambling disorder was reported in 3 % of the PD sufferers; moreover, they also discovered in PD sufferers an incidence range of 6 % to 14 % of other impulse control disorders (uncontrollable sexuality: 10 %, compulsive shopping: 6 %, and uncontrollable eating: 14 %). Moreover, a logistic regression assay concluded that the next factors were linked to an elevated impulse control disorder frequency among PD patients: younger than 68 years, use of type B monoamine oxidase inhibitor or dopaminergic system agonist. They also found a tendency: patients with impulse control disorder signs were exposed to high doses of dopamine compared to those sufferers without them.

It has also been reported that impulse control diseases, including uncontrollable gambling, shopping, eating and hyper sexuality, are also found in PD patients (Weintraub, 2009). Weintraub affirmed there is a relationship between impulse control disorders and the following conditions: male gender, younger age, use of dopamine agonists, earlier age of PD beginning, background of uncontrollable impulses symptoms before the onset of PD, individual or family background of substance abuse disorder, bipolar disorder, and an impulsive personality.

Furthermore, other related work from the Weintraub research group performed a study in a cluster of ( $n=3090$ ) subjects with idiopathic PD in the United States and Canada to estimate the prevalence of different impulse control disorders. This study also evaluated the link between impulse control disorders, dopamine-replacement treatment, and other clinical traits (Weintraub et al., 2010). The study found that impulse control disorders were found in roughly 14 % of PD sufferers. Specifically, it found a 6 % of compulsive shopping, 5 % of gambling disorder, 4.3 % of binge eating disorder, and 4 % of compulsive sexual behavior in PD patients. Furthermore, 3.9 % of PD patients had two or more impulse control disorders. Other variables related to a higher incidence of impulse control disorders in PD patients were: younger age, never been married, dopamine

agonist treatment, use of levodopa, actual tobacco smoking, and a family background of gambling problems. This study concluded that the treatment with dopamine agonists in PD patients was linked to a roughly 2 to 3.5 fold augmented odds of displaying an impulse control disorder.

On the other hand, a work by Isella's research group proposed that the relationship between PD and gambling disorder could be explained by the effect of aging processes in some cognitive functions (including executive functioning); subsequently this disruption of cognitive functioning could induce risky and gambling behaviors (Isella et al., 2008). This study contrasted Iowa Gambling Test performances of 40 young, 40 old healthy adults, and 18 subjects affected by mild gravity dementia of the frontal lobe. Moreover, it was found that decision-making skill deteriorated with age; furthermore, this deterioration was very similar to the type found in conditions of executive impairment due to neurodegeneration. Besides, it proposed that potential deficits in focused attention during lengthy tasks could be the subjacent disrupted decision-related factor in natural aging (Isella et al., 2008).

It is important to mention the work by Zamarian's research group (Zamarian, Sinz, Bonatti, Gamboz, & Delazer, 2008), even though it did not include subjects with PD, because it explored the impact of aging on decision (under ambiguity or under risk conditions). A considerable number of PD patients can be classified as old in terms of age, based on this, the study compared a group of young versus older adults by means of the Probability-Associated Gambling task and the Iowa Gambling Task. It found no significant discrepancies between both clusters in the Probability-Associated Gambling task. A possible interpretation is that older subjects were able to make decisions, if full problem information was provided (about probability options, related benefits and losses). Moreover, older fellows displayed lower Iowa Gambling Task's execution compared to young adults. This possibly implied that older subjects had more trouble in making suitable judgments under ambiguous conditions. Indeed, in the Iowa Gambling Task subjects were unaware of the rules for winning or losing and had to grasp it by trial and error (experience). This investigation insinuated that older subjects could elaborate suitable decisions if full information about the decision context was provided (Zamarian et al., 2008).

Other studies have pointed out the strong relationship between gambling disorder and PD. For

instance, a study contrasted a group of PD patients with active impulse control disorder symptoms ( $n=22$ ) against a group of PD patients without active impulse control disorder symptoms ( $n=19$ ), regarding the relevance of dopaminergic agonist therapy on risk-taking behavior. The study applied the Balloon Analogue Risk Task (Claassen et al., 2011) and concluded that dopaminergic augmentation of hazard-taking conduct was a possible causative for the appearance of impulse control disorder in PD patients (Claassen et al., 2011). Also, another investigation contrasted a group of fellows with comorbid gambling disorder and PD ( $n=15$ ) against a group of fellows with gambling disorder and without PD ( $n=45$ ; Jiménez-Murcia et al., 2012). The main differences between both groups were that the members of the first group were older and displayed later onset of gambling behaviors dysfunction, decreased alcohol consumption, augmented bingo playing, and reduced indexes of hostility compared to the second group (Jiménez-Murcia et al., 2012).

Another research compared a group of fellows with gambling disorder ( $n=51$ ) against matched controls ( $n=57$ ), based on a series of tests (Iowa Gambling Task, Stroop Task and Go/NoGo Task; Kertzman et al., 2011). The main difference found was that fellows with gambling disorder displayed significant differences in blocks 3, 4 and 5 of the Iowa Gambling Task; specifically, subjects with gambling disorder learned the Iowa Gambling Task slower than controls, and had augmented detrimental options. Furthermore, this was not explained by deficits in inhibition response (Stroop Test), nor by the amount of commission mistakes (Go/NoGo Task; Kertzman et al., 2011).

Furthermore, another investigation ( $n=22$ ) evaluated subjects with advanced idiopathic PD and implanted electrodes (subthalamic nucleus) for the purpose of exploring the effect of deep brain stimulation on the inclination to chase losses (Rogers et al., 2011). It concluded that temporary stimulation alters the judgment of collected losses during gambling events in idiopathic PD patients. On the other hand, a clinical research in PD patients ( $n=353$ ) reported an association between PD and compulsive symptoms (Verbaan et al., 2009). Compulsive symptoms appeared in 19% of the patients, and frequencies of 10% for compulsive shopping/gambling, and sexual preoccupation were found (Verbaan et al., 2009).

Another recent study compared the electroencephalographic responses of three groups of subjects during the completion of a gambling task: PD patients

with impulse control disorder ( $n=12$ ), PD patients without impulse control disorder ( $n=12$ ), and healthy controls ( $n=14$ ; Carriere et al., 2016). This investigation concluded that impulse control disorder in PD patients was linked to a weaker control of fronto-central theta power by recompense valence, and to a greater fronto-central theta power after high and unanticipated outcomes; also, it was linked to a reversal of the effect of hazard on beta oscillations (Carriere et al., 2016). However, because the relatively small size of the sample (12 to 14 subjects per group), the findings should be considered with carefulness.

A recent research contrasted two groups of subjects: PD patients with gambling disorder history ( $n=37$ ), and PD patients without gambling disorder (matched for disease and dopaminergic therapy) that serve as controls ( $n=21$ ), based on the personality profile of the MMPI-2 (Brusa et al., 2016). The study found that PD patients with gambling disorder displayed higher values on the validity scales (L, F, and K) and specific content scales (cynicism and bizarre ideation) compared to the control group; this personality profile fits more in the cluster A personality disturbance of the DSM-5. According to Brusa et al.'s report, potential consequences of starting dopaminergic treatment in PD patients with this personality profile should be considered, because of the potential risk of displaying gambling disorder (or other impulse control disorders; Brusa et al., 2016).

Moreover, a recent case report ( $n=2$ ) proposed that the relationship between PD and impulse control disorder (hypersexuality and gambling) was explained by dopamine based treatment (Nelis, Berendse, & van den Heuvel, 2016). It reported that after decreasing the dopamine agonist medication, the symptoms of hypersexuality and gambling diminished. However, one limitation of this study is the reduced sample size ( $n=2$ ), hence, the result should be considered with caution.

### **Conclusions of the experimental work about the association between gambling disorder and PD**

The following tendencies may summarize the analysis of the previously mentioned reports:

- 1) Treatments or conditions that increase the agonism of dopamine receptor in PD patients was a variable linked to a higher probability of gambling

disorder or impulse control disorder (for instance: hypersexuality, compulsive eating or compulsive shopping). For instance, treatment with dopaminergic drugs like Pramipexole - a partial/full D2/D3/D4 receptor agonist (Riba et al., 2008), Piribedil - a D2/D3 receptor agonist and D4 receptor antagonist (Micheli et al., 2015), Aripiprazole - a D2/D3/D4 receptor partial agonist (Gaboriau et al., 2014), and higher dosages of anti-Parkinsonian drugs (levodopa, dopamine equivalents or levodopa equivalents; Pontieri et al., 2015) have shown relatedness to gambling disorder in PD patients. On the other hand, dopamine related treatments like high dosages of anti-Parkinsonian drugs (levodopa, dopamine equivalents, levodopa equivalents; Pontieri et al., 2015), levodopa or dopamine agonists (Weintraub et al., 2010), type B monoamine oxidase inhibitors (Pérez-Lloret et al., 2012), increase the incidence of other impulse control disorders in PD patients based on different studies. On the other hand, deep brain stimulation (sub-thalamic nucleus) in advanced stage PD patients alters the judgment during “chasing losses” (Rogers et al., 2011).

- 2) The incidence of gambling disorder in PD patients can be partially explained by aging effects on cognitive processes, based on the works of Isella et al. (2008) and Zamarian et al. (2008). Specifically, the disruption of the decision processes (executive function) is underlined by the inability to sustain attention during complex tasks (Isella et al., 2008). Moreover, the effect of aging on decision processes depends on the degree of ambiguity of the task. Taking together the findings of Isella (Isella et al., 2008) and Zamarian (Zamarian et al., 2008) research groups, the next relationship can be stated: if the rules of win and lose, and the probability options are clear (unambiguous condition), the effects of aging are non significant. However, if the rules of win and lose, and the options of probabilities are not clear (should be grasped by trial and error or experience), then the effect of aging on decision process is more impairing.
- 3) Other factors that could increase the probability of gambling disorder in PD patients are: novelty seeking, personal or family background of alcohol abuse disorder (Voon et al., 2007), younger age at PD beginning (Siri et al., 2010; Voon et al., 2007), male gender (Siri et al., 2010), longer term of disease, more severe psychotic symptoms, more

severe anxiety, more severe depression (Pontieri et al., 2015), older age, later onset of gambling disorder, and augmented bingo playing (Jiménez-Murcia et al., 2012).

- 4) On the other hand, possible variables that could increase the incidence of other impulse control disorders (for instance: hypersexuality, compulsive eating or compulsive shopping) in PD patients are: younger age of PD disease onset (Pérez-Lloret et al., 2012; Weintraub, 2009; Weintraub et al., 2010), male gender (Weintraub, 2009), unmarried (Weintraub et al., 2010), longer PD duration (Pontieri et al., 2015), mental disorder-related factors like disorder's severity (psychotic, anxiety or depression; Pontieri et al., 2015), impulsiveness, personal history of a disorder (substance abuse, bipolarity or impulse control; Weintraub, 2009), and current cigarette smoking (Weintraub et al., 2010). Finally, the presence of family background of a disorder —substance abuse, bipolarity (Weintraub, 2009), or gambling disorder (Weintraub et al., 2010)— could also increase the probability of an impulse control disorder in a PD patient.
- 5) A potential approach for treating gambling disorder and other impulse control disorders in PD patients is the activation of the subthalamic nucleus combined with the reduction of dopaminergic treatment (Castrìo et al., 2015).
- 6) In terms of neuropsychological and psychometric characteristics, the studies showed that PD sufferers with a gambling disorder (compared to those without a gambling disorder) displayed more impairment in visual spatial memory (at a long term range), disruption of frontal brain functioning (Santangelo et al., 2009); disruption in sets shifting and spatial planning (Vitale et al., 2011); higher scores in the validity scales (L, F and K) and content scales (cynicism and bizarre ideation) of the MMPI-2 (Brusa et al., 2016). However, another study differed (Siri et al., 2010), and instead found intact cognitive functioning in PD patients with a gambling disorder. In effect, these subjects showed better results in the Rey Auditory Verbal Learning Test, verbal phonemic fluencies, verbal semantic fluencies, and attentive matrices.

### General final conclusions

- 1) There is a high comorbidity between gambling disorder and ADHD, ranging the incidences roughly

between 20 % and 30 %. Also, subjects with ADHD have a high incidence of gambling disorder (46.2 %, based on one scientific report), and this tendency is also found in adolescent stage.

- 2) Subjects with comorbid gambling disorder and ADHD (compared to those without ADHD) show the next differences: more severe gambling, more psychiatric comorbidities, early start of gambling conducts, higher impulsivity, higher caffeine consumption, poorer response restraint and personal control, impaired decision-making, low self-esteem, depressive moods, higher emotional instability, interpersonal sensitivity, stress proneness, and augmented cognitive distortions.
- 3) The presence of ADHD in subjects with gambling disorder implies more challenges for screening, assessment and treatment of patients.
- 4) Treatments or conditions that increase the agonism of dopamine receptor in PD patients was a variable linked to a higher probability of gambling disorder or impulse control disorder (for instance: hypersexuality, compulsive eating or compulsive shopping).
- 5) Other conditions that explain the higher incidence of gambling problems in subjects with PD are: the effects of aging on cognitive processes (decision processes, executive function), novelty seeking, background (personal or family) of alcohol abuse disorder, younger age of PD onset, male gender, longer term disease, severe psychotic symptoms, severe anxiety, severe depression, and older age.
- 6) The gambling disorder has also comorbidities with other disorders (not the main subject of this review) like: nicotine use disorder, substance use problem, humor disorder, anxiety ailments, and antisocial personality disorder.

## Limitations of the present revision

The present revision only includes publications that are in English or Spanish language (at least the abstract). It means that works in other languages (e.g., Russian, French or other) were not included because of the author's translation skill limitations. Also, some of the studies have a reduced sample size, so the findings have to be considered with caution.

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