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INDIRIZZO: PSICOLOGIA SOCIALE E DELLA PERSONALITÀ

PATHOLOGICAL GAMBLING: COMPULSIVE-IMPULSIVE SPECTRUM DISORDER, BEHAVIOURAL ADDICTION, OR BOTH?

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Riassunto

Il Gioco d'azzardo patologico (GAP) è una condizione cronica e progressiva, definita come "una condotta persistente e ricorrente di gioco maladattivo"; attualmente è incluso tra i Disturbi del controllo degli impulsi (non altrove classificati) nel *Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition - Text Revision* (DSM-IV-TR). I criteri diagnostici per il GAP richiamano sia quelli tipici dei Disturbi da uso di sostanze (DUS) sia quelli che caratterizzano i disturbi compulsivi (in particolare, quelli del Disturbo ossessivo compulsivo [DOC]).

I termini *compulsività* e *impulsività* vengono di norma utilizzati in maniera interscambiabile per definire le difficoltà nel controllo del comportamento che determinano la messa in atto di condotte psicopatologiche in maniera ripetuta e persistente; tuttavia, con essi si fa riferimento a due costrutti distinti. Per compulsività si intende la "tendenza a mettere in atto comportamenti ripetitivi in modo automatico o stereotipato, al fine di prevenire eventuali conseguenze negative, che determina compromissione del funzionamento"; d'altro canto, l'impulsività viene generalmente descritta come la "predisposizione a reagire a stimoli interni o esterni in maniera rapida e non pianificata, prestando scarsa considerazione a ciò che di negativo può derivare, per sé e per gli altri, dall'esecuzione di tali azioni".

Nella fenomenologia del GAP sono coinvolte caratteristiche sia compulsive che impulsive; vari autori hanno indagato tali aspetti avvalendosi primariamente di strumenti quali l'osservazione clinica e la somministrazione di questionari di autovalutazione. Sulla base della letteratura, il GAP può essere concettualizzato sia

come un disturbo appartenente allo *spettro compulsivo-impulsivo*, sia come una *dipendenza comportamentale*. Entrambi questi quadri teorici sono stati presi in considerazione per la futura categorizzazione del GAP all'interno del DSM-5: comprendere quale sia il migliore è fondamentale da un punto di vista diagnostico. Sebbene i due approcci non siano mutualmente esclusivi, infatti, adottare l'uno piuttosto che l'altro ha importanti risvolti a livello clinico.

Di recente si è riconosciuta la necessità di integrare indicatori di tipo sia fenotipico (i.e. fenomenologici) sia endofenotipico (i.e. comportamentali/fisiologici) nel corso dell'*assessment* psicodiagnostico. Gli *endofenotipi* sono delle misure del funzionamento neuropsicologico, neurofisiologico e biochimico dell'individuo; di conseguenza, anomalie riscontrabili a livello endofenotipico riflettono la presenza di una compromissione nei processi cognitivi sottostanti. E' stato suggerito che la presenza di *deficit* in due funzioni esecutive mediate dalla corteccia prefrontale, quali l'abilità di inibizione della risposta motoria e l'abilità di presa di decisione, sia implicata nelle difficoltà di auto-regolazione comportamentale (i.e., comportamenti compulsivi e impulsivi) che caratterizzano particolari categorie di individui. Da questo punto di vista, i comportamenti di tipo compulsivo e impulsivo sarebbero da intendersi come: a. la conseguenza dell'emissione di una risposta precoce, messa in atto prima che uno specifico stimolo sia stato completamente processato, o il fallimento nell'inibizione di una risposta già iniziata; oppure b. la presenza di processi decisionali disfunzionali, che persistono indipendentemente dal fatto che le conseguenze del comportamento attuato siano negative o non ottimali. Per tale motivo, misure cognitive delle abilità di inibizione della risposta motoria e di presa di decisione potrebbero rappresentare promettenti indicatori endofenotipici della regolazione comportamentale; è stato infatti

ipotizzato che le problematiche comportamentali manifestate da giocatori d'azzardo, pazienti con DOC e individui con DUS siano legate alla presenza di *deficit* in tali funzioni.

La presente tesi di dottorato è stata realizzata sulla base di queste considerazioni, e alla luce del fatto che un confronto diretto tra giocatori d'azzardo, pazienti con DOC e individui con DUS possa rappresentare una via percorribile al fine di identificare la classificazione diagnostica più adatta per il GAP.

Un gruppo di pazienti con GAP è stato messo a confronto con un gruppo di pazienti con DOC, un gruppo di dipendenti da alcol e uno di individui sani avvalendosi sia di questionari di autovalutazione che di prove cognitive atte a valutare compulsività e impulsività. Gli obiettivi principali erano l'indagine di somiglianze e differenze tra i tre gruppi clinici in tali dimensioni, e l'analisi degli di stili di risposta di ciascun gruppo alle prove cognitive. Per misurare l'abilità di inibizione della risposta motoria è stato impiegato un paradigma Go/Nogo, mentre per valutare i processi di presa di decisione si è utilizzato l'Iowa Gambling Task (IGT).

Inoltre, i dati relativi a prove *self-report* e cognitive di un piccolo gruppo di giocatori d'azzardo sono stati confrontati con quelli ottenuti da un gruppo di *croupier*. Il gioco d'azzardo rappresenta l'attività principale per entrambe le categorie di individui; inoltre, è stato riscontrato che i *croupier* hanno un rischio di sviluppare condotte di gioco d'azzardo problematico o patologico maggiore rispetto a quello rilevato nella popolazione generale. Di conseguenza, esaminare caratteristiche di compulsività e impulsività in tale gruppo di individui può rivelarsi utile al fine di individuare i fattori potenzialmente coinvolti nello sviluppo del disturbo.

I risultati principali hanno evidenziato maggiori livelli sia di compulsività che di impulsività nei pazienti con GAP rispetto ai controlli sani. Inoltre, i tre gruppi clinici si sono caratterizzati per punteggi molto simili tra loro nei questionari di autovalutazione, sia rispetto alle caratteristiche compulsive che a quelle impulsive. I tre gruppi clinici non hanno dimostrato la presenza di *deficit* nell'abilità della risposta motoria. Per quanto riguarda i processi di presa decisionale, invece, i pazienti con GAP e i dipendenti da alcol hanno mostrato una prestazione complessivamente deficitaria rispetto ai controlli sani, mentre nei pazienti con DOC non si sono riscontrate difficoltà. La prestazione dei giocatori d'azzardo e dei dipendenti da alcol si è caratterizzata per un declino verso la fine della prova, il che è indicativo della presenza di *deficit* nei processi di mantenimento dell'apprendimento: entrambi i gruppi tendono quindi a preferire le scelte svantaggiose a quelle vantaggiose.

Dal confronto tra pazienti con GAP e *croupier* è emerso che i primi si caratterizzavano per la presenza di compulsività rispetto agli individui sani, mentre i secondi non hanno mostrato differenze rispetto ai controlli. Sia i giocatori che i *croupier* hanno invece riportato punteggi di impulsività auto-riferita comparabili e significativamente superiori rispetto a quelli ottenuti dal gruppo di controllo. Rispetto alle prove cognitive, i tre gruppi hanno ottenuto prestazioni simili. Tuttavia, l'analisi dei profili di apprendimento all'IGT ha evidenziato come i pazienti con GAP abbiano conseguito una prestazione tendenzialmente deficitaria rispetto agli altri gruppi; inoltre i *croupier*, a differenza dei controlli sani, non hanno mostrato un miglioramento nell'ultimo blocco della prova. Ciononostante, tali differenze non raggiungono la significatività statistica.

Sulla base dei presenti risultati, è possibile trarre alcune conclusioni.

In primo luogo, quanto emerso dalla somministrazione dei questionari di autovalutazione suggerisce che sia l'ipotesi dello spettro compulsivo-impulsivo, sia la concettualizzazione del GAP come dipendenza comportamentale potrebbero essere adeguate ai fini della categorizzazione del disturbo: infatti, caratteristiche di compulsività e impulsività coesistono nei pazienti con GAP. Inoltre, le numerose somiglianze riscontrate tra pazienti con GAP, individui con DOC e dipendenti da alcol forniscono ulteriore sostegno alla possibilità di includere queste tre condizioni in un medesimo spettro di disturbi.

D'altro canto, i risultati ottenuti tramite l'IGT hanno messo in luce che giocatori d'azzardo e dipendenti da alcol si caratterizzano per *deficit* analoghi. Ciò è in linea con i dati di letteratura, che riportano la presenza di simili alterazioni nel funzionamento dei circuiti cerebrali sottostanti all'abilità di presa di decisione in queste due categorie cliniche; da questo punto di vista, quindi, classificare il GAP come una dipendenza potrebbe essere più appropriato. I dati emersi dal confronto tra pazienti con GAP e *croupier* sembrano inoltre in linea con tale ipotesi, dal momento che alcuni dei probabili fattori di vulnerabilità per le dipendenze (personalità impulsiva e processi di presa decisionale potenzialmente alterati) sono stati osservati anche in una categoria di individui sani particolarmente a rischio di sviluppare il disturbo. Tuttavia, data la scarsa numerosità campionaria, questo risultato è da intendersi come puramente preliminare; è auspicabile che ulteriori indagini vadano ad approfondirne la validità.

Quanto emerso dal presente lavoro consente pertanto di affermare che entrambe le classificazioni proposte sono appropriate, a seconda che si utilizzino indicatori fenotipici o endofenotipici. La conduzione di altri studi si rende necessaria, al fine di chiarire quale sia la categoria diagnostica migliore per l'inquadramento del GAP.

Abstract

Pathological gambling (PG) is a chronic and progressive condition, defined as "persistent and recurrent maladaptive gambling behaviour"; it is currently classified among the Impulse control disorders (Not Elsewhere Classified) in the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition - Text Revision (DSM-IV-TR). The diagnostic criteria for PG resemble those of both Substance use disorders (SUDs) and Compulsive disorders (in particular, Obsessive compulsive disorder [OCD]).

The terms *compulsivity* and *impulsivity* are interchangeably used to describe difficulties in self-control leading to repetitive psychopathological behaviours; nonetheless, they represent two distinct constructs. Compulsive behaviours are driven by "a tendency to perform unpleasantly repetitive acts in a habitual or stereotyped manner to prevent perceived negative consequences, leading to functional impairment", whereas impulsivity has been described as "a predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences of these reactions to the impulsive individual or others". Features of both compulsivity and impulsivity are involved in PG phenomenology, and a large body of literature investigated these aspects mainly making use of clinical observation and results obtained through self-report questionnaires. PG can be conceptualized as a *compulsive-impulsive spectrum disorder* or as a *behavioural addiction*: these two theoretical frameworks have been proposed for PG categorization in DSM-5, thus and understanding which of them is better suited to PG symptoms is relevant for diagnostic

classification issues. Although these two approaches are not mutually exclusive, adopting one rather than the other has important clinical implications.

Recently, the importance of integrating phenotypic (i.e. phenomenological) and endophenotypic (i.e. behavioural/physiological) indicators in psychodiagnostic assessment has been highlighted. *Endophenotypes* are measures of the individual neuropsychological, neurophysiological and biochemical functioning, and consequently anomalies in endophenotypes are supposed to reflect impairments in the underlying neurocognitive processes. Impairments in motor inhibition ability and difficulties in delaying gratification and decision making, which are prefrontally-mediated cognitive functions, have been suggested to underlie problems in behavioural regulation (i.e. compulsive and impulsive behaviours). From this perspective, both compulsive and impulsive behaviours would represent: a. the performance of an action before its complete processing or the failure of interrupting already activated actions; b. a dysfunction in behavioural choices, which are perpetrated despite bad consequences for the individual. Therefore, cognitive measures of motor inhibition and decision making abilities may represent promising endophenotipic indicators of behavioural regulation, and deficits in these functions are hypothesized to underpin PG, OCD, and SUDs.

The present dissertation was conducted in the light of these considerations, and following the recommendation that directly comparing PGs with OCD patients and individuals with SUDs can represent a viable way to identify the most suitable classification for PG.

A group of treatment-seeking PGs was compared with patients with OCD, Alcohol dependents (ADs) and healthy controls (HCs) on both self-report

questionnaires and cognitive measures of compulsivity and impulsivity. The main aims were to investigate similarities and differences between clinical groups in such measures, as well as potentially different patterns of response in cognitive tasks. The Go/Nogo task was used to assess motor inhibition ability, whereas the Iowa Gambling Task (IGT) was administered to evaluate decision making processes.

A preliminary comparison between small groups of PGs and croupiers on the same measures was also conducted; croupiers were chosen as gambling represents a relevant activity for both groups of individuals, and also in the light of the higher risks of developing problem or pathological gambling observed in casino employees than in general population. Consequently, the study of compulsivity and impulsivity in croupiers may be helpful in identifying the factors potentially involved in the development of PG.

The main results showed that PGs reported higher levels of both self-reported compulsivity and impulsivity than healthy individuals. Furthermore, a number of similarities between PGs, OCD patients and ADs in the phenotypic measures of both dimensions was observed. No evidence of impaired motor inhibition ability in PGs, OCD patients or ADs emerged. In regards to decision making processes, deficits in the IGT performance were found in PGs and ADs, whereas OCD patients did as good as HCs. Both PGs and ADs were characterized by a decline of their performance towards the end of the task, which indicated difficulties in the maintenance of learning to shift from disadvantageous to advantageous decisions.

The comparison between PGs and croupiers revealed that the former obtained higher scores on measures of compulsivity, whereas the latter did not differ from HCs. However, both PGs and croupiers reported similar and higher self-reported impulsivity

than HCs. As regards the cognitive tasks, no significant difference between groups emerged; nonetheless, IGT profiles of learning showed that PGs had a poor performance and croupiers differed from HCs in that they did not improve in the last block of the task.

Several conclusions may be drawn from present results.

First of all, data from self-report measures suggest that both the compulsive-impulsive spectrum hypothesis and the behavioural addiction one might be adequate for PG categorization, as compulsivity and impulsivity co-occur in PGs. Furthermore, the numerous analogies emerged between PGs, OCD patients and ADs further support to include the three of them in a common spectrum of disorders.

On the other hand, IGT findings highlighted the presence of similar deficits in PGs and ADs. This result is in line with literature reporting dysfunctions in the brain circuitry underlying decision making ability, and therefore it supports the conceptualization of PG as an addictive disorder. Data emerged from the comparison between PGs and croupiers seem also to be consistent with this hypothesis, as probable vulnerability factors for addictions (i.e. impulsivity personality trait and potentially altered decision making processes) have been observed also in healthy individuals at risk for the development of PG. However, given the small samples sizes further studies are recommended.

To conclude, results from the present dissertation indicate that both classifications are equally appropriate for PG, depending on the adopted indicators. Other studies are required to further clarify which is the best diagnostic category for PG.

Contents

Part I- Literature review

Chapter 1

Pathological gambling

1.1. Diagnostic and clinical aspects

1.1.1. Diagnosis

Pathological gambling (PG) is defined as "persistent and recurrent maladaptive gambling behaviour" (American Psychiatric Association [APA], 1994) and is a chronic and progressive condition, which was first recognized as a psychiatric disorder in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; APA, 1980). In the DSM-III it was classified among the Impulse control disorders (Not Elsewhere Classified), and it maintained this categorization also in the next Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV; APA, 1994) and Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition - Text Revision (DSM-IV-TR; APA, 2000).

The Impulse control disorders (i.e. PG, Trichotillomania, Kleptomania, Pyromania, and Explosive-Intermittent Disorder) are grouped together in the light of a common essential feature, that is the failure to resist an impulse, urge, or temptation (APA, 2000). The diagnostic criteria for PG (Table 1.1) were modeled on those for Substance use disorders (SUDs), because of the observed phenomenological similarities between PG and SUDs (Lesieur & Rosenthal, 1991): for example, criterion A.2 clearly reflects the phenomenon of "tolerance" characterizing SUDs, criterion A.3 refers to

"relapse", whereas criterion A.4 is related to the "withdrawal syndrome". Growing evidence supporting the addictive nature of PG have been recently reported (for a detailed review, see paragraph 2.4), and "Gambling Disorder" has been proposed to be reclassified into the "Substance Use and Addictive Disorders" category in the DSM-5 (APA, 2012).

Table 1.1. DSM-IV-TR diagnostic criteria for PG (Code 312.31).

A. Persistent and recurrent maladaptive gambling behaviour as indicated by five (or more) of the following:
1. is preoccupied with gambling (e.g., preoccupied with reliving past gambling experiences, handicapping or planning the next venture, or thinking of ways to get money with which to gamble)
2. needs to gamble with increasing amounts of money in order to achieve the desired excitement
3. has repeated unsuccessful efforts to control, cut back, or stop gambling
4. is restless or irritable when attempting to cut down or stop gambling
5. gambles as a way of escaping from problems or of relieving a dysphoric mood (e.g., feelings of helplessness, guilt, anxiety, depression)
6. after losing money gambling, often returns another day to get even ("chasing" one's losses)
7. lies to family members, therapist, or others to conceal the extent of involvement with gambling
8. has committed illegal acts such as forgery, fraud theft, or embezzlement to finance gambling
9. has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling
10. relies on other to provide money to relieve a desperate financial situation caused by gambling
B. The gambling behavior is not better accounted for by a Manic Episode.

It is to note that some of the DSM-IV-TR criteria for PG also resemble those of "compulsive disorders", i.e. the preoccupation with gambling (criterion A.1) recalls the obsessive thoughts typically reported by individuals suffering from Obsessive compulsive disorder (OCD); moreover, gambling may be performed as a means to cope with negative feelings (criterion A.5): the same mechanism underlies the development and maintenance of compulsions (an in-depth description of compulsive aspects of PG is provided in paragraph 2.1).

The DSM-IV-TR diagnostic criteria also take into account all the psychosocial problems deriving from pathological gambling behaviours, including marital and financial problems, impaired occupational functioning (i.e. absenteeism, job loss, poor performance), and resort to illegal acts.

Criterion B highlights the importance of distinguishing PG from gambling secondary to mania, as the phenomenon of "chasing losses" can be observed also in individuals with Bipolar disorder (during manic episodes).

Furthermore, differential diagnosis of PG includes a distinction between "pathological" and "social" gambling (that is, individuals no longer gamble after the occurrence of adverse consequences) and suggests to verify whether individuals also suffer from Parkinson's disease, as pathological gambling behaviours have been recognized as one of the side effects of dopamine agonist administration (Grant & Odlaug, 2010).

1.1.2. Co-occurring disorders

PG frequently occurs in comorbidity with SUDs (Kessler et al., 2008), in particular with alcohol (Cunningham-Williams, Cottler, Compton, & Spitznagel, 1998; Gerstein et al., 1999; Petry, Stinson, & Grant, 2005; Welte, Barnes, & Wieczorek, 2001) and tobacco dependence (Crockford & el-Guebaly, 1998; Grant & Potenza, 2005). Also anxiety (Black & Moyer, 1998; Petry et al., 2005) and mood disorders (Grant & Kim, 2001; Petry et al., 2005; Rømer Thomsen, Callesen, Linnet, Kringelbach, & Møller, 2009; Kennedy et al., 2010) are quite common in pathological gamblers (PGs), and high rates of attempted/completed suicide are reported (Ledgerwood & Petry, 2004). Among personality disorders, Obsessive compulsive, Paranoid, and Antisocial are the more prevalent within individuals suffering from PG (Petry et al., 2005). Lastly, PGs generally report reduced quality of life (Grant & Kim, 2005) and severe health problems, especially cardiac and liver diseases (Morasco & Petry, 2006; Morasco, Vom Eigen, & Petry, 2006).

1.1.3. The progression of Pathological gambling

Lesieur and Rosenthal (1991) provided a descriptive definition of the main phases characterizing the "career" of the pathological gambler, based on the original model by Custer (1982). PG cannot be intended as a homogenous disorder (see paragraph 1.3.6); nonetheless, its clinical course is similar across sufferers and four main stages have been identified:

1) The "winning" phase. Males are more likely to endorse this phase. Early wins, generally a "big one", strongly foster individuals in engaging with gambling; wins are attributed to personal ability rather than to chance, and individuals experience

increased self-esteem and a sense of power and omnipotence. Thoughts about potential future wins and success are quite frequent in this phase; time is increasingly devoted to gamble at the expense of family and friends. In case of losses, experienced as threats for their self-esteem, individuals start to "chase" them to the point that "chasing losses" becomes a proper obsession. A vicious circle leads gamblers to the next phase.

2) The "losing" phase. Losses are unexpected, intolerable, and attributed to bad luck; "chasing" is the predominant aspect in this stage. In the attempt to win back losses, gamblers begin to bet and lose higher and higher amounts of money; they start to ask for money in order to pay creditors, intimate relationships become difficult and family members accept to pay debts in return for the promise to stop gambling.

3) The "desperation" phase. The individual may engage with illegal activities, i.e. frauds, embezzlements, thefts, bad cheques, in order to pay debts: these acts are conceived as "short-term" strategies with the idea that an oncoming win will solve the situation. Problems with sleep and food, as well as severe troubles with family members and public authorities lead the gambler to think about leaving and starting a new life or, more frequently, about suicide.

4) The "giving up" phase. Hopelessness is the essential feature of this phase: gamblers realize that they will never be able to stop, and they no longer care. They are only interested in gambling, no matter if they will lose. After this phase PGs, especially those encouraged and supported by their family members or friends, can start to think about seeking treatment and trying to reorganize their own lives (Custer, 1982; Lesieur & Rosenthal, 1991).

1.2. Epidemiology and gender differences

The precise prevalence rate of PG is still unknown, as only a scarce number of large studies has been conducted to date (Kallick, Suits, Deilman, & Hybels, 1979; Gerstein et al., 1999; Petry et al., 2005; Welte et al., 2001); the different instruments adopted to establish a diagnosis of PG and the diverse time frames characterizing those studies further complicate the identification of the exact prevalence of the disorder (Grant & Odlaug, 2010). In the United States population, prevalence is estimated around 1% (Petry et al., 2005); rates ranging from .42% to 5.45% have been reported with respect to various forms of disordered gambling (i.e. PG and problem gambling).
In Italy, problem gambling prevalence has been found to vary between the .7% (EURISPES, 2009) and the 1.2% (EURISPES, 2007), but no systematic prevalence study has been conducted to date.

The onset of the disorder is generally in adolescence or in early adulthood (especially in men; Ibanez, Blanco, De Castro, Fernandez-Piqueras, & Saiz-Ruiz, 2003a; Shaffer, Hall, & Vander Bilt, 1999); rates tend to decrease in older adults and spontaneous recovery is frequent. The course is characterized by periods of abstinence and relapse (Grant & Potenza, 2004; Slutske, 2006). PG is more frequent among males than females (males:females ratio = 2:1; Petry, 2006; Potenza, 2006). Women usually engage in the addictive behaviour at a later age than men, but the progress to problematic levels is more quick ("telescoping"; Potenza, 2006; Potenza, Koran, & Pallanti, 2009). Male gamblers are more likely to show antisocial personality traits, substance abuse, and marital problems than female gamblers (Grant & Odlaug, 2010); furthermore, men tend to prefer "strategic" types of gambling (i.e. sports betting,

blackjack) than women, and this difference has been attributed to higher levels of sensation-seeking behaviours potentially characterizing the former (Potenza et al., 2001b; Vitaro, Arseneault, & Tremblay, 1997). Lastly, women usually report to gamble for self-regulatory purposes (i.e., reducing stress or bad mood), whereas men generally do not perform gambling behaviours to obtain such a relief (Grant & Kim, 2001; Ladd & Petry, 2002; Potenza et al., 2001b).

1.3. Etiology

Johansson, Grant, Kim, Odlaug and Götestam (2009) critically reviewed all the literature pertaining the risk factors for PG; they concluded that those most well-established comprise: a. demographic factors, in particular young age and male gender; b. cognitive distortions; c. sensory characteristics, specifically a preference for speed and sound (typical of slot machines or video lottery terminals); d. schedules of reinforcement; e. delinquency and illegal acts.

The main etiological factors potentially involved in PG are discussed as follows.

1.3.1. Genetics

Results from family studies generally agree in demonstrating that first-degrees relatives of PGs are more likely to show PG that first-degrees relatives of unaffected individuals (Black, Monahan, Temkit, & Shaw, 2006; Ibanez, Blanco, & Saiz-Ruiz, 2002), and that people with PG are more likely to have an affected parent (Gambino, Fitzgerald, Shaffer, Renner, & Courtage, 1993). Genetics studies also support the notion

of a possible genetic transmission of PG (Eisen et al., 1998; Winters & Rich, 1998). Further evidence in regards to genetics are discussed in Chapter 2 (2.3 and 2.4).

1.3.2. Neurobiology

Neurotransmitters. Studies on neurotransmitter systems have mainly focused on noradrenalin (related to aspects of arousal), serotonin (linked to impulsivity and behavioural control) and dopamine (associated with reward and reinforcements). Increased noradrenalin function (Bergh, Eklund, Sodersten, & Nordin, 1997; Potenza, 2008; Roy et al., 1988) and decreased serotonin function (Nordin & Eklundh, 1999; Potenza, 2008) have been found. Mixed and unclear results regarding the alterations in dopamine function (increased vs decreased levels) have been reported (Bergh et al., 1997; Meyer et al., 2004; Potenza, 2008); studies on PG consequent to treatments with dopamine agonist medications in Parkinson's disease further support the involvement of this neurotransmitter in PG (Voon et al., 2007; Weintraub et al., 2006).

Neurocircuitry. To date, a scarce number of neuroimaging studies have been conducted to investigate potential alterations in cerebral structures in regards to PG. Potenza et al. (2003b) observed that PGs, compared with control subjects, showed a decreased activation in the frontal and orbitofrontal (OFC) cortex, in the caudate, in the basal ganglia, and thalamus after viewing gambling scenarios. Moreover, a diminished activation of the ventromedial prefrontal cortex (vmPFC) was observed in correspondence of the viewing of intense gambling cues. Another study (Potenza et al., 2003a) also found a decreased activation of the vmPFC in PGs when performing a task assessing cognitive control. Reuter et al. (2005) compared PGs and healthy individuals in a task simulating gambling and reported that the former were characterized by a

deactivation of the right ventral striatum during wins and by a deactivation in the vmPFC. Another study highlighted that PGs showed an increased activation of the right dorsolateral PFC, right parahippocampal gyrus and left occipital cortex when exposed to gambling cues (Crockford, Goodyear, Edwards, Quickfall, & el-Guebaly, 2005). Lastly, Hollander et al. (2005) reported higher activations in the cingulate gyrus, the putamen, the prefrontal areas and the primary visual cortex in PGs playing a computerized blackjack, especially associated with monetary rewards. Studies assessing the relationship between impaired decision making ability and cerebral function in PG suggested that alterations in the vmPFC (Clark et al., 2008), ventral striatum (Li, Lu, D'Argembeau, Ng, & Bechara, 2010), anterior cingulate cortex (Campbell-Meiklejohn, Woolrick, Passingham, & Rogers, 2008; Dalley, Everitt, & Robbins, 2011), and insula (Clark et al., 2008; Clark, Lawrence, Astley-Jones, & Gray, 2009) function may be involved in PG phenomenology.

Overall, these results suggest the participation of diverse circuitries in PG, such as the *reward circuitry* (ventral striatum, especially the nucleus accumbens*)*, the *motivational circuitry* (PFC, thalamus, basal ganglia), the *memory circuitry* (hyppocampus), and the *executive control circuitry* (OFC and PFC).

Further evidence in regards to neurobiology are discussed in Chapter 2 (2.3 and 2.4).

1.3.3. Behavioural factors

The mechanisms of classical and operant conditioning have been claimed to play a crucial role in both enhancing the engagement in gambling behaviours and

establishing habitual patterns of gambling (Blaszczynski & Nower, 2002). The main implications are discussed as follows.

Classical conditioning. Gambling is generally associated with increased physiological arousal; the environmental cues typically related to gambling behaviours (flashing lights, loud noises, the chime of coins) easily become conditioned stimuli, thus stimulating physiological arousal and the urge of gamble (Clark, 2010).

Operant conditioning. The operant mechanisms influence the performance of gambling behaviours even more strongly than the classical ones:

- The main positive reinforcement involved in PG is obviously money. Moreover, other typologies of stimuli have been identified as highly rewarding for PGs, and thus as potentially implicated in the onset and maintenance of gambling behaviours (McCown & Chamberlain, 2000): a. social stimuli (socializing with people sharing the same interests); b. material values (for example, drinks for free generally served in casinos); c. environmental stimuli (pleasant auditory and visual stimuli); d. cognitive stimuli (the "near-misses");
- Early and big wins are highly rewarding and drive the individual to gamble again and again (Johansson et al., 2009);
- Intermittent wins are generally allocated on a variable ratio: this intermittent reinforcement/reward schedule of reinforcement is particularly resistant against extinction and is capable of generating states of physiological arousal, thus it seems to be crucial in the development of PG (Blaszczynski & Nower, 2002; Johansson et al., 2009).
- Negative reinforcement principles are involved in the maintenance of gambling behaviours as negative affects, such as boredom, distress, anxiety or depressive states,

are relieved by the exciting nature of gambling (Blaszczynski & Nower, 2002; Clark, 2010). Furthermore, once the habit is established, resisting the urge to gamble causes aversive emotions; at that point, compulsive gambling is performed in order to reduce such a distress (Blaszczynski & Nower, 2002).

1.3.4. Cognitive factors

Cognitive models of PG highlight the importance of cognitive biases, i.e. cognitive distortions, irrational beliefs, and erroneous perceptions, in the development and maintenance of the disorder (Ladouceur & Walker, 1996; Toneatto, Blitz-Miller, Calderwood, Dragonetti, & Tsanos, 1999). Experimental psychology extensively demonstrated that humans generally show difficulties in processing probability and randomness (Tversky & Kahneman, 1971); therefore, they are prone to develop such cognitive biases which are typically further promoted by the characteristics of gambling games (Clark, 2010). The two main cognitive errors displayed by PGs regard (Ladouceur, 2004; Toneatto & Gunaratne, 2009): a. gambling outcomes can be controlled by the gambler (primary illusory control); b. gambling outcomes are predictable by the gambler (secondary illusory control). Cognitive distortions enhance the probability of developing a series of irrational beliefs mainly concerning: a. *illusion of control* (over-confidence in personal control over the gambling; gambling is intended as a game of skill rather than as a game of chance); b. *illusory causalities and correlations* (unrelated events are thought to be associated); and c. *interpretative biases* (attributional biases, i.e. attributing wins to dispositional factors, such as own skills).

The "Gambler's Fallacy" and the "Near-miss effect" are two examples of phenomena based on the illusion of correlation. The first one consists in the belief that a

win is more likely (or "due") after a long series of losses; the second one refers to the temporal proximity between a loss and a win, which is particularly salient to the gambler who perceive him/herself to be constantly nearly winning (Griffiths, 1991). Both these erroneous beliefs lead the gambler to go on with the gambling, as they give him/her the perception of being mastering the game (Clark, 2010).

Illusions of personal control and illusionary correlations give reason of the superstitions characterizing PGs (Jacobsen, Knudsen, Krogh, Pallesen, & Molde, 2007). Superstitions have been classified as follows (Toneatto & Gunaratne, 2009):

- talismanic superstitions, that consist in believing that specific objects are associated with good luck and therefore enhance the chance of winning;
- behavioural superstitions, relying on the belief that performing certain ritual behaviours will help in positively affecting the gambling outcomes;
- cognitive superstitions, referring to the belief that certain mental states can play a role in increasing the chance of winning (i.e. optimism, prayer), and to the existence of "hot" and "cold" numbers.

The most common interpretative biases characterizing PGs include: a. the evidence that past wins are more easily recalled than past losses (the flashing lights and loud noises generally accompanying wins probably mediate this memory bias; Clark, 2010); b. the idea of having a "winning tendency" mainly due to early wins (which determine high expectancies of winning) and to relatively recurrent past wins (Jacobsen et al., 2007); and c. the "hindsight bias", that is attributing a loss to a wrong decision, which could have been avoided (Toneatto & Gunaratne, 2009).

1.3.5. Social factors

Poor economic conditions, low socio-economic status and delinquency have been identified among the social factors potentially involved in the development of PG (Vitaro, Brendgen, Ladouceur, & Tremblay, 2001; Welte, Barnes, Tidwell, & Hoffman, 2008). Furthermore, widowed and divorced individuals (Petry et al., 2005), as well as people who started to approach gambling in early life (Kessler et al., 2008), are more likely to develop problems with gambling. Lastly, increased rates of PG seem to be associated with increased availability and legalization of gambling activities (Crockford & el-Guebaly, 1998).

1.3.6. An integrate model: The Pathway Model of Gambling

The model proposed by Blaszczynski and Nower (2002) represents an attempt to integrate neurobiological, personality, developmental, cognitive, behavioural and environmental factors, with the aim of providing a conceptual framework capable of explaining the onset and the course of PG. The basic idea is that PG is a heterogeneous disorder: common ecological, behavioural and cognitive processes underlie gambling behaviour but, depending on the involved pathway, three different subtypes of PGs can be identified. These distinct typologies differ in regards to demographic features, vulnerability factors and etiological processes.

The main common variables refer to: a. Availability and access to gambling; such a factor guarantees the social acceptance of gambling and incentives individual to gamble; b. Classical and operant conditioning; c. Cognitive distortions.

The three subtypes identified by Blaszczynski and Nower (2002) are supposed to lay on a severity continuum in the light of specific vulnerability factors. The model

posits that, starting from similar ecological factors, gambling can proceed through one of the three postulated pathways; at the end, the conditioning processes and the distorted cognitions act so that habituation, chasing and gambling behaviours appear phenomenologically similar across the diverse subtypes.

The "Behaviourally conditioned problem gamblers" constitute the less severe subtype. They are not characterized by premorbid psychological problems or vulnerabilities, and their behaviour is mostly affected by the influence of both conditioning processes and distorted cognitions. They can start to gamble at any age, and gambling is performed for socialization (they go to gamble with family members or friends). The loss of control over behaviour is generally a transient state, and the course of PG is characterized by an alternation of regular/heavy gambling. Negative affects, such as anxiety or depression, may be present as a consequence of the pathological behaviour. Individuals included in this category are generally motivated to enter treatment and show good compliance.

The "Emotionally vulnerable problem gamblers" are characterized by premorbid anxiety or mood disorders, impaired coping and problem solving abilities and generally report a negative personal history. Their emotional instability is attributed to both biological and psychological vulnerabilities. These PGs perform gambling behaviours as self-regulatory strategies, in order to escape from negative affects or to increase subjective arousal. They are more resistant to treatment, because of the positive and negative rewards associated with gambling.

The "Antisocial impulsivist problem gamblers" represent the most disturbed and severe subtype of PGs. They are characterized by both biological (i.e. neurological or neurochemical dysfunctions), and psychological (i.e. high levels of impulsivity and

antisocial personality disorder) vulnerabilities. They generally show a series of behavioural problems in addition to gambling, such as substance abuse (particularly alcohol) and criminal behaviours; their impulsivity is generally worsened by co-occurring negative emotions. The onset of PG is typically earlier than in the other two subtypes and the course is characterized by binge episodes. Motivation and compliance to treatment are particularly low.

1.4. Treatment

1.4.1. Psychological treatments

Behavioural therapy. The main behavioural techniques adopted with PGs deal with the identification of gambling triggers and the development of rewarding activities alternative to gambling (Grant & Odlaug, 2010). Imaginal desensitization (i.e. aimed at resisting/reducing the urges to gamble) has been demonstrated to be an effective strategy (McConaghy, Armstrong, Blaszczynski, & Allcock, 1983; 1988; McConaghy, Blaszczynski, & Frankova, 1991), but the maintenance of positive outcomes is unclear (McConaghy et al., 1988).

Cognitive therapy. Cognitive therapy for PG includes psychoeducation, irrational cognition awareness training and cognitive restructuring (Grant & Odlaug, 2010; Toneatto, 2002; Toneatto & Gunartne, 2009). It aims at changing the patient's beliefs regarding perceived control over randomly determined events, and helps the patient understand that the laws of probability, rather than ritualistic behavior, control the outcome of gambling. The use of self-monitoring diaries is also particularly frequent

and aims to educate the patients in identifying the triggers and the consequences of gambling behaviours (Toneatto, 2002). Both individual (combined with relapse prevention; Ladouceur et al., 2001; Sylvain, Ladouceur, & Boisvert, 1997) and group (Ladouceur et al., 2003) cognitive therapy is effective in the short and in the long term.

Cognitive-behavioural therapy. Cognitive-behavioural therapy (CBT) for PG mainly consists in the integration of the cognitive and behavioural techniques previously reported, as well as the inclusion of other specific strategies either to improve treatment compliance (i.e. problem solving training, identification of the barriers to change), and to cope with daily life stressors (i.e. assertiveness training, relaxation techniques). The effectiveness of CBT in the treatment of PG has been proved by several randomized control trials (Grant & Odlaug, 2010; Potenza et al., 2009).

Motivational Interviewing. The Motivational Interviewing (Miller & Rollnick, 1991) is an empathic approach aiming to enhance patients' motivation to change their behaviours and to overcome the ambivalence typically associated with the process of change. It is generally used with individuals suffering from SUDs (Potenza et al., 2009). Several studies demonstrated its effectiveness also in PGs (Dickerson, Hinchy, & England, 1990; Hodgins, Currie, el-Guebaly, & Peden, 2004; Hodgins & Holub, 2007).

Gamblers Anonymous. Gamblers Anonymous is a 12-step program for people that have a gambling problem, modeled on the Alcoholics Anonymous; it is a self-help group where PGs may share their experience and hope with each other that they may solve their common problem and help others to recover from a gambling problem (Potenza et al., 2009). Positive effects of participation in these groups have been reported (Hodgins, Peden, & Cassidy, 2005; Petry et al., 2006).

1.4.2. Pharmacological treatments

To date, no pharmacological treatment for PG has been officially approved by the Food and Drug Administration. Nonetheless, the effectiveness of various medications has been tested and promising results have been reported. In the light of the heterogeneity of the disorder and of the different cerebral circuits involved in PG phenomenology, opioid antagonists, antidepressants, atypical antipsychotics, mood stabilizers, and glutamatergic agents have been considered as drugs potentially effective in treating PG (Grant & Odlaug, 2010).

Chapter 2

Compulsive and impulsive aspects of Pathological gambling: phenomenological features and theoretical models

To date, the terms *compulsivity* and *impulsivity* have been interchangeably used in psychiatric, neurologic and psychological literature to describe difficulties in self-control which lead to repetitive psychopathological behaviours; nonetheless, they represent two distinct constructs (Leeman & Potenza, 2012; van den Heuvel et al., 2010). Compulsive behaviours are defined as repetitive, rigid and stereotyped goal-directed actions; individuals refer to feel driven to perform them in order to prevent or reduce some uncomfortable feelings, such as anxiety and discomfort (APA, 2000). Compulsive behaviours are generally anticipated by strong urges, which individuals have difficulties to resist. OCD is the prototype of compulsive disorders; nonetheless, compulsive features have been claimed to be involved also in SUDs, Personality disorders and Schizophrenia (Goldstein & Volkow, 2002; Lubman, Yücel, & Pantelis, 2004). On the other hand, impulsivity relates to the repetitive execution of maladaptive behaviours despite the potentially negative consequences deriving from their performance; thus, impulsive acts can be intended as rapid and unplanned reactions to particular internal or external stimuli, aimed at obtaining immediate pleasure of gratification (Kertzman et al., 2008; Moeller, Barratt, Dougherty, Schmitz, & Swann,

2001). All the disorders classified among the ICDs in the DSM-IV-TR are impulsive conditions; moreover, impulsivity has been identified as a central feature of certain Personality disorders (in particular, Antisocial and Borderline), SUDs, Bipolar disorder and Attention-deficit hyperactivity disorder (Grant & Potenza, 2006).

Grant and Potenza (2006) highlighted that in psychological and psychiatric literature there is a lack of agreement in regards to the relationship between these two constructs; some authors argued that compulsive and impulsive traits may co-occur among the same psychopathology (Fineberg et al., 2010; Stein & Hollander, 1995), whereas other models tend to conceptualize them as two similar but distinct dimensions (Leeman & Potenza, 2012).

Features of compulsivity and impulsivity are involved in PG phenomenology, and different theoretical approaches based on compulsivity and impulsivity have been proposed in literature. PG can be mainly conceptualized as a *compulsive-impulsive spectrum disorder* or as a *behavioural addiction*: understanding which of these two frameworks is better suited to PG symptoms is relevant for its future diagnostic classification in the DSM-5. These two approaches are not mutually exclusive; they rather provide different ways to interpret the same compulsive and impulsive phenomenological features shown by PGs.

One of the main risks of trying to define the "most appropriate classification" is that clinical and personality psychology frequently provide circular explanations: "[…] circular explanation involves using a description of an event as an explanation of that same event […] Circular explanations tend to reify the to-be-explained performance into a property causing that same performance" (Boag, 2011, pp. 225-227). For

example, “PGs are impulsive because they act without considering the consequences of their actions”.

Nonetheless, adopting one framework rather than the other have important implications for treatment, and international literature has been working in order to identify the most adequate for PG (Potenza et al., 2009).

2.1. Pathological gambling and compulsivity

Compulsive behaviours have been described as driven by “a tendency to perform unpleasantly repetitive acts in a habitual or stereotyped manner to prevent perceived negative consequences, leading to functional impairment” (Fineberg et al., 2010, p. 591), or as “actions inappropriate to the situation which persist, have no obvious relationship to the overall goal and which often result in undesirable consequences” (Dalley et al., 2011; p. 680). Thus, three critical components seem to be involved in defining compulsivity: a. persistence of behaviours (perseveration); b. repetitive behaviours are goal-oriented, but often they are not logically related with the goal they aim to attain; c. performing such behaviours may result in negative consequences.

From a phenomenological point of view, the three above-mentioned aspects are clearly entailed in PGs’ behaviours. As a matter of fact: a. gambling is a repeatedly performed behaviour and individuals suffering from this disorder report difficulties in both resisting and controlling actions. Moreover, gambling-related behaviours, such as getting money to gamble or handicapping, are repetitively performed, thus reflecting problems in inhibiting behaviours (Grant & Potenza, 2006; Potenza et al., 2009); b. PGs

often report anxiety or sadness as triggers of their gambling (Potenza et al., 2003a). In this respect, gambling behaviours resemble the compulsions typical of OCD as they are performed with the aim of reducing unpleasant feelings, rather than to fulfill the purpose they are supposed to accomplish, i.e. gaining money (Grant & Kim, 2001; Ladd & Petry, 2002); c. Impairment deriving from pathological gambling is well-documented and impacts on the personal, familial and occupational functioning (Dell'Osso, Altamura, Allen, Marazziti, & Hollander, 2006; Grant & Potenza, 2004).

Other PG phenomenological features have been claimed to be related to the dimension of obsessionality/compulsivity. PGs frequently report repetitive and intrusive thoughts about gambling, similar to OCD obsessions (Grant & Potenza, 2006; Potenza et al., 2009); furthermore, gambling behaviours can be associated with obsessive thoughts, and therefore they are performed to reduce the anxiety and distress caused by obsessions (APA, 2000; van den Heuvel et al., 2010). Lastly, individuals suffering from PG often endorse rituals associated with their gambling, as gambling on certain slot machines, wearing particular clothes when gambling, carrying specific objects for good luck or betting on "good numbers"; these ritualistic behaviours are the reflection of superstitious beliefs and, as a consequence, they are believed to be capable of influencing gambling outcomes (Grant & Potenza, 2006; Jacobsen et al., 2007; Toneatto & Gunaratne, 2009).

In order to systematically verify to what extent PG compulsivity features resemble those of OCD, some studies investigating OCD symptoms and beliefs in samples of PGs (Blaszczynski, 1999; Frost, Meagher, & Riskind, 2001) or directly comparing PG and OCD patients in regards to these constructs (Anholt et al., 2004; Bottesi, Ghisi, Boz, Sica, & Sanavio, 2011a) were conducted. The self-report measures

used in these studies are questionnaires originally developed to assess OCD symptoms and beliefs:

1) The Padua Inventory (Sanavio, 1988), comprising 4 subscales measuring obsessions and compulsions: Impaired control over mental activities (assesses excessive doubting and ruminations), Washing, Checking, and Impaired control over motor activities (measures urges and worries associated with motor behaviour, i.e. violent impulses);

2) The Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989), investigates several dimensions in relation to obsessions and compulsions, i.e. time spent, interference, distress, resistance, and control associated with OCD symptoms, and provides three scores (Obsessions, Compulsions, and Total score);

3) The Obsessive Compulsive Inventory-Revised (OCI-R; Foa et al, 2002), measures the distress caused by OC symptoms. The inventory is made up of six subscales: washing, checking, ordering, obsessing, hoarding, and mental neutralizing;

4) The Obsessive Beliefs Questionnaire (OBQ; Obsessive Compulsive Cognitions Working Group [OCCWG], 1997; 2001), assessing six domains of core dysfunctional beliefs believed to play a crucial role in the onset and maintenance of OCD: Perfectionism, Inflated responsibility, Over-importance of thoughts, Control of thoughts, Overestimation of threat, and Intolerance of uncertainty.

Blaszczynski (1999) found that PGs obtained significantly higher scores on the Impaired control over mental activities and the Impaired control over motor activities subscales of the Padua Inventory than a group of healthy controls; on the contrary, no differences between groups in the Washing and Checking subscales emerged. Frost et al. (2001) compared pathological and light gamblers on the Y-BOCS and observed

higher OCD symptom severity, as measured by the three scores, in the former than in the latter. Furthermore, PGs reported more avoidance behaviours and urges to engage in violent behaviours to themselves and others than the other group.

Anholt et al. (2004) directly compared PGs and OCD patients making use of the Padua-R (a revised version of Padua Inventory; van Oppen, Hoekstra, & Emmelkamp, 1995) and the OBQ; they also included a clinical (panic disorder) and a nonclinical control group. Main results revealed that PGs showed significantly lower levels of OCD symptom severity (Padua-R) than OCD patients, whereas their scores were similar to those obtained by healthy participants; nonetheless, they reported scores similar to those of OCD patients, and significantly higher than those of the control groups, in all the OBQ domains, except for Overestimation of threat. Consistently, Bottesi et al. (2011a) found that OCD patients showed higher OCD symptom severity, as measured by the OCI-R, than both PG and healthy control groups; moreover, OCD and PG groups obtained comparable and significantly higher scores on the Perfectionism and Excessive control of thoughts subscales of OBQ-R (Dorz, Novara, Pastore, Sica, & Sanavio, 2009; Novara, Dorz, Pastore, Sica, & Sanavio, 2011) than controls.

Findings from these studies are mixed, but overall they support the presence of specific compulsive-related aspects in PGs. In particular, compulsivity features emerged in the forms of fears of losing control over both mental and physical behaviour and dysfunctional cognitive beliefs related to perfectionism and control of thoughts; this last result is in line with the typically present illusions of control over gambling outcomes and cognitive superstitions characterizing pathological gamblers (Toneatto & Gunaratne, 2009).

2.2. Pathological gambling and impulsivity

Impulsivity is a multifaceted construct which has been described as "a predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences of these reactions to the impulsive individual or others" (Moeller et al., 2001; p. 1784). As for compulsivity, key issues emerge from this definition: a. predisposition: impulsivity is intended as part of a complex behavioural pattern, rather than as a single action; b. lack of planning/premeditation: impulsive behaviours occur in the absence of a conscious judgment of the consequences of actions. This is a critical aspect because lack of forethought differentiates impulsive behaviours from compulsive ones, in that the latter imply planning before actions are performed (Moeller et al., 2001).

Two main dimensions underlying impulsive behaviours have been recently identified: difficulties in inhibiting/interrupting behaviours and problems involving behavioural choices, referring to more and less automatic (i.e. non conscious) processes, respectively (Dalley et al., 2011; Potenza & Wit, 2010; see chapter 3). Independent of the dimension considered, the aim of impulsive behaviours is the pursuit of reward (Leeman & Potenza, 2012).

The phenomenology of PG is clearly characterized by impulsive features: PGs show problems in self-regulating their behaviour, and specifically in inhibiting the urge for gambling (Goudriaan, Oosterlaan, De Beurs, & Van den Brink, 2007). Moreover, they continue to perform risky behaviours, i.e. gambling, despite the knowledge of having a persistent problem and the related adverse consequences (el-Guebaly, Mudry, Zohar, Tavares, & Potenza, 2011). Harm to occupation and personal/familiar

relationships (mainly due to chasing losses and laying about losses), seek a financial bailout, committing illegal acts to obtain money are some examples of negative consequences of pathological gambling (MacLaren, Fugelsgang, Harrigan, & Dixon, 2011). Lastly, gambling is considered a reward-seeking behaviour by individuals suffering from PG, who often report to gamble to achieve excitement and gratification (Blasczczynski, 1999; Grant & Kim, 2003; Schmitz, 2005); thus, endorsing gambling activities is generally ego-syntonic and hedonistic in nature for PGs, and urges to gamble are generally described as pleasurable, at least in the first phases of the disorder (Potenza et al., 2009; Stein & Lochner, 2006). All these phenomenological features clearly parallel those characterizing SUDs, and this is why PG has been suggested to be conceptualized as a behavioural addiction (Holden, 2001; Petry, 2006; Potenza, 2006). Further analogies between PG and SUD will be discussed in paragraph 2.4.

A number of studies investigated self-reported impulsivity among PGs (for a an exhaustive meta-analytical review, see MacLaren et al., 2011). Different definitions of impulsivity and compulsivity have been provided in psychological literature, and different facets of those constructs have been stressed on the basis of the adopted theoretical framework. As a consequence, several self-report measures aimed at assessing these personality features have been developed, and each of them emphasizes different constitutive dimensions of both constructs. A brief description of the main instruments employed to assess impulsive features is provided as follows:

1) The Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975), measures a general impulsivity factor (*broad impulsiveness*), which is constituted by 4 different personality traits: risk-taking, non-planning, liveliness and narrow impulsiveness. The last one refers to impulsive behaviours such as acting before

thinking or not considering both pros and cons of actions before performing them (Eysenck & Eysenck, 1977);

2) The Big Five Questionnaire (BFQ; Caprara, Barbaranelli, Borgogni, & Perugini, 1993), defines two different personality dimensions involving impulsive aspects: neuroticism, which refers to the individual's abilities of both inhibiting impulsive reactions in conflictual situations and regulating emotions and anxiety; conscientiousness, which depicts two traits involved in impulse control, i.e. scrupulosity (reliability and precision) and persistence (ability to complete tasks and commitments);

3) The Sensation Seeking Scale (SSS; Zuckerman, 1971), focuses on the construct of sensation seeking, defined as the need of novelty, various and complex sensations and experiences. Therefore, it assesses the tendency to take physical or social risks to achieve those sensations. The sensation seeking dimension comprises four personality traits: thrill- and adventure-seeking, experience-seeking, disinhibition and boredom susceptibility;

4) The Temperament and Character Inventory (TCI; Cloninger, Svrakic, & Przybeck, 1993), is quite often used to measure novelty seeking, harm avoidance, reward dependence and persistence. All these personality traits are relevant to both impulsivity and compulsivity;

5) The Barratt Impulsiveness Scale (BIS-11; Barratt, 1965; Patton, Stanford, & Barratt, 1995), measures 3 different dimensions of impulsivity: motor activation, which reflects the tendency to act without thinking; attention, referring to a lack of concentration/attention and to impulsive decision making; lack of planning, which expresses a poor orientation towards future (Patton et al., 1995).

6) The Urgency, Premeditation, Perseverance and Sensation Seeking (UPPS; Whiteside, Lynam, Miller, & Reynolds, 2005), integrates 4 dimensions of impulsivity assessed by most of the self-report measures previously described: Negative urgency; Low premeditation; Low perseverance; Sensation seeking.

In the last decade, two models of impulsivity have been developed with the aim of integrating all the dimensions investigated by these self-report measures into a whole framework: the Urgency, Premeditation, Perseverance and Sensation Seeking Model (UPPS; Whiteside & Lynam, 2001) and the Hierarchical Structural Model (HSM; Markon, Krueger, & Watson, 2005). The UPPS model comprises an empirically derived set of four dimensions of impulsivity: i) Negative urgency, reflecting the tendency towards emotionally motivated rash actions. It is associated with the Urgency facet of Neuroticism of the BFQ and the Attention scale of the BIS-11; ii) Low premeditation, which refers to the tendency to act without thinking about consequences of behaviours and is positively associated with the Eysenck Impulsivity Scale of the EPQ, the Impulsiveness scale of the TCI, and the Nonplanning scale of the BIS-11, whereas it is negatively associated with the Deliberation sub-dimension of the Conscientiousness scale of the BFQ; iii) Low Perseverance, which reflects the tendency to interrupt non-rewarded behaviours and is associated with high scores on the Boredom susceptibility scale of the SSS and with low scores on the Self-discipline facet of the Conscientiousness scale of the BFQ; iv) Sensation seeking, referring to the tendency to engage in sensation-seeking behaviours. It is associated with high scores on the Venturesomeness scale of the EPQ, the Excitement seeking facet of the Extraversion scale of the BFQ, and the Disinhibition scale of the SSS.

Differently, the HSM put together a variety of personality traits related to impulsivity, as measured by self-report questionnaires, and two measures of personality disorders: the Schedule for Nonadaptive and Adaptive Personality (SNAP; Clark, 1993) and the Dimensional Assessment of Personality Pathology (DAPP; Livesley & Jackson, 2002). Four levels of analysis of personality structure have been identified. The third one is particularly relevant to PG, as it includes personality dimensions defined Unconscientious disinhibition and Disagreeable disinhibition, and it comprises features similar to the psychological traits measured by the Neuroticism, low Agreeableness, and low Consciousness facets of the BFQ; the Harm avoidance, low Cooperativeness, and Novelty seeking of the TCI; the Neuroticism-anxiety, Agression-hostility, and the Impulsive sensation seeking dimensions of the Alternative Five model by Zuckerman, Kuhlman, Joireman, Teta and Kraft (1993).

The meta-analysis by MacLaren et al. (2011) was conducted on 44 studies which investigated impulsivity traits among PGs; they adopted the UPPS and the HSM as theoretical frameworks for literature search; therefore, they included all the studies that made use of the previously described self-report measures assessing impulsivity. Substantial effects for personality features related to the Negative Urgency and Low Premeditation factors emerged, whereas no effects for the traits associated with Low Perseverance and Sensation Seeking ones were found. Furthermore, in regards to the levels of HSM the analysis revealed significant effects for the traits associated with Unconscientious disinhibition, Disagreeable disinhibition, and Negative Affect (Neuroticism) dimensions.

To summarize, self-reported impulsivity has been demonstrated to represent a crucial personality dimension in relation to PG. Specifically, results from a broad meta-

analysis highlighted that a. acting on the spur of the moment, b. acting without thinking, and c. affective states related to neuroticism are relevant in characterizing PG personality profile. On the contrary, the psychological traits associated with sensation-seeking did not result as much important (MacLaren et al., 2011).

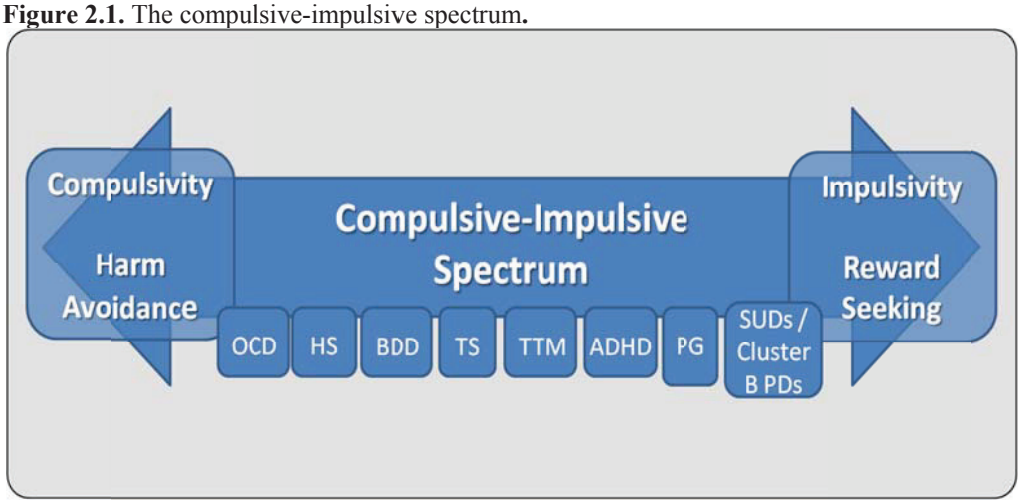
2.3. The Compulsive-impulsive spectrum hypothesis

Several authors observed that the need to perform particular behaviours in a rigid, repeated and stereotyped manner was a clinical characteristic shared by a number of psychopathological disorders; therefore, they hypothesized that these disorders could be part of a *compulsive-impulsive spectrum* and proposed a dimensional trans-nosographic model (Hollander & Wong, 1995a; 1995b; McElroy, Phillips, & Keck, 1994; Oldham, Hollander, & Skodol, 1996). In addition to phenomenological resemblances, these disorders were found to be also similar in regards to the underlying genetic, chemical, immunological, and anatomical substrates (Stein, 2000).

Compulsivity and impulsivity were defined as the two opposite poles of such a continuum; as a consequence, the disorders mainly characterized by harm and risk avoidance, increased levels of anxiety and difficulties in the inhibition of behaviours were located on the compulsive end, whereas those typified by risk and pleasure seeking, lack of control and behavioural disinhibition were located on the impulsive one (Hollander & Wong, 1995a; 1995b). The disorders originally included in this continuum were: OCD (compulsive pole), Hypochondriasis, Body dismorphic disorder, Anorexia, Depersonalization disorder, Tourette syndrome, Trichotillomania, Pathological

gambling, Hypersexuality disorder and Borderline and Antisocial personality disorders (impulsive pole). Other disorders have been hypothesized to pertain the continuum during years (i.e. van den Heuvel et al., 2010). Figure 2.1. summarizes the main disorders included in the compulsive-impulsive spectrum.

Figure 2.1. The compulsive-impulsive spectrum**.**



Note: OCD=Obsessive compulsive disorder; HS=Hypocondriasis; BDD=Body dismorphic disorder; TS=Tourette's Syndrome; TTM=Trichotillomania; ADHD=Attention deficit/hyperactivity disorder; PG=Pathological gambling; SUDs=Substance use disorders; Custer B PDs=Cluster B Personality disorders.

The relative collocation of each disorder among the continuum was based on the amount of compulsivity and impulsivity characterizing each disorder (Blaszczynski, 1999). From a neurobiological perspective, increased serotoninergic and frontal functioning were supposed to underlie OCD, while impulsive personality disorders would be related to a decreased serotoninergic and frontal functioning (Lochner & Stein, 2006). Furthermore, the disorders laying on the continuum were hypothesized to share both compulsive and impulsive features that is, compulsivity and impulsivity could be interpreted as distinct and sometimes orthogonal factors, each contributing to varying degrees across the disorders. Both compulsive and impulsive features may

occur simultaneously in the same disorder, or at different time points within the same disorder (Grant & Potenza, 2006). In other words, some OCD patients might score high both in compulsivity and impulsivity measures, whereas individuals suffering from other disorders included in the spectrum might show a reversed pattern (Fineberg et al., 2010; Lochner & Stein, 2006; Stein, 2000; Stein & Hollander, 1995).

Recent literature seems to support this perspective. For example, Ettelt et al. (2007) observed high levels of cognitive impulsiveness among OCD patients; in particular, measures of cognitive impulsiveness were associated with aggressive obsessions and checking behaviours. Furthermore, Potenza (2007) compared PGs, OCD patients and healthy controls on self-report measures and found that both clinical groups reported high levels of both impulsivity and harm avoidance. Evidence supporting the complex relationship between compulsivity and impulsivity in PG also emerged in a study by Blanco et al. (2009), which examined the changes in compulsive and impulsive features among PG individuals after 12 weeks of treatment with paroxetina; PGs were administered the Padua Inventory previous and after treatment. Results revealed significant decreases in the Impaired control over mental activities subscale (a measure of obsessionality/compulsivity), as well as in the Impulsiveness subscale of the EPQ, after treatment; furthermore, PG symptom severity after treatment was correlated only with changes in the Impulsiveness scale scores. These results suggest that compulsivity and impulsivity interact in a complex fashion, as both dimensions had relevance with respect to treatment outcome, but impulsivity emerged as more related with gambling severity (Blanco et al., 2009).

Lastly, neuroanatomical models highlighting the overlap between two distinct functional systems support the notion of the compulsive-impulsive spectrum (Fineberg

et al., 2010). In the compulsive circuit, the caudate nucleus is thought to drive compulsive behaviours, whereas the OFC would play a role in controlling and inhibiting them; in the same way, the ventral striatum/nucleus accumbens shell would drive impulsive behaviours, while the anterior cingulate/vmPFC might control and inhibit them in the impulsive circuit. These two circuits are interconnected and differentially modulated by neurotransmitters (Brewer & Potenza, 2008; Robbins, 2007). Therefore, the tendency to perform compulsive or impulsive acts is supposed to depend on anomalies in these cerebral structures: specifically, hyperactivity in the striatal components or hypoactivity in the prefrontal regions (Fineberg et al., 2010).

Some studies provided only moderate support to the inclusion of PG into the compulsive-impulsive spectrum. For example, Kim and Grant (2001) investigated novelty seeking, reward dependence, and harm avoidance traits among PG individuals, OCD patients and healthy controls: PGs reported higher levels of novelty seeking, impulsiveness, and extravagance, whereas showed less anticipatory worry, harm avoidance, and fear of uncertainty than OCD patients. The Authors concluded that the two disorders were characterized by more difference than similarities in personality traits, thus suggesting substantial differences between PG and OCD; however, they pinpointed that analyzing these results form a dimensional personality perspective may be overinclusive (Kim & Grant, 2001). Other two studies comparing PGs' and OCD patients' personality characteristics (Anholt et al., 2004; Bottesi et al., 2011a) only partially sustained the compulsive-impulsive spectrum hypothesis, in that no similarities in (symptomatic) compulsivity measures emerged. A recent meta-analytical study assessing the relationship between PG and OCD was performed with the aim to test the

validity of the compulsive-impulsive spectrum hypothesis (Durdle, Gorey, & Stewart, 2008). Comorbidity, familiarity, and prevalence issues were taken into account. In line with the compulsive-impulsive spectrum hypothesis, a strong relationship between PG and OCD traits was observed; furthermore, low effect sizes for comorbidity rates between disorders emerged, thus suggesting that the two psychopathologies are distinct but share common features. Nonetheless, no data supporting familiarity between disorders were found. In the light of these results, Durdle et al. (2008) stated that the inclusion of PG in the compulsive-impulsive spectrum was only partially supported.

Furthermore, a number of evidence in contrast with this proposal have been reported. Some argue that one of the main arguments for not including PG and OCD into the same classification is that gambling behaviours are mainly driven by the research of pleasure and gratification; therefore, PG sufferers often experience ego-syntonic feelings. On the contrary, OCD symptoms are ego-dystonic in nature, as distress and fears of harm usually motivate performing compulsions and regret and guilt frequently follow compulsive behaviours (Potenza et al., 2009).

In addition, results concerning rates of co-occurrence between PG and OCD are inconsistent: the rate of comorbid OCD in PG patients was found to range between 1% to 20% (Argo & Black, 2004); nonetheless, the St. Luis Epidemiologic Catchment Area study (Cunningham-Williams et al., 1998) failed in detecting relationships between the disorders, as an odd-ratio of .6 emerged. Also studies investigating the occurrence of PG in samples of OCD patients did not reveal important relationships between disorders: Grant, Mancebo, Pinto, Eisen and Rasmussen (2006b) found low rates of both current and lifetime prevalence of PG (.3% and 1%, respectively); rates of both current and past PG lower than 1% were observed by Hollander et al. (1997) in a

sample of 2000 OCD patients. Furthermore, two family studies (Bienvenu et al., 2000; Black, Moyer, & Schlosser, 2003) did not find associations between PG and OCD.

Genetic and neurobiological studies also provided findings mainly supporting differences rather than analogies between PG and OCD. The allelic variants of the 5HT transporter gene have been observed in both PG and OCD, but the short allele was found to be associated with PG, whereas the long one was associated with OCD (Hemmings & Stein, 2006; Ibanez, De Castro, Fernandez-Piqueras, & Saiz-Ruiz, 2003b); furthermore, several studies did not observe alterations of this allele (reviewed by Hemmings and Stein, 2006). Hyperactivity in the frontostriatal circuitry characterizes OCD (Mataix-Cols & van den Heuvel., 2006), whereas hypoactivity in the same circuitry has been observed in PG (Reuter et al., 2005; Potenza, 2006). A different involvement of the same neurotransmitters also distinguishes PG from OCD: in the former, pro-serotoninergic agents improved mood leading to euphoric states (Potenza & Hollander, 2002), whereas in the latter they worsened symptoms (Pauls, Mundo, & Kennedy, 2002). Consequently, Selective Serotonin Re-uptake Inhibitors (SSRI) are the gold standard pharmacological treatment for OCD, whereas their utility in PG is less clear (Potenza et al., 2009).

2.4. Pathological gambling as a Behavioural addiction

The term *addiction* derives from the Latin *addicere*, which means "bound to" or "enslaved by", and psychiatric and psychological literature traditionally adopted it when referring to impaired control over substance use behaviours (Maddux & Desmond, 2000). More recently, this expression has been extended to other behaviours

characterized by difficulties in behavioural regulation which lead to harmful effects; in this respect, the term *addiction* seems more appropriate than *dependence*, as it also includes the adverse consequences on individual, familiar and social spheres that are usually related to these behaviours (Potenza, 2006).

Potenza (2006) identified three core elements of addiction: a. craving states preceding behaviours; b. impaired control over behaviours; c. continued behavioural engagement in spite of negative consequences. This definition fits with the phenomenological features of PG, therefore it has been suggested to consider it as a *behavioural/nonsubstance addiction* that is, addiction to non-drug behaviours (Frascella, Potenza, Brown, & Childress, 2010; Holden, 2001; Petry, 2006; Potenza, 2006), with possible re-categorization in DSM-5 among the "Substance Use and Addictive Disorders" (APA, 2012).

A review of the main evidence supporting the idea of PG as a behavioural addiction is provided.

Phenomenology. PGs, as well as drug addicts, frequently report the occurrence of tolerance and withdrawal symptoms. Tolerance symptoms in PG consist in the need for increased intensity of gambling over time, and urges/cravings to gamble are frequently experienced while abstaining from the behaviour, thus defining a withdrawal syndrome (Blanco, Moreyra, Nunes, Saiz-Ruiz, & Ibanez, 2001; Grant, Brewer, & Potenza, 2006a). Repeated unsuccessful to control, cut back or quit gambling, as well as feeling irritable and restlessness when trying to reduce or stop the behaviours are frequently endorsed by PGs (Potenza, 2006); it is noteworthy that all these aspects are currently reported as inclusionary diagnostic criteria in the DSM-IV-TR (APA, 2000).

As previously discussed, there is evidence that PG sufferers are characterized by both impulsive and compulsive features. Differently from the compulsive-impulsive hypothesis, which posits the co-occurrence of impulsive and compulsive traits within disorders, the most recent models of addiction suggest the involvement of an "impulsivity-compulsivity shift" in addictive behaviours (Brewer & Potenza, 2008; Dalley et al., 2011; Everitt & Robbins, 2005; Fineberg et al., 2010; Potenza, 2008). This means that addictive behaviours are originally novelty/reward driven and motivated by positive reinforcement mechanisms (impulsive); later, impulsive behaviours shift to compulsivity that is, they become more habit-driven and they are performed because they are negatively rewarded (el-Guebaly et al., 2011; Leeman & Potenza, 2012). As a matter of fact, in the first stages PG symptoms are ego-syntonic in nature: pleasure, relief and gratification are the most important drives to gamble (APA, 2000). However, the motivational factors underlying gambling behaviour tend to change over time: initially, PGs gamble to earn money; later, they report to gamble "just to gamble"; finally, they need to gamble in order to reduce the urges to gamble and the associated distress (Brewer & Potenza, 2008; Chambers, Bickel, & Potenza, 2007). Therefore, PG symptomathology tends to shift towards ego-dystony, which is also due to the awareness of the difficulties in refraining from gamble, as well as the negative consequences of gambling behaviours. Nonetheless, it is worthy to note this shift from impulsive to compulsive behaviours can be differently defined as "the occurrence of compulsivity and impulsivity at different time points", as stated in the compulsive-impulsive spectrum hypothesis (Grant & Potenza, 2006).

Lastly, both PGs and drug dependents usually report high scores in self-report measures of impulsivity (Blaszczynski, Steel, & McConaghy, 1997; Potenza et al., 2003b; 2009).

Epidemiology. PG resembles SUDs also in regards to gender differences. Males are more likely to present the disorder than females: the observed men:women ratio is 2:1, which similar to that characterizing SUDs, in particular alcoholism (Petry, 2006; Potenza, 2006; Potenza, Kosten, & Rounsaville, 2001a; Potenza et al., 2001b); it is to note that the males:females ratio for OCD is lower (1:1; APA, 2000). Another commonality with alcohol dependence (AD) is the gender-related phenomenon of "telescoping" (Lynch, Roth, & Carroll, 2002; Potenza et al., 2001a; 2001b; Tavares, Zilberman, Beites, & Gentil, 2001). Furthermore, clinical course of PG and SUDs is also quite similar. Higher rates of the disorder are generally observed in adolescence and young adulthood, whereas they tend to be low in old adulthood (Chambers & Potenza, 2003; Shaffer, Hall, & Vander Bilt, 1999a; Wagner & Anthony, 2002). In particular, many people tend to spontaneously recover at later ages (Slutske, Jackson, & Sher, 2003).

Lastly, high rates of comorbidity between PG and SUDs have been found (Crockford & el-Guebaly, 1998; Grant & Potenza, 2004; McCormick, Russo, Ramirez, & Taber, 1984; Petry et al., 2005). PGs make use of more tobacco and alcohol, and are more likely to fulfill the criteria for tobacco/alcohol abuse and/or dependence, than non-gamblers (Cunningham-Williams et al., 1998; Kessler et al., 1994). For example, Petry et al. (2005) observed comorbid alcohol use disorder in 70% of PGs, whereas over 30% of PG sufferers reported a SUD. Furthermore, substance abusers frequently also suffer from PG (Petry, 2001; Spunt, Lesieur, Hunt, & Cahill, 1995).

Social factors. Similar social factors are involved in both PG and SUDs: both disorders impact a large social network, including family, friends, colleagues and social/health services (Lobsinger & Beckett, 1996; Potenza, 2006). Moreover, cultural attitudes can influence the endorsement of gambling and substance use (i.e. tobacco smoking, alcohol consumption), as they are culturally-based and socially accepted (Potenza et al., 2001a); an association between increased rates of PG and increased availability and legalization of gambling activities has been observed (Crockford & el-Guebaly, 1998).

Genetics and neurobiology. Results from a twin epidemiological study suggest a genetic link between PG and SUDs, in particular alcoholism: data from the Vietnam Era Twin registry reported that the 12-20% of genetic and the 3-8% of environmental risks for PG overlapped with those of AD (Shah, Eisen, Xian, & Potenza, 2005; Slutske et al., 2000). Similarities between PG and SUDs have also been suggested by molecular genetic studies: increased frequency of the D2A1 allele of the D2 dopamine receptor gene was found in PGs, and even higher frequencies were observed in PGs with comorbid SUDs (Comings, 1998). It is to note that this allele is associated with impulsive, compulsive, and addictive behaviours (Blum et al., 1995).

In regards to biochemistry, serotoninergic (Fineberg et al., 2010; Potenza, 2001; Schlosser, Black, Repertinger, & Freet, 1994) and dopaminergic (Grant et al., 2006a) deficits seem to underlie both PG and AD symptoms. Furthermore, dysregulations in the endogenous opioids system are supposed to be involved in both PG and alcohol use disorders (Grant et al., 2006a); consistently, opioid antagonists such as naltrexone and nalmefene are effective in reducing both PG- and alcohol-related symptoms (Grant et al., 2006c; Kim, Grant, Adson, & Shin, 2001; Mason, Salvato, Williams, Ritvo, &

Cutler, 1999). Shared neurocircuitry is also supposed to underlie both PD and SUDs: anomalies in frontostriatal circuits' functioning, and specifically diminished activation in the vmPFC and in the dopaminergic mesolimbic pathway linking the ventral tegmental area to the nucleus accumbens, are hypothesized to be responsible of the impulsive choice and reward-seeking behaviours characterizing both SUDs and PG (Everitt & Robbins, 2005; Potenza, 2006; 2008; Reuter et al., 2005; Volkow & Fowler, 2000; Williams & Potenza, 2008; Wrase et al., 2007).

Psychological treatments. Psychological and behavioural interventions originally developed to treat SUDs have been also introduced in the treatment of PG (Brewer et al., 2008; Petry, 2005). The most effective are: the 12-step program Gamblers Anonymous, modeled after Alcoholics Anonymous; motivational enhancement and interviewing, and cognitive behavioural therapy (Potenza et al., 2009).

2.5. Alternative models

The "addictive" or "reward dependent" spectrum

Several psychopathological conditions have been suggested to be included in a spectrum of disorders characterized by "reward dependent" behaviours, driven by preoccupations, urges or cravings. These are: alcohol and substance abuse, PG, Eating disorders, Hypersexual behaviour, and excessive physical exercise (Lochner & Stein, 2006). The inclusion of OCD in such a framework was controversial; nonetheless, several authors highlighted a number of phenomenological commonalities between OCD and, for example, AD (Anton, 2000; Modell, Glaser, Cyr, & Mountz, 1992). In

particular, similar difficulties in behavioural inhibition have been suggested to underlie both disorders, thus OCD compulsions and alcohol cravings would both represent failures in motor inhibition ability. Moreover, Vehreul, Van Den Brink and Geerlings (1999) identified three different types of alcohol craving: *reward craving*, *relief craving* and *obsessive craving*, the latter defined as the loss of control over behaviours consequent to alcohol-related obsessional thoughts. Despite such phenomenological overlaps between disorders, the idea of this spectrum of addictive disorders has not been further developed.

The obsessive-compulsive spectrum

A categorical framework partially consistent with the compulsive-impulsive spectrum hypothesis is the Obsessive-compulsive spectrum disorders (OCSDs) approach (Hollander, 1993). Several of the disorders included in the ICDs category of DSM were grouped into such a spectrum, in consideration of the phenomenological and neurobiological commonalities, as well as the patterns of familial transmission and treatment responses, shared by these disorders. Later, Hollander and Rosen (1999) divided the spectrum into four clusters. One of them was characterized by impulsive behaviours, and included PG, Pyromania, Sexual compulsions, and Compulsive buying. The main features endorsed by individuals included in this cluster was the experience of arousal, pleasure and gratification feelings as a consequence of their behaviours (Hollander & Rosen, 1999). Evidence supporting this framework came from a further cluster analysis performed by Lochner et al. (2005), who were mainly interested in investigating OCD heterogeneity. They suggested that the study of comorbidities could represent a promising way to identify OCD symptom subtypes: indeed, different OCD

subtypes might be associated with different comorbid psychopathologies, and these associations might be due to common underlying biological mechanisms. Furthermore, such an approach was thought to represent an useful means to establish which of the OCSDs could be classified as more or less closely related to OCD (Lochner & Stein, 2006). Therefore, a cluster analysis of comorbid OCSDs in patients with a primary diagnosis of OCD was performed and three main cluster emerged: "Reward deficiency" (comprising PG, Trichotillomania, Tourette syndrome, and Hypersexual disorder), "Impulsivity" (comprising compulsive shopping, Kleptomania, and Eating disorders), and "Somatic" (comprising Body dismorphic disorder and Hypochondriasis). Cluster I was characterized with an earlier onset of OCD, presence of tics, and harm related and/or sexual/religious obsessions and compulsions; dopaminergic deficits would be involved in the phenomenological features typical of this cluster. A history of childhood emotional abuse, prevalence of female gender, higher levels of OCD severity and novelty-seeking personality traits typified Cluster II; serotoninergic system dysfunctions might be related to this cluster. Lastly, Cluster III resulted associated with somatic obsessions and compulsions and poor insight; no specific psychobiological features have been related with this cluster (Lochner et al., 2005).

These results provide interesting ideas concerning the conceptualization of these psychological disorders; hypothesizing the existence of different clusters of disorders is not in contrast with the compulsive-impulsive spectrum hypothesis. Rather, different disorders might lay on different points of the continuum on the basis of the characteristics of the cluster they are part of; in this respect, the space defined by the OCSDs can be intended as multidimensional (Stein & Lochner, 2006). Furthermore, postulating the existence of "Reward deficiency" cluster within the OCSDs allows to

consider the possibility of interpreting specific compulsive behaviours as forms of behavioural addiction.

Chapter 3

The role of inhibitory control and decision making in behavioural regulation: An endophenotype approach to Pathological gambling

3.1. The endophenotype approach to the study of psychiatric disorders

Previous chapter focused on the description of compulsive and impulsive aspects of PG. This description was mainly based on phenomenology and on studies which made use of self-report questionnaires, that are phenotypic indicators. On the other hand, *endophenotypes* can be defined as internal phenotypes, as they are "intermediate measures (or markers) between top-level symptoms and bottom-level genetic contributions […] closer to the underlying neuropathology than top-level symptoms or clinical phenotype" (Chamberlain, Blackwell, Fineberg, Robbins, & Saahakian, 2005, p. 401). Therefore, endophenotypes are intended as measures of the individual neuropsychological, neurophysiological and biochemical functioning; consequently, anomalies in endophenotypes are supposed to reflect impairments in the underlying neurocognitive processes (Gottesman & Gould, 2003).

Several authors claimed the importance of integrating phenotypic and endophenotypic indicators in psychodiagnostic assessment (Chamberlain et al., 2005; Goudriaan et al., 2008), as they can provide information pertaining to different

channels, i.e. verbal (subjective) and behavioural/physiological (objective) respectively. This is in line with the basic idea that psychological assessment has to be considered in its multidimensionality, and horizontal integration (the combination of information deriving from different channels) has to be taken into account in order to help the clinician in formulating targeted diagnostic hypotheses (Sanavio, Bertolotti, Michielin, Vidotto, & Zotti, 2008).

Self-report measures allow the researcher to collect a great amount of information pertaining a wide range of attitudes and behaviours in a short period of time, and they give the opportunity to evaluate the subjective experience of clinical symptoms; moreover, self-report data analysis permits to identify distinct behavioural patterns. Nonetheless, some shortcomings intrinsic in their use are: their reference to self-reported behaviours/cognitions (which may not correspond to objective reality); a complete certainty about truthfulness of answers is impossible to achieve (reliability is lowered); administering them in different time-points can be inadequate (Moeller et al., 2001). Furthermore, speculating about putative associations between obtained scores and underlying neurobiological mechanisms is difficult (Chamberlain & Sahakian, 2007). On the contrary, the assessment of psychological constructs availing of endophenotypic measures, i.e. computerized behavioural tasks, allows the collection of more objective data, as well as the possibility to jointly investigate neural correlates through neuroimaging or transcranial magnetic stimulation (Chamberlain & Sahakian, 2007); furthermore, behavioural measures have been found to be sensitive to changes in impulsivity during treatment and to be predictive of treatment outcomes as well as relapse (Dom, De Wilde, Hulstijn, & Sabbe, 2007; Goudriaan et al., 2008). Gottesman and Gould (2003) also stressed the usefulness of employing endophenotypic measures

for assessment purposes, as they can be helpful in enhancing the understanding of the neurobiology and genetics underlying psychological disorders, thus establishing a biological underpinning for diagnosis and classification.

3.2. The involvement of motor inhibition and decision making abilities in behavioural regulation

Impairments in motor inhibition ability and difficulties in delaying gratification and decision making have been suggested to underlie problems in behavioural regulation (i.e. compulsive and impulsive behaviours; Aragues, Jurado, Quinto, & Rubio, 2011; Bechara, 2003; Dalley et al., 2011; Dawe, Matthew, & Loxton, 2004; de Wit & Richards, 2004; el-Guebaly et al., 2011; Fineberg et al., 2010; Potenza & Wit, 2010; Yücel & Lubman, 2007). They both are prefrontally-mediated cognitive functions (they mainly involve the circuits described in paragraph 2.3). In particular, the tendency to pre-potent motor disinhibition is mediated through the right inferior frontal (RIF) cortex (and specifically, the pars opercularis, Brodmann area 44) and the basal ganglia (and specifically, the globus pallidus), and modulated by the neurotransmitter norepinephrine, whereas impulsive decision making is mediated through the OFC and subcortical connections, and modulated by serotonin at the cortical level and dopamine at the subcortical one (Aragues et al., 2011; Fineberg et al., 2010).

The first authors suggesting that these two main dimensions might be involved in behavioural dysregulation were Dawe et al. (2004) and de Wit & Richards (2004). Through the integration of the most recent personality theories and developments in

neurosciences to that time, they identified two components of impulsive/compulsive behaviours: a. behavioural disinhibition or rash impulsiveness, which refers to difficulties in both initiating and inhibiting motor responses. Consequently, impulsive/compulsive behaviours would represent the performance of an action before its complete processing and evaluation ("acting without thinking") or the failure of interrupting current actions (problems in response inhibition); b. consequence sensitivity or impulsive decision making, referring to impulsivity in terms of behavioural choices which are perpetrated despite bad consequences for the individual, i.e. preferring to obtain small but immediate rewards rather than big but delayed ones. Motor inhibition deficits have been hypothesized to account for impaired decision making; nonetheless, research findings are inconsistent (Kertzman, Lidogoster, Aizer, Kotler, & Dannon, 2011).

3.3. Cognitive measures of motor inhibition and decision making abilities

Cognitive measures of motor inhibition and decision making abilities represent promising endophenotypic indicators of behavioural regulation and have been largely employed in research on PG (Goudriaan et al., 2008). The mainly used paradigms are described below.

3.3.1 Motor inhibition ability

Among the neuropsychological measures of motor inhibition ability, the Go/Nogo task and Stop-Signal task are regarded the most valid and reliable

(Chamberlain & Sahakian, 2007; Chambers, Garavan, & Bellgrove, 2009; Oosterlan, Logan, & Sergeant, 1998).

Go/Nogo task

In the Go/Nogo task (Drewe, 1975) subjects are asked to respond as quickly as possible to target stimuli (Go trials), by performing a simple motor response (generally pressing a button), and to refrain from responding to distractor cues (Nogo trials). The behavioural data usually collected are the number of errors (omissions: the subject does not react to the Go stimulus; commissions: the subject reacts to the Nogo stimulus) and reaction times (RTs; milliseconds taken to respond to Go stimulus and on Nogo trials). Studies with nonclinical subjects found faster RTs on Nogo conditions than on Go conditions, suggesting that commission errors may be quick guesses or premature responses (Falkenstein, Hoormann, & Hohnsbein, 1999; Falkenstein, Koshlykova, Kiroj, Hoormann, & Hohnsbein, 1995). As a consequence, commission errors in the Go/Nogo task are generally regarded an index of poor motor inhibition control (Bohne, Savage, Deckersbach, Keuthen, & Wilhelm, 2008).

Stop-Signal Task

The Stop-Signal task (Logan, Cowan, & Davis, 1984) differs from Go/Nogo task as it measures the ability of inhibiting a pre-activated motor response. In this task subjects are required to perform a visual discrimination task, i.e. emitting different motor responses according to the stimuli (go signals) they are presented with. Instructions stress that motor reactions have to be as quick as possible. In a number of trials, a stop signal (generally, an auditory stimulus) is presented after a go signal: when

the stop signal occurs, subjects have to refrain from responding to the go signal. Finally, the calculation of an algorithm allows to measure the time internally spent to inhibit the pre-activated response; this period of time is defined Stop-Signal Reaction Time (SSRT). The longer the SSRT, the more impaired the ability to inhibit motor responses. Other behavioural indicators of performance are the number of errors and the mean RTs associated with go signals (Logan et al., 1984).

3.3.2. Decision making ability

One of the mostly used measures of decision making is the Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994). It consists of four desks of cards that, when turned, reveal a combination of gains and losses (measured in monetary rewards). Participants are given an initial budget (usually $2000/2000 €) and they are required to increase this amount as much as possible by choosing cards from any of the four decks; they are told that they are free to switch from any deck to another. The task is designed so that two decks are advantageous, and choosing consistently cards from them results in a net gain: wins are quite low, as well as penalty amounts. The two advantageous decks are different as one is characterized by a more frequent, but smaller in magnitude, punishment than the other. On the contrary, the other two decks are considered disadvantageous and choosing consistently from them leads to a net loss: each card from the disadvantageous decks can provide high rewards and high punishments. As for the two advantageous decks, the punishment is more frequent and of smaller magnitude in one deck than in the other. Participants are not told about the total number of trials (100) before starting the task, whereas they are informed that some of the decks are advantageous and some disadvantageous. A total gain score is

computed at the end of the task by subtracting the total number of card selected from the advantageous minus disadvantageous decks; the lower the score, the higher the impairments in decision making ability. Furthermore, partial net-scores are usually computed for each block of 20 cards (Bechara et al., 1994).

Brand, Recknor, Grabenhorst and Bechara (2007) pinpointed that two types of decision making are involved in task execution: a. "under ambiguity decision", characterizing the first phase of task (first 40 trials), as decisions have to be made without knowledge of the nature of outcomes and the probability of gains and losses; b. "decision under risk", typical of the second phase (last 60/40 trials), where participants should have learnt the risks associated with distinct decks and therefore they should be aware of the consequences of choosing from one deck than the other (Brand et al., 2007; Kertzman et al., 2011).

3.4. Motor inhibition and decision making deficits as putative endophenotypic markers of compulsive and impulsive disorders

Motor inhibition deficits are hypothesized to underpin PG, OCD, and SUDs (Fineberg et al., 2010), and impaired performance on the IGT has been observed in PG, OCD and AD (el-Guebaly et al., 2011). The main evidence are reviewed as follows.

3.4.1. Pathological gambling

Motor inhibition ability

A few studies investigated motor inhibition ability in PG through Go/Nogo paradigms; overall, results support the existence of inhibitory deficits. Goudriaan, Oosterlaan, de Beurs and Van den Brink (2005) found that PGs, individuals with Tourette syndrome and Alcohol dependents (ADs) performed a significantly higher number of commission errors than healthy controls; no differences between clinical groups emerged. Fuentes, Tavares, Artes and Gorenstein (2006) also observed significantly more commission errors in PGs than in healthy controls. Kertzman et al. (2008) integrated the Go/Nogo paradigm with the continuous performance test (CPT; requires to identify and respond to a Go stimulus) and found that PG sufferers showed both more omission and commission errors, as well as slower RTs, than healthy controls. Similar results emerged in a later study conducted by the same research group: PGs performed more omission errors and were slower than healthy individuals, whereas no differences in the number of commission errors emerged (Kertzman et al., 2011). Lastly, Bottesi et al. (2011a) observed that both PG sufferers and OCD patients executed more omission errors that healthy controls, even when age and education level were partialled out. Omission errors are generally considered a measure of inattention rather than of behavioural inhibition deficits (Halperin, Sharma, Greenblatt, & Schwartz, 1991), thus results from these studies suggest that PG sufferers may be also characterized by attentive problems. An alternative explanation for the slow performance showed by PGs posits that slowness, as well as omission errors, could be the product of a conflict between automatic and voluntary behaviour, due to deficits in the organization of stimulus-response schemata (Kertzman et al., 2008).

Studies assessing motor inhibition ability in PGs making use of the Stop-Signal task provided mixed results. Goudriaan, Oosterlaan, de Beurs and van den Brink (2006) compared the performance of PG sufferers, individuals with Tourette syndrome, ADs and healthy controls and found that the three clinical groups showed SSRTs significantly slower than the control one; no differences between clinical groups emerged. The same PG sufferers entered a follow-up study, aimed to investigate whether motor inhibition deficits and problems in decision making were related with relapse (Goudriaan et al., 2008). Results revealed that only motor inhibition deficits were significant predictors of relapses. Also the studies by Reena (2008) and Ledgerwood et al. (2012) found inhibitory deficits in PGs who, compared with healthy controls, showed a significantly slower performance on a Stop-Signal task and on modified version of the Stop-Signal task (GoStop Impulsivity Paradigm; Dougherty, 2003), respectively. Lawrence, Luty, Bodgan, Sahakian and Clark (2009) made a comparison between PGs, ADs and healthy controls and found that ADs performed worse than PGs who, in their turn, were more impaired than healthy controls. Lastly, Odlaug, Chamberlain, Kim, Schreiber and Grant (2011) explored motor inhibition ability through the Stop-Signal task in a community sample; participants were classified as PGs, gamblers-at-risk and no-risk gamblers on the basis of scores obtained at the Structured Clinical Interview for Pathological Gambling (SCI-PG; Grant, Steinberg, Kim, Rounsaville, & Potenza, 2004). Results highlighted that PGs showed longer SSRTs than both the other groups.

On the other hand, several studies failed in detecting poor inhibitory control in PG sufferers. Ledgerwood, Alessi, Phoenix and Petry (2009) did not find differences between PGs (with and without an history of substance abuse) and healthy controls in

performance on the Stop-Signal task; furthermore, those who reported substance use problems in the past did not differ from those who did not report it. Lastly, Grant, Chamberlain, Schreiber, Odlaug and Kim (2011) did not observe any difference between at-risk gamblers and social/non-problem gamblers neither in SSRTs nor in RTs for Go Trials.

Decision making ability

Studies aiming to investigate decision making ability in PGs through the IGT generally led to consistent results, highlighting the presence of deficits.

Cavedini, Riboldi, Keller, D'Annucci and Bellodi (2002b) observed that healthy controls overall selected more cards from the advantageous decks than PGs, and that the former rapidly learnt to choose cards from those decks. On the contrary, PGs started to select cards alternatively from advantageous and disadvantageous decks, shifting to the disadvantageous ones towards the end of the task. Goudriaan et al. (2005) compared the performance PGs, ADs, patients with Tourette syndrome and healthy controls. They found that PGs showed a higher response speed and less response shifting after losses than the other three groups; moreover, both PGs and ADs made more disadvantageous choices and demonstrated less conceptual knowledge of the advantageous decks than the other two groups. Linnet, Røjskjær, Nygaard and Maher (2006), using a modified version of the IGT (i.e. the Mouse Game), observed a lower total net-score in PGs than in healthy controls. The analysis of the adopted strategies revealed that PGs did not perform more disadvantageous sequences than healthy controls; rather, they performed less advantageous sequences and showed a lower ratio of good – bad choice sequences than controls. Forbush et al. (2008) did not find any difference between PGs and healthy

controls in the overall net-score, but they reported that PGs did not shift towards advantageous card selection, whereas controls did. An impaired learning was also observed by Kertzman et al. (2011) and Ledgerwood et al. (2012). The former found significant differences between PGs and healthy controls in blocks 3-5: PGs continued to choose more frequently from disadvantageous decks all over the task, thus obtaining lower net-scores (Kertzman et al., 2011). Similarly, results from the other study revealed that non treatment-seeking PGs had a variable performance, characterized by a slower learning than healthy controls (Ledgerwood et al., 2012)

In the light of the deficits showed by PGs when executing the IGT, several authors assessed whether impaired decision making ability, as measured by the IGT, was predictive of PG severity (Forbush et al., 2008), relapse (Alvarez-Moya et al., 2011; Goudriaan et al., 2008) and dropout (Alvarez-Moya et al., 2011). Results suggest that performance on the IGT is not a significant predictor neither of PG severity nor of relapse (Alvarez-Moya et al., 2011; Forbush et al., 2008; Goudriaan et al., 2008), whereas impairment on the task was associated with higher risk of dropout but only at a trend level (Alvarez-Moya et al., 2011). Rather, poor response inhibition and perseveration for reward (as measured by the Card Playing Task; Newman, Petterson, & Kosson, 1987) resulted predictive of relapse in a group of PGs (Goudriaan et al., 2008), whereas poor spatial working memory was a predictor of dropout during treatment (Alvarez-Moya et al., 2011).

3.4.2. Obsessive compulsive disorder

Motor inhibition ability

A number of studies have used Go/Nogo paradigms to assess motor inhibition ability in OCD individuals; results are inconsistent. Bannon, Gonsalvez, Croft and Boyce (2002; 2006) conducted two studies comparing OCD patients and individuals suffering from Panic disorder and found that the former performed more commission errors than the latter. Furthermore, a subgroup of remitted OCD patients were administered the same Go/Nogo task 1.40 (SD = 0.52) years after the end of treatment; no difference between the two performances (symptomatic vs remitted phase) emerged, thus suggesting the trait-like nature of motor inhibition symptoms in OCD (Bannon et al., 2006). Two further studies (Bottesi, Ghisi, Sica, & Sanavio, 2012a; Penadés et al., 2007) proved that OCD patients performed more commission errors than healthy controls in a Go/Nogo task. Recently, Abramovitch, Dar, Schweiger and Hermesh (2011a) reported that OCD patients performed slower RTs than healthy controls on a different typology of Go/Nogo task, namely the Expanded Go-Nogo test. Furthermore, the same Authors compared OCD patients, individuals with attention deficit/hyperactivity disorder (ADHD) and healthy controls in the same Go/Nogo task and found that OCD and ADHD patients performed more commission errors that healthy controls, whereas they did not differ each other (Abramovitch, Dar, Hermesh, & Schweiger, 2011b). On the other hand, Johannes et al. (2001) and Bohne et al. (2008) compared OCD patients with individuals suffering from Tourette syndrome and healthy controls on one hand, and patients with Trichotillomania and healthy individuals on the other one; no differences between OCD patients and healthy controls in the behavioural performance emerged from both studies. Many other studies failed in detecting

behavioural differences between OCD patients and healthy controls (Hermann, Jacob, Unterecker, & Fallgatter, 2003; Kim, Kim, Yoo, & Kwon, 2007; Maltby, Tolin, Worhunsky, O'Keefe, & Kiehl, 2005; Ruchsow et al., 2005; 2007); nonetheless, anomalies in the event-related potentials (ERP) components usually related to commission errors (ERN/Ne, N200, P300; Hermann et al., 2003; Kim et al., 2007; Ruchsow et al., 2005; 2007) and hyperactive anterior cingulated cortex (ACC) during task execution (Hermann et al., 2003; Maltby et al., 2005) were observed in OCD groups.

Studies using the Stop-Signal task generally agreed in finding impaired inhibitory control in OCD patients. Penadés et al. (2007) observed slower SSRTs in OCD patients than healthy controls; Chamberlain, Fineberg, Blackwell, Robbins and Sahakian (2006) reported that OCD individuals' performance was similar to that of patients with Trichotillomania, and both clinical groups were significantly more impaired than healthy participants. Chamberlain et al. (2007) reported that unaffected first-degree relatives of OCD patients and OCD probands did not differ significantly in the performance at the Stop-Signal task; in addition, both groups showed significantly longer SSRTs than comparison subjects without a known family history of OCD. Boisseau et al. (2012) compared OCD patients, individuals with Eating disorders and healthy controls: those with OCD were characterized by slower SSRTs than healthy individuals, and showed more omission errors than those suffering from Eating disorders.

Decision making ability

Mixed results emerged from studies investigating decision making ability through the IGT among OCD patients. Cavedini et al. (2002a) found that OCD patients selected a significantly higher number of cards from the disadvantageous decks than both healthy controls and patients with Panic disorder; furthermore, OCD individuals did not shift in card selection from disadvantageous to advantageous decks. Healthy controls and patients with Panic disorder did not differ neither in card selection nor in the adopted strategy (they both showed a learning effect over time). Within the OCD group, those characterized by a poor treatment response performed worse than those positively responding to treatment. A poorer performance in OCD patients (in terms of both total and partial net-scores and no shifting in card selection) compared to healthy controls was also found by Starcke, Tuschen-Caffier, Markowitsch and Brand (2009). A following study performed by the same Authors further highlighted more disadvantageous choices in OCD patients that in healthy participants; in particular, the OCD group was characterized by lower net-scores in blocks 3 and 5 (Starcke, Tuschen-Caffier, Markowitsch, & Brand, 2010). Lastly, a group of OCD patients overall performed significantly worse (less advantageous choices) than a group of healthy subjects (Cavedini, Zorzi, Piccinni, Cavallini, & Bellodi, 2010) and lower net-scores (total score and second fifth cards) were observed in a large sample of Brazilian OCD patients compared with healthy controls (da Rocha, Alvarenga, Malloy-Diniz, & Corrêa, 2011). A further support of decision making impairments characterizing OCD came from two studies using the IGT in unaffected first-degrees relatives of OCD patients (Cavedini et al., 2010; Viswanath, Janardhan Reddy, Kumar, Kandavel, & Chandrashekar, 2009): results highlighted that OCD relatives selected a higher number

of cards from disadvantageous decks than both healthy controls' relatives (Cavedini et al., 2010; Viswanath et al., 2009) and healthy probands (Cavedini et al., 2010).

On the other hand, several authors did not find deficits in the IGT performance when assessing OCD patients. Nielen, Veltman, de Jong, Mulder and den Boer (2002) reported that individuals with OCD and healthy controls exhibited a similar performance, both shifting to the more advantageous decks over time. Also Lawrence et al. (2006) failed in detecting overall differences between OCD patients and healthy controls during the IGT. Nonetheless, they found that patients with higher hoarding symptomatology were characterized by a poorer performance. Lastly, Krishna et al. (2011) did not report any impairment in regards to decision making processes when comparing medication-naïve and never-treated OCD patients with matched healthy controls.

3.4.3. Alcohol dependence

Motor inhibition ability

Only a few recent studies assessed motor inhibition ability in ADs, and they all reported difficulties in motor inhibition. Goudriaan et al. (2005; 2006) found that ADs showed inhibitory deficits in both Go/Nogo task (high number of commission errors) and Stop/Signal task (slow SSRTs); Lawrence et al. (2009) reported that ADs were characterized by longer SSRTs in a Stop-Signal task, than PGs and healthy controls. Bottesi et al. (2011b) reported a positive correlation between the number of commission errors on a Go/Nogo task and the self-reported levels of craving in a group of ADs. A later study (Bottesi, Imbeck, Gentile, & Ghisi, 2012b), however, showed that a group of ADs performed more omission errors and longer RTs than matched healthy controls; no

associations between alcohol craving and Go/Nogo task performance emerged.

Decision making ability

One of the earliest studies testing decision making ability through the IGT in ADs was performed by Mazas, Finn and Steinmetz (2000). They compared four groups of participants: ADs with comorbid antisocial personality (ASP), ADs without comorbid ASP, individuals diagnosed with ASP and without AD, and a control group (no AD neither ASP). Overall, results showed an impaired performance in ADs, in terms of more disadvantageous choices; however, the impairment was no longer related with AD when including ASP in the analyses. In a further study, Dom, De Wilde, Hulstijn, van den Brink and Sabbe (2006) made a comparison between: ADs with comorbid Cluster B Personality disorders (PDs), ADs with comorbid Cluster A and Cluster C PDs, ADs without comorbid PDs, and healthy controls. All the ADs were abstinent. They found that all the clinical groups showed a similar performance over blocks that is, they did not learn to shift from disadvantageous to advantageous decks, whereas controls improved over time. Furthermore results highlighted that, among the ADs, those with comorbid Cluster A or Cluster C PDs performed significantly better than the other two groups; the worse performance was observed in the ADs with comorbid Cluster B PDs. Another study (Miranda, MacKillop, Meyerson, Justus, & Lovallo, 2009) investigating the contribution of ASP in the performance of ADs on the IGT revealed that ADs with and without comorbid ASP performed poorly (total net-score) than healthy controls; however, the two clinical groups showed different patterns, as those without ASP were characterized by a delayed, but not absent, shift from disadvantageous to advantageous decisions, whereas those with ASP showed

difficulties in the maintenance of the learning (Miranda et al., 2009).

Fein, Klein and Finn (2004) reported that a group of abstinent ADs obtained a significantly lower total net-score in comparison with a group of healthy controls; the total net-score in the AD group was negatively correlated with the duration of alcohol use and with the duration of peak alcohol use. Goudriaan et al. (2005) found that abstinent ADs selected a significantly lower number of cards from the advantageous decks than healthy controls (ADs had a performance similar to that showed by the PG group). However, differently from PGs, ADs learnt to choose cards from low-risk decks over time (but selecting them less frequently than healthy controls). Furthermore, both ADs and PGs were characterized by less conceptual knowledge of the advantageous decks, i.e. they had difficulties in identifying the advantageous decks, when interviewed at the end of the task. Consistently with the study by Goudriaan et al. (2005), Nöel, Bechara, Dan, Hanak and Verbank (2007) reported that abstinent ADs picked more cards from the disadvantageous decks than healthy controls. However, they also observed a decline in the ADs performance in the last block of the IGT, thus suggesting a return to a disadvantageous strategy at the end of the task and a lack of learning. Salgado et al. (2009) reported that abstinent ADs obtained lower total and partial (on blocks 2, 4 and 5) net-scores than and healthy controls; however, they only performed t-tests for independent samples using net-scores as dependent variables, so they did not investigate learning effects. More recent studies (Bottesi et al., 2012b; Kim, Sohn, & Jeong, 2011; Tomassini et al., 2012) further support the existence of decision-making deficits in abstinent ADs, in terms of both a greater number of cards selected from the disadvantageous decks and a more impaired performance on the later stages of the IGT (in the last two blocks, Kim et al., 2011; in the second and in the last two blocks,

Tomassini et al., 2012) than healthy controls. Lastly, a prospective study conducted on college students highlighted that disadvantageous decision making on the IGT was a predictor of heavy drinking after two years (Goudriaan, Grekin, & Sher, 2011).

Part II- Empirical research

Chapter 4

Investigating phenotypic and endophenotypic indicators of compulsivity and impulsivity in Pathological gamblers

4.1. General aims and hypotheses

The present exploratory research was designed to better understand the compulsive and impulsive features characterizing PG, thus contributing to the current debate about its classification.

Bottesi (2012) and Grant and Potenza (2006) highlighted that clinical research should focus on similarities and differences between PG, OCD and SUDs (exhaustively reviewed in Chapter 2) to identify the most appropriate classification of PG in DSM-5: nonetheless, to date such a comparison has not been performed. Furthermore, as previously stressed in Chapter 3, the integration of phenotypic and endophenotypic indicators in clinical practice is crucial as it allows to gather information from different channels (Chamberlain et al., 2005; Goudriaan et al., 2008), thus leading to multidimensionality in psychological assessment (Sanavio et al., 2008).

In the present study, PGs were compared with patients with OCD, ADs and healthy controls (HCs) on both phenotypic and endophenotypic measures of compulsivity and impulsivity. OCD and AD were chosen as clinical control groups

since the former represents the prototype of Compulsive disorders, whereas the latter shows genetic and neurobiological links with PG. The main aims were to detect similarities and differences between clinical groups in self-report and cognitive measures of compulsivity and impulsivity, as well as potentially different patterns of response in cognitive tasks.

A second preliminary study was also conducted: a small group of PGs was compared with a group of croupiers and HCs on the same measures adopted in the main study. Croupiers share with PGs the interest for gambling, and gambling clearly represents a relevant daily activity for both groups; they also spend the most of the day in the same environment. Furthermore, several studies showed higher risks of developing problem or pathological gambling in gaming workers than in general population (Hing & Gainsbury, 2011; Hu, Luk, Leong, & Van, 2012; Lee, LaBrie, Rhee, & Shaffer, 2008; Shaffer, Vander Bilt, & Hall, 1999b; Wu & Wong, 2008). It is not clear whether this is better accounted by environmental or dispositional factors; thus, examining compulsivity- and impulsivity-related aspects in such a nonclinical population may provide useful information to identify the factors potentially involved in the development of PG. Such a dimensional approach has proved to be valuable in research on OCD (Burns, Formea, Keortge, & Sternberger, 1995).

In particular, it is reasonable to assume that croupiers are characterized by lower levels of compulsive features than PGs, in that compulsivity is generally associated with egodystony (see paragraphs 2.1 and 2.4), but higher than HC, as very often croupiers have to perform stereotyped and repetitive actions because of their job. Furthermore, higher levels of impulsivity in croupiers than in HCs are expected. Lastly, it will be

explored whether motor inhibition and decision making abilities in croupiers are similar or different from those characterizing PGs. To the Author's knowledge, to date compulsivity and impulsivity in samples of croupiers have not been investigated.

4.2. Study 1 - Compulsivity and impulsivity: a comparison between Pathological gamblers, patients with OCD and Alcoholics

4.2.1. Method

Participants

Clinical individuals originally recruited were patients with DSM-IV-TR diagnosed PG (PG group; N=44), OCD (OCD group; N=22), and AD (AD group; N=75) as their most severe problem.

They were recruited from the following outpatient and inpatient mental health clinics:

- PG: *Società Italiana di Intervento sulle Patologie Compulsive (SIIPAC)*, Bolzano (N=14); *Casa di Cura Parco dei Tigli*, Teolo - Padova (N=6); *Servizio per le Tossicodipendenze*, Castrovillari - Cosenza (N=8), Firenze (N=4), Portogruaro - Venezia (N=5); *Associazione Orthos*, Siena (N=7).

- OCD: *Casa di Cura Villa Margherita*, Arcugnano - Vicenza (N=10); *Casa di Cura Parco dei Tigli,* Teolo - Padova (N=1); *Istituto di Terapia Cognitiva e Comportamentale*, Padova (N=8); *Servizio di Terapia Cognitiva e Comportamentale (Liripac)*, Padova (N=3).

- AD: *Casa di Cura Parco dei Tigli,* Teolo - Padova (N=40); *Servizio per le Tossicodipendenze*, Mirano – Venezia (N=35).

General exclusion criteria were the presence of severe neurological or internistic pathologies, current or past psychotic disorder, and mental retardation. Patients with secondary comorbid Axis-I or Axis-II diagnoses were included**.** Specific inclusion criteria were: PGs had to score ≥5 at the South Oaks Gambling Screen (SOGS; Lesieur & Blume, 1987; Italian version by Gheradri, Lesieur, & Blume, 1992) and not to report

comorbidities with OCD and AD; OCD patients had to score ≥16 at the Yale–Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989; Italian version by Pancheri, 1992) and not to have comorbid PG or AD; ADs had to score ≥5 at the Alcohol Use Disorders Discrimination Test (AUDIT; Bohn, Babor, & Kranzler, 1995; Italian version by Piccinelli et al., 1997), to be detoxified for at least 2 weeks and not to report comorbid PG or OCD. After being assessed, suitable patients participating the study were 40 PGs, 22 OCD patients, and 40 ADs. Sixty-two out of 102 patients (60.8%) were medicated (17 PGs, 12 OCD patients, and 33 ADs).

Healthy controls (HCs) originally recruited were 75 community individuals enrolled in different towns of Northern, Central and Southern Italy. To be included in the study, HCs had neither to fulfill diagnostic criteria for any psychiatric disorder nor to take any medication. Participants were excluded from the study whether they showed: high levels ($z>1.64$) of depression, as measured by the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996; Italian version by Ghisi, Flebus, Montano, Sanavio, & Sica 2006); high levels ($z>1.64$) of anxiety, as investigated by the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988; Italian version by Sica, Coradeschi, Ghisi, & Sanavio, 2006) and the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990; Italian version by Morani, Pricci, & Sanavio, 1999); high levels ($z>1.64$) of obsessive-compulsive symptoms, as assessed by the Padua Inventory (Sanavio, 1988); scores beyond the cut-offs at the SOGS and/or at the AUDIT. The final HC group was made up of 47 individuals.

Groups differed in several demographic variables: gender (all groups were mainly composed by males, except for ADs); age (OCD patients were significantly younger than participants included in the other 3 groups); marital status and occupation

(OCD patients were mainly single and students, respectively). Furthermore, as expected the clinical samples scored significantly higher than HCs on BDI-II, BAI, and PSWQ (Table 4.1).

Table 4.1. Demographic and clinical variables of the four groups.

	PG	OCD	AD	HC	χ^2/F	df	p	post-hoc
Age	40.01 (12.05)	31.27 (11.58)	47.15 (10.43)	43.06 (11.94)	9.18	3,146	<.001	PG=AD=HC<OCD
Years of education	11.79 (4.06)	12.40 (2.83)	10.29 (3.06)	10.87 (3.10)	2.36	3,146	.07	PG=OCD=AD=HC
Gender (% of males)	95	72.7	50	78.7	21.96	3	<.001	-
Marital Status (% of married/cohabitant)	26.9	5.1	25.6	42.3	25.90	9	.002	-
Occupation (% of full-time employed)	27.9	8.8	16.2	47.1	69.15	18	<.001	-
BDI-II	13.87 (9.72)	18.40 (10.43)	15.18 (9.48)	2.28 (2.82)	28.34	3,146	<.001	PG=OCD=AD>HC
BAI	10.75 (10.49)	14.05 (12.21)	13.78 (10.67)	3.23 (2.79)	12.25	3,146	<.001	PG=OCD=AD>HC
PSWQ	47.33 (12.47)	58.58 (13.42)	47.80 (11.94)	32.89 (4.39)	33.59	3,146	<.001	OCD>PG=AD>HC

Means (standard deviations) for continuous variables are reported.
Note: post-hoc = Bonferroni post-hoc.

Measures

Self-report screening instruments

The *South Oaks Gambling Screen* (SOGS; Lesieur & Blume, 1987; Gheradri et al., 1992) is a 20-item self-report measure used to screen for PG. A cut score of 5 or more indicates that the individual is a Probable Pathological Gambler (PPG), whereas a score of 3-4 indicates that the respondent may have "some problems with gambling".

The *Alcohol Use Disorders Discrimination Test* (AUDIT; Bohn et al., 1995; Piccinelli et al., 1997) is a 10-item questionnaire designed to identify people with alcohol dependence. A cut-off point of 7/8 has been identified as an optimal value for general population screening of at-risk drinking (Reinert & Allen, 2007); Piccinelli et al. (1997) suggested that 5 was a better cut-off point for screening in Italian population.

The *Yale–Brown Obsessive Compulsive Scale* (Y-BOCS; Goodman et al., 1989; Pancheri, 1992) is an instrument investigating several dimensions characterizing obsessions and compulsions (the amount of time consumed, interference with daily functioning, distress, resistance, and control associated with OCD symptoms). It provides three scores: one for the severity of obsessions, one for the severity of compulsions, and a total score (obsessions plus compulsions). A cut-off point of 16 (total score) indicates clinically significant levels of OCD (Baer, Brown-Beasley, Sorce, & Henriques, 1993; Rosenfeld, Dar, Anderson, Kobak, & Greist, 1992).

The *Beck Depression Inventory-II* (BDI-II; Beck et al., 1996; Ghisi et al., 2006) is a 21-item self-report scale assessing the severity of affective, cognitive, motivational, vegetative, and psychomotor components of depression. The BDI-II has excellent internal consistency (original version: α=.93 for students and α=.92 for clinical individuals; Italian version: α=.80 for students and α=.87 for depressed patients), and test-retest reliability in student samples (original version (1-week): r=.93; Italian version (1-month): r=.76). Good Cronbach's alphas were observed also in the present study (PG: α=.87; OCD: α=.94; AD: α=.89; HC: α=.78).

The *Beck Anxiety Inventory* (BAI; Beck et al., 1988; Sica et al., 2006) is a 21-item self-report questionnaire measuring the severity of physiological anxiety symptoms. Excellent psychometric properties were observed in both the original (internal consistency: α=.92; 1-week test-retest reliability: r=.75 in a community sample) and the Italian version (internal consistency: α=.89, α= .87, and α=.81 in undergraduates, community and anxious patients, respectively; 1-month test-retest reliability: r=.62 in a student sample). Reliability proved to be good also in groups participating the present research (PG: α=.93; OCD: α=.94; AD: α=.89; HC: α=.73).

The *Penn State Worry Questionnaire* (PSWQ; Meyer et al., 1990; Morani et al., 1999) is a 16-item inventory designed to assess trait worry. Psychometric properties of the instrument proved to be good in both undergraduate and clinical samples (Meyer et al., 1990); in an Italian community sample Cronbach's alpha resulted .85 (Morani et al., 1999). Internal consistency was acceptable also in the present study (PG: α=.86; OCD: α=.87; AD: α=.87; HC: α=.66).

Self-report measures of compulsivity and impulsivity

The *Padua Inventory* (PI; Sanavio, 1988) is a 60-item self-report instrument made up of 4 subscales assessing OCD symptoms: Impaired control over mental activities (excessive doubting and ruminations), Washing (fears of contamination and compulsions aimed to prevent infections and illnesses), Checking compulsions, and Impaired control over motor activities (urges and worries associated with overt behaviour). The questionnaire demonstrated good psychometric properties: internal consistency (Total score) resulted α=.90 for males and α=.94 for females, and test-retest reliability (1-month) was r=.78 for males and r=.83 for females (Sanavio, 1988).

The *Obsessive Beliefs Questionnaire-87* (OBQ-87; OCCWG, 1997; 2001; Italian version by Sica et al., 2004) consists of 87 items which investigate the six dysfunctional beliefs supposed to be involved in the onset and maintenance of OCD (OCCWG, 1997). Such beliefs seem also to characterize the cognitive style of people suffering from other Anxiety and Eating disorders (Frost, Novara, & Rhéaume, 2002; Sica et al., 2004; Taylor, Kyrios, Thordarson, Steketee, & Frost, 2002). The Italian version of the questionnaire is also made up of 6 subscales (Sica, Coradeschi, Sanavio, Dorz, & Ghisi, 2003): Perfectionism (the belief that the "perfect solution" for a problem exists and that

things must be done in the perfect manner), Overestimation of threat (exaggerating the severity of a negative outcome as well as its probability of occurrence), Control of thoughts (the belief that having complete control over intrusive thoughts, images, and impulses is important, feasible and desirable), Thought-action fusion (TAF; the belief that thoughts are important *per se* and equivalent to actions), Responsibility-Omission (feeling responsible not to have prevented a potentially harmful situation) and Responsibility-Harm (feeling responsible when performing an action interpreted as negative or immoral). The subscales of the original version demonstrated good internal consistency ($.71<\alpha<.93$) and test-retest reliability (r ranging from .75 to .90; OCCWG, 1997). As regards the Italian version, internal consistency of the subscales was between .85 and .93 for OCD patients and between .74 and .89 for university students; 1-month test-retest reliability was evaluated in students and correlation coefficients ranged between r=.69 and r=.87 (Sica et al., 2004).

The *Barratt Impulsiveness Scale*-11 (BIS-11; Patton et al., 1995; Italian version by Fossati, Di Ceglie, Acquarini, & Barratt, 2001) is a 30-item self-report scale designed to measure general impulsivity taking into account its multi-factorial nature. In particular, the original version investigates three separate components of this construct: Motor impulsiveness (i.e. acting "on the spur of the moment"), Attention (i.e. the ability to focus attention on one task at hand), and Nonplanning impulsiveness (i.e. not to consider the consequences of actions before performing them). The Italian version of the BIS-11 is composed by three slightly different subscales: Motor impulsiveness/Attention; Perseverance/Lack of delay in obtaining gratification; Nonplanning impulsiveness. Psychometric properties of the original version proved to be good (Patton et al., 1995). Internal consistency and 2-month test-retest reliability of

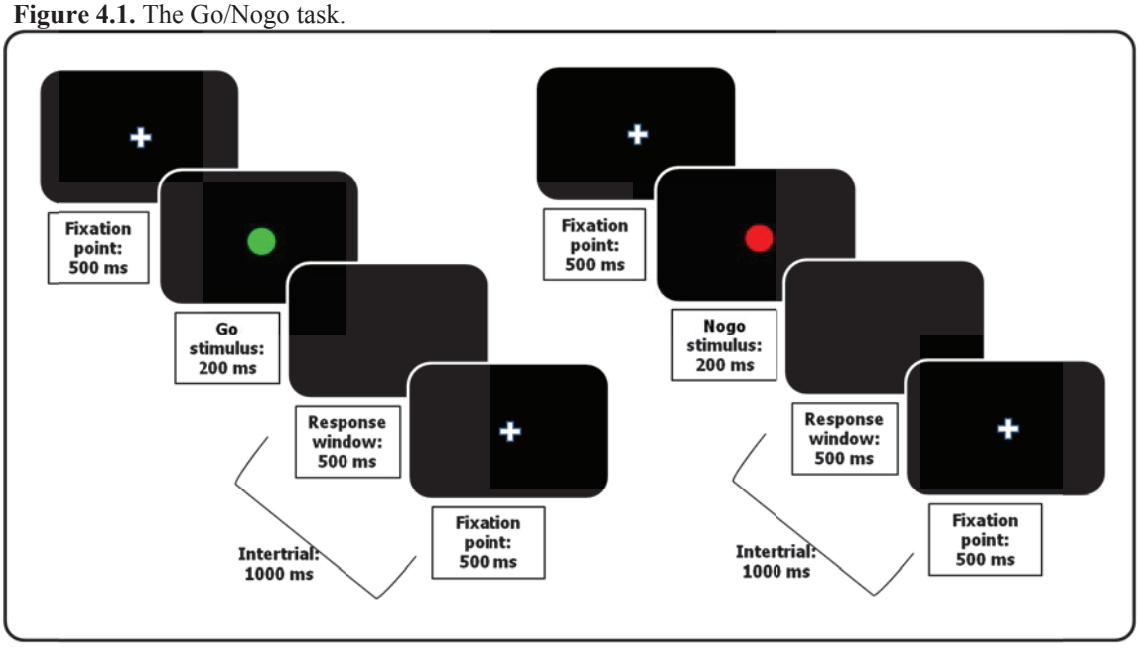
the BIS-11 Total score were also tested in Italian undergraduate students: they were good, α=.79 and r=.89, respectively (Fossati et al., 2001).

Cognitive tasks

The *Go/Nogo task* was chosen as it is one of the most well-characterized paradigms designed to detect response inhibition deficits (Aron, 2007; Dillon & Pizzagalli, 2007; Nigg, 2000), capable of identifying orbitofrontal and ventral prefrontal deficits in humans and animals and not involving a memory component (Maltby et al., 2005). The paradigm adopted in the present study included a practice sequence (composed of 20 stimuli, 15 Go and 5 Nogo) to ensure the instructions were understood followed by 4 experimental blocks. Each block consisted of 100 stimuli (75 Go and 25 Nogo), presented in a randomized order on a computer screen placed at a distance of 120 cm from the subject. The Go stimulus was a green circle and the Nogo stimulus was a red circle (both measuring 40 pixels in diameter). The stimulus duration was set at 200 ms and the stimulus presentation was preceded by a fixation point (white cross) of 500 ms duration; the response window was of 500 ms and so the interstimulus interval was set at 1000 ms (Figure 4.1). Participants were instructed to press the space bar on the keyboard with the index finger of their dominant hand as soon as possible whenever the Go stimuli appeared on the screen and to refrain from responding to the Nogo stimuli. The instructions emphasized both speed and accuracy. Participants were informed that they would receive feedback on each error by a sound. Behavioral performance was defined as: the number of omission errors (false negative; no response to Go stimuli within the response window); the number of commission errors (false positive; failures

to withhold response to Nogo stimuli); and the RTs associated with correct Go trials and commission errors.

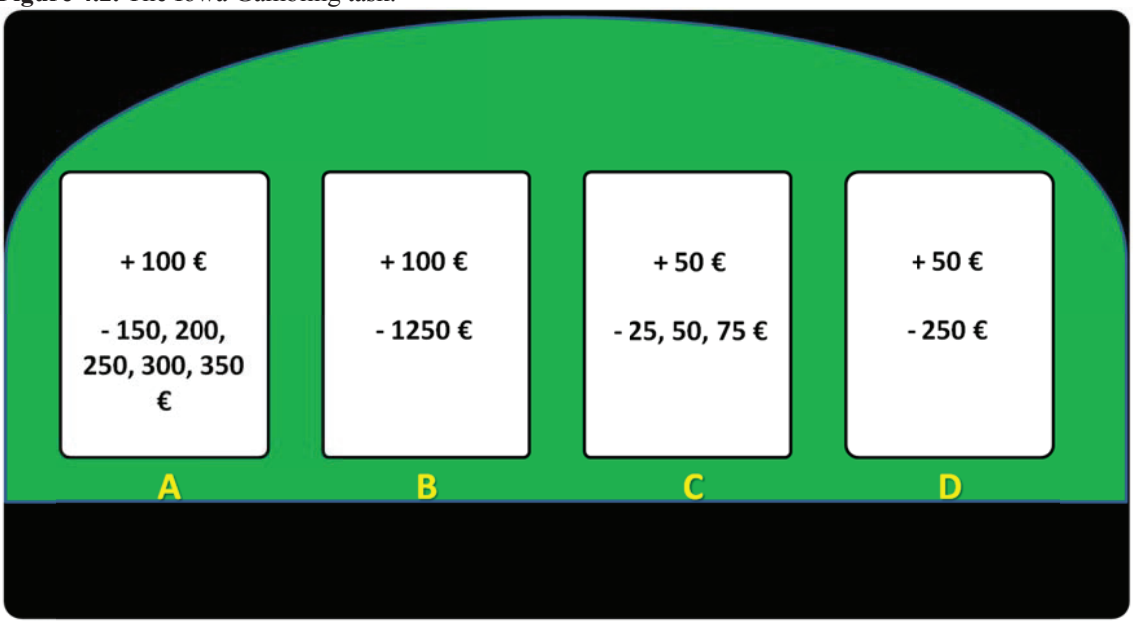
Figure 4.1. The Go/Nogo task.



The *Iowa Gambling Task (IGT)* employed in the present study was the original paradigm designed to measure decision making by Bechara et al. (1994). Participants were presented with four desks of cards on the screen of the computer and instructions required to increase an initial virtual budget of 2000 € by turning cards one-by-one. The IGT began with a practice sequence made up of 12 stimuli in order to allow participants to become familiar with the task, followed by the experimental block consisting of 100 trials. Subjects were told that there was no time limitation to complete the task, whereas they were not informed about the number of trials. The two decks on the right (C and D) were the advantageous ones, whereas the disadvantageous decks (A and B) always appeared on the left of the screen (Figure 4.2). The four decks were constructed as

described in paragraph 3.3.2. The measures obtained at the end of the IGT were 6: a total net-score, computed by subtracting the number of cards chosen from the disadvantageous decks from the number of cards chosen from the advantageous ones; 5 partial net-scores, obtained by dividing the overall performance in 5 blocks of 20 card selections.

Figure 4.2. The Iowa Gambling task.



Procedure

Before entering the study all individuals were informed of the study's aims and gave their written informed consent (Appendix). All participants first completed a short questionnaire collecting socio-demographic data (Appendix). They then completed the self-report measures, administered in a rotated sequence to control for order effects, and the two cognitive tasks. Both the tasks were implemented in E-Prime (version 1.1). Questionnaires and cognitive tasks were administered in a counterbalanced order. The entire assessment took about one hour.

The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional board of the Department of General Psychology at the University of Padova.

Data screening and statistical analyses

Missing data (<1%) in questionnaires were replaced with the participant's mean score on the respective measure.

All measures were screened for univariate and multivariate normality. The identified univariate outliers were winsorized using the method "next highest observation plus one" (as recommended by Field, 2009). The distributions on these measures were then considered normal according to figures of skew and kurtosis.

Cronbach's alphas were also calculated for each subscale of the PI, OBQ-87, and BIS-11 in order to test their reliability in each of the four groups. Almost all subscales showed acceptable (α>.60; Theorell, Michélsen, & Nordemar, 1993) to excellent (α>.90) internal consistency in all samples; the only exceptions were the PI subscale Impaired control over motor activities and the BIS-11 subscales Perseverance/Lack of delay in obtaining gratification and Nonplanning impulsiveness (Table 4.2). Removal of item 57 ("I feel I have to make special gestures or walk in a certain way") from the PI subscale Impaired control over motor activities improved the reliability of the scale (α=.60) in both OCD and HC samples, whereas internal consistency for the PG and the AD groups did not change; thus, item 57 was removed when computing the subscale score. Differently, analyses did not indicate that removal of any item would have significantly improved the internal consistency of the BIS-11 subscales Perseverance/Lack of delay in obtaining gratification and Nonplanning

impulsiveness. Therefore, only the BIS-11 Total score was included in subsequent analyses.

As regards the Go/Nogo task, RTs lower than 150 ms (accidental responses) were excluded.

Table 4.2. Cronbach's alphas for the PI, OBQ-87 and BIS-11 total and subscales scores.

	PG	OCD	AD	HC	N° of items
PI Total	.96	.95	.93	.90	60
PI Mental control	.93	.93	.92	.68	17
PI Washing	.85	.96	.84	.89	11
PI Checking	.93	.89	.94	.66	8
PI Motor control	.92	**.47**	.82	**.40**	7
OBQ-87 Total	.98	.97	.94	.96	87
OBQ-87 Perf.	.91	.88	.68	.81	14
OBQ-87 Resp. Harm	.90	.88	.74	.84	13
OBQ-87 Overest. threat	.87	.90	.82	.76	11
OBQ-87 Control thoughts	.89	.90	.85	.92	14
OBQ-87 Resp. Omission	.79	.90	.71	.68	6
OBQ-87 TAF	.63	.87	.75	.76	6
BIS-11 Total	.73	.70	.83	.63	30
BIS-11 Motor/Attention	.76	.81	.72	.75	10
BIS-11 Perseverance/lack of delay	**.40**	**.21**	.62	**.45**	12
BIS-11 Nonplanning	.64	**.40**	.72	**.44**	8

Note: Mental control=Impaired control over mental activities; Motor control=Impaired control over motor activities; Perf.=Perfectionism; Resp. Harm=Responsibility-Harm; Overest. threat=Overestimation of threat; Control thoughts=Control of thoughts; Resp. Omission=Responsibility-Omission.

A two-way Multivariate Analysis of Variance (MANOVA) with group and medication (yes/no) as the independent variables was conducted. The dependent variables were: the PI and OBQ-87 subscales scores; the BIS-11 Total score; the IGT Total net-score; the behavioural data obtained in the Go/Nogo task. Effect sizes (partial η^2) were also calculated. To analyze the between-subjects effects and the Group×Medication interaction, pairwise comparisons based on estimated marginal means with Bonferroni corrections for multiple comparisons were conducted. All the

dependent variables scores were transformed into Z-scores. Mean (SD) raw scores obtained by the four groups on all measures, as well as correlations between dependent variables (on the total sample), are reported in the Appendix. Moreover, Go/Nogo task performances of the 4 samples were further investigated by performing Pearson's correlations between the total number of errors and mean RTs (Go + Nogo trials), and the number of commission errors and mean RTs on Nogo trials for each group. Bohne et al. (2008) made use of this procedure to identify different profiles of performance on the Go/Nogo task in clinical groups.

Lastly, a 4(group)×5(IGT blocks 1-5) mixed model analysis of variance (ANOVA) was performed to analyze the profile of the IGT performances of the 4 groups. Raw IGT partial net-scores were used. Pairwise comparisons were executed based on estimated marginal means with Bonferroni corrections for multiple comparisons. SPSS version 17 was used to analyze the data.

4.2.2. Results

4.2.2.1. Differences between groups in self-report and cognitive measures

Multivariate tests revealed a significant effect of group [Pillai's trace $F_{(48,330)}$=2.75; p<.001; partial η^2=.286] and a significant interaction Group×Medication [Pillai's trace $F_{(32,218)}$=2.07; p=.001; partial η^2=.233], whereas the effect of medication was not significant [Pillai's trace $F_{(16,108)}$=1.70; p=.06; partial η^2=.202]. Tests of between-subjects effects (group and medication) are reported in Table 4.3.

As far as concerns differences between groups, pairwise comparisons revealed that:

- the three clinical groups scored significantly higher than HCs on the PI subscales Impaired control over mental activities and Checking (all ps<.01), whereas no differences between PG, OCD and AD groups emerged;
- OCD patients obtained significantly higher scores than the other three groups on the PI subscale Washing (all ps<.01); PGs and ADs did not differ, but PGs scored significantly higher than HCs (p=.005), whereas ADs obtained scored comparable with those of HCs;
- PGs scored higher than HCs in the PI subscale Impaired control over motor activities (p=.04);
- the three clinical groups scored significantly higher than HCs on the OBQ-87 subscales Perfectionism and Overestimation of threat (all ps<.01), whereas no differences between PG, OCD and AD groups emerged;

Table 4.3. Between-subjects effects tests. Mean (SD) Z-scores obtained by the 4 groups (medicated and unmedicated) in all measures.

		Medication status	PG	OCD	AD	HC	$F_{(3,122)}$	p	partial η^2	Pairwise comparisons
PI	Mental control	no	.19(1.01)	-.04(.73)	.27(1.01)	-.74(.24)	6.08	.001	.129	PG=OCD=AD>HC
		yes	.24(1.11)	1.15(1.26)	.12(.71)					
		total	.21(1.03)	.86(1.25)	.14(.74)					
	Washing	no	.26(.93)	1.32(1.99)	.12(.97)	-.54(.47)	10.04	<.001	.197	OCD>PG>HC PG=AD; AD=HC
		yes	.14(.87)	1.00(1.74)	-.12(.61)					
		total	.22(.89)	1.08(1.74)	-.09(.66)					
	Checking	no	.05(1.08)	-.34(.67)	.34(1.64)	-.61(.27)	2.42	.07	.056	PG=OCD=AD>HC
		yes	.38(1.06)	.87(1.12)	.14(1.00)					
		total	.17(1.07)	.57(1.14)	.16(1.08)					
	Motor Control	no	.43(1.82)	-.35(.00)	-.26(.21)	-.32(.15)	1.67	.18	.039	PG>HC OCD=AD=HC
		yes	.21(.84)	.14(.95)	.18(1.20)					
		total	.34(1.50)	.02(.84)	.12(1.12)					
OBQ-87	Perf.	no	.04(.78)	.54(1.36)	.77(.72)	-.63(.60)	7.07	<.001	.147	PG=OCD=AD>HC
		yes	.27(1.33)	.30(.81)	.03(.95)					
		total	.13(1.01)	.36(.93)	.13(.95)					
	Resp. Harm	no	.15(.65)	-.77(.65)	.80(.58)	-.49(.86)	3.90	.01	.087	PG=AD>HC OCD=HC
		yes	.19(1.53)	.29(1.01)	.24(.82)					
		total	.16(1.04)	.02(1.03)	.32(.82)					
	Overest. threat	no	.14(1.84)	.00(1.09)	.91(.68)	-.74(.44)	8.27	<.001	.168	PG=OCD=AD>HC
		yes	.36(1.27)	.76(1.07)	.21(.88)					
		total	.22(1.01)	.57(1.09)	.31(.88)					
	Control thoughts	no	.16(.82)	-.98(.72)	.53(.67)	-.61(.86)	3.68	.01	.082	PG=AD>HC OCD=HC
		yes	.34(1.28)	.53(.83)	.22(.85)					
		total	.23(1.00)	.15(1.04)	.26(.83)					
	Resp. Omission	no	-.04(.87)	-.67(.87)	1.28(.47)	-.55(.46)	5.99	.001	.128	PG=AD>HC OCD=HC
		yes	.50(1.45)	.47(1.16)	.10(.91)					
		total	.16(1.13)	.18(1.18)	.26(.95)					
	TAF	no	.19(.83)	-.19(1.46)	-.05(.62)	-.23(.87)	1.32	.27	.031	PG=OCD=AD=HC
		yes	.30(1.20)	-.23(1.15)	.13(1.12)					
		total	.23(.96)	-.22(1.18)	.11(1.06)					
BIS-11	Total score	no	.32(1.05)	-.40(1.22)	-.31(.94)	-.65(.67)	6.62	<.001	.139	PG=OCD>HC AD=HC
		yes	.87(.81)	.44(1.06)	.24(1.01)					
		total	.54(.99)	.32(1.08)	.17(1.0)					
IGT	Total net score	no	-.39(1.00)	-.19(.51)	.12(.65)	.57(1.33)	4.34	.006	.096	PG<HC PG=OCD=AD OCD=AD=HC
		yes	-.41(.85)	-.12(.58)	-.22(.49)					
		total	-.40(.93)	-.14(.55)	-.18(.52)					
Go/Nogo task	n° omission	no	-.33(.44)	-.62(.13)	1.08(1.56)	-.39(.43)	3.75	.01	.084	PG=OCD=HC AD>PG=HC
		yes	-.10(.55)	.64(1.50)	.29(1.35)					
		total	-.24(.49)	.33(1.41)	.40(1.38)					
	n° commission	no	-.22(.89)	-.54(.39)	.42(1.49)	-.13(.66)	.30	.82	.007	PG=OCD=AD=HC
		yes	.01(.82)	.50(1.52)	-.05(.89)					
		total	-.13(.86)	.24(1.40)	.01(.98)					
	RTs Go Trials	no	-.14(.99)	-.43(.70)	.91(1.04)	-.46(.86)	3.82	.01	.085	PG=OCD=HC AD>HC
		yes	-.04(.96)	.17(.88)	.31(.93)					
		total	-.10(.96)	.02(.86)	.39(.95)					
	RTs Nogo Trials	no	-.17(.89)	-.54(.56)	1.13(1.24)	-.27(.88)	3.74	.01	.084	PG=OCD=HC AD>PG=HC
		yes	-.13(1.01)	.25(1.12)	.33(1.04)					
		total	-.16(.92)	.05(1.05)	.44(1.09)					

Note: Mental control=Impaired control over mental activities; Motor control=Impaired control over motor activities; Perf.=Perfectionism; Resp. Harm=Responsibility-Harm; Overest. threat=Overestimation of threat; Control thoughts=Control of thoughts; Resp. Omission=Responsibility-Omission.

- PGs and ADs showed significantly higher scores than HCs in the OBQ-87 subscales Responsibility-Harm, Control of thoughts and Responsibility-Omission (all ps<.01). No differences between PG, OCD and AD groups emerged, and OCD patients scored similarly to HCs;

- PGs and OCD patients scored higher than HCs on the BIS-11 Total score ($p<.001$ and $p=.02$, respectively). No differences between PG, OCD and AD groups emerged, and ADs scored similar to HCs;

- PGs overall performed worse than HCs at the IGT ($p<.001$). No differences between PG, OCD and AD groups emerged, and OCD patients and ADs performances were comparable to that of HCs;

- on the Go/Nogo task PGs performed similar to OCD patients and HCs; ADs made more omission errors and were slower on Nogo trials than both PGs and HCs, and were slower on Go trials than HCs (all $ps<.01$).

The test of between-subjects effects also highlighted that medicated subjects reported higher scores than unmedicated ones on the BIS-11 Total score ($p=.04$).

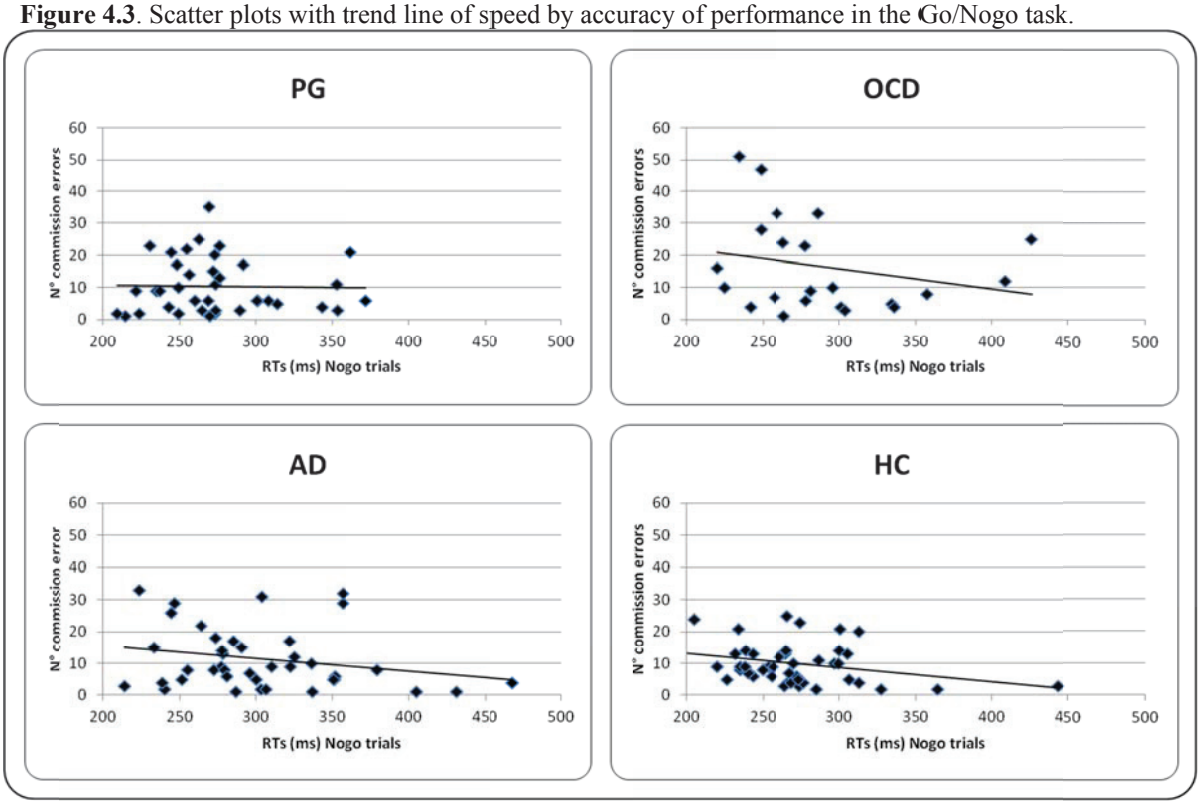
Lastly, the Group×Medication interaction resulted significant in regards to the OBQ-87 subscales Control of thoughts ($p=.02$) and Responsibility-Omission ($p<.001$), and the number of omission errors ($p=.01$) at the Go/Nogo task. Pairwise comparisons showed that unmedicated PGs and unmedicated ADs had higher scores than HCs on the OBQ-87 subscale Control of thoughts ($p=.01$ and $p=.04$, respectively). Furthermore, unmedicated ADs scored higher than the other groups on the OBQ-87 subscale Responsibility-Omission, and performed more omission errors on the Go/Nogo task (all $ps<.05$).

4.2.2.2. Analysis of Go/Nogo task performances

No association between the total number of errors on the Go/Nogo task and mean RTs (on both Go and Nogo trials) emerged in any of the 4 groups (all ps>.05).

In regards to the impulsive errors, the correlation between the number of commission errors and mean RTs on Nogo trials was negative and significant only in the HC group (r = -.31; p = .04). Scatter plots are reported in Figure 4.3.

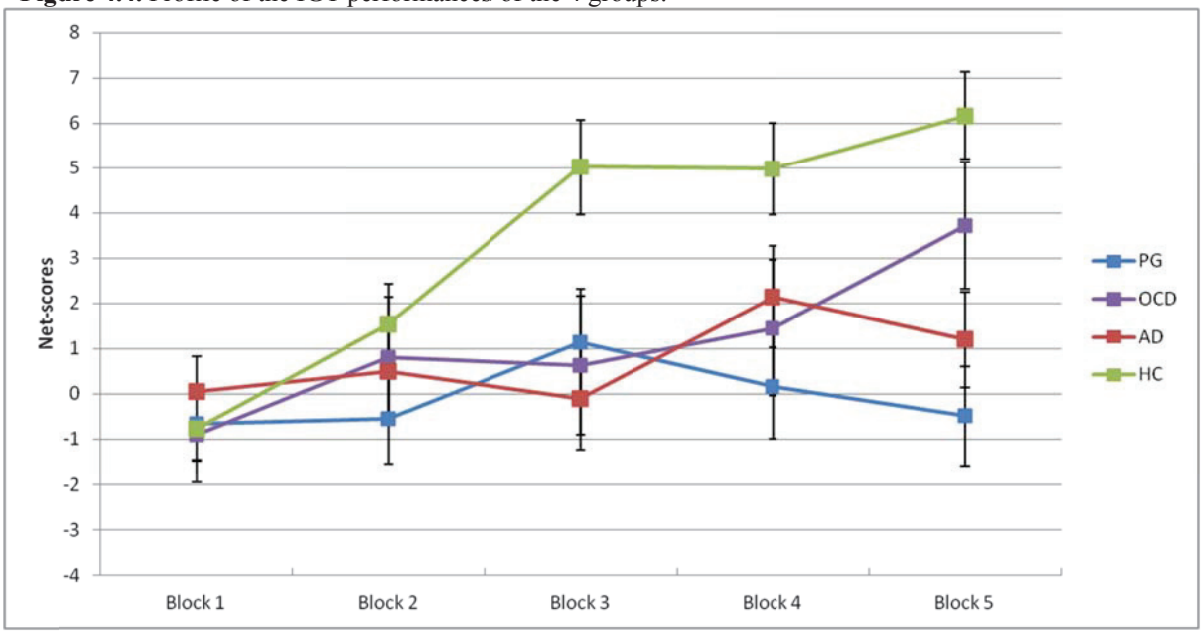
Figure 4.3. Scatter plots with trend line of speed by accuracy of performance in the Go/Nogo task.



4.2.2.3. Analysis of IGT profiles

As medication did not affect overall IGT performance (4.2.2.1), it was not entered as between-groups factor in the mixed model ANOVA. IGT profiles are reported in Figure 4.4.

Figure 4.4. Profile of the IGT performances of the 4 groups.



The analysis revealed a significant main effect of group [$F_{(3,142)}$=6.13, p=.001, partial η^2=.12]: PGs and ADs overall performed worse than HCs, whereas OCD patients performance did not differ from that showed by other participants. Furthermore, a significant main effect of block was observed [$F_{(4,568)}$=6.99, p<.001, partial η^2=.05]: performance on block 1 was overall significantly worse than performance on block 3, 4, and 5. Lastly, the Group×Block interaction was significant [$F_{(12,568)}$=2.40, p=.005, partial η^2=.05], in that ADs performed worse than HCs in block 3, PGs performed worse than HCs in block 4, and both PG and ADs performed worse than HCs in block 5. Mean IGT partial net-scores for the 4 groups are reported in Table 4.4.

Table 4.4.. Mean (with respective standard errors) IGT partial net-scores for the 4 groups.

NET SCORES	PG	OCD	AD	HC	$F_{(3,142)}$	p	partial η^2	Bonferroni post-hoc
Block 1	-.65(.8)	-.91(1.04)	.05(.77)	-.77(.71)	.28	.84	.006	PG=OCD=AD=HC
Block 2	-.54(1.02)	.82(1.32)	.5(.98)	1.53(.9)	.79	.50	.016	PG=OCD=AD=HC
Block 3	1.14(1.19)	.64(1.54)	-.1(1.14)	5.02(1.05)	4.33	.006	.084	PG=OCD=AD PG=OCD=HC AD<HC
Block 4	.16(1.16)	1.46(1.5)	2.15(1.11)	4.98(1.03)	3.49	.02	.069	PG=OCD=AD OCD=AD=HC PG<HC
Block 5	-.49(1.09)	3.73(1.42)	1.2(1.05)	6.17(.97)	7.97	<.001	.143	PG=OCD=AD OCD=HC PG=AD<HC
Total	-.08(.65)	1.16(.84)	.76(.62)	3.37(.57)	6.13	.001	.115	PG=OCD=AD OCD=HC PG=AD<HC

4.2.3. Summary of results

The main aim of Study 1 was to compare PGs with OCD patients, ADs, and HCs on both phenotypic and endophenotypic indicators of compulsivity and impulsivity, in order to understand which features are mainly involved in PG.

In regards to self-report measures, results highlighted that PGs are characterized by higher levels of both compulsive and impulsive features than HCs; a number of similarities between PGs, OCD patients and ADs in both dimensions were also observed.

As far as concern the Go/Nogo task, PGs performed similar to OCD patients and HCs, whereas ADs performed worse than PGs and HCs; in particular, ADs made more omission errors (especially those unmedicated) and were slower than both PGs and HCs. A further investigation of Go/Nogo task performance (speed by accuracy for impulsive errors) failed in detecting any peculiar pattern of response in the clinical groups. However, in HC group a negative correlation between number of commission

errors and RTs on Nogo trials emerged, thus indicating that nonclinical subjects performed on a continuum ranging from a "fast and inaccurate performance" to a "slow and accurate performance".

The IGT profiles revealed that PGs did not learn to shift from disadvantageous to advantageous decks over the task, and showed difficulties in maintaining the learning, thus resulting in an overall bad performance. Similarly, performance of ADs was poor but, differently from PGs, ADs were characterized by a delayed, and not totally absent, shift from disadvantageous to advantageous decisions (net-score increases in block 4). A decline on block 5 was observed in both PG and AD groups. No differences between OCD patients and HCs emerged.

Overall, findings from self-report measures support the co-occurrence of compulsivity and impulsivity in PGs; consequently, conceptualizing PG as a compulsive-impulsive spectrum disorder or a behavioural addiction seems to be equally adequate. Furthermore, present results also sustain the existence of a compulsive-impulsive spectrum, including distinct disorders (i.e., OCD, PG, and AD) characterized by different amounts of both dimensions.

Nonetheless, results from the IGT suggest that cognitive mechanisms of PGs are more similar to those characterizing ADs rather than to those typical of OCD, thus supporting the hypothesis of impaired decision making ability as endophenotype for addictive disorders.

4.3. Study 2 - Compulsivity and impulsivity: a comparison between Pathological gamblers and croupiers

4.3.1. Method

Participants

Twenty croupiers were recruited through the *Centro Formazione Croupier,* Abano Terme (PD). Exclusion criteria were the same applied in Study 1 to participants included in the HC group (paragraph 4.2.1). Two subjects were excluded as they reported a score of 3 or 4 at the SOGS, and 3 individuals did not enter the study because of high levels of depression, anxiety, or worry.

Forty-five participants were finally included in Study 2: 15 croupiers, 15 PGs and 15 HCs. Data from PGs and HCs were randomly selected from those collected in Study 1. Groups differed in years of education (croupiers had an higher education level than HCs) and marital status (all croupiers were single). PGs reported higher levels of depression and worry than the other groups (Table 4.5). 46.7% of PGs were medicated.

Table 4.5. Demographic and clinical variables of the three groups.

	PG	CR	HC	χ^2/F	df	p	post-hoc
Age	32.33 (8.53)	28.80 (7.21)	33.80 (7.65)	1.62	2,42	.21	PG=CR=HC
Years of education	12.53 (3.33)	14.72 (2.84)	11.93 (2.84)	3.37	2,42	.04	PG=CR; PG=HC CR>HC
Gender (% of males)	93.3	100	93.3	1.05	2	.59	-
Marital Status (% of married/cohabitant)	40	0	46.7	9.30	2	.01	-
Occupation (% of full-time employed)	57.1	53.3	73.3	7.21	8	.51	-
BDI-II	9.67 (7.32)	3.73 (3.51)	1.93 (2.71)	10.04	2,42	<.001	PG>CR=HC
BAI	9.47 (10.16)	5.57 (4.34)	3.60 (2.58)	3.11	2,42	.06	PG=CR=HC

	PG	CR	HC	χ^2/F	df	p	post-hoc
PSWQ	44.27 (11.77)	35.13 (6.97)	30.01 (4.52)	11.31	2,42	<.001	PG>CR=HC

Note: post-hoc = Bonferroni post-hoc. CR = croupiers.

Measures and Procedure

The same measures and procedure of Study 1 were adopted.

Data screening and statistical analyses

Data from croupiers were screened as described in Study 1. Reliability of self-report measures (PI, OBQ-87, and BIS-11) was tested. In the light of results emerged in Study 1, Cronbach's alphas for the modified PI subscale Impaired control over motor activities (without item 57) and the BIS-11 Total score were calculated in the croupiers sample and were used in the analyses. Internal consistency for all scales was acceptable/good (.70<α <.90).

A one-way MANOVA with group as the independent variable was conducted. The dependent variables were the same as in Study 1. Effect sizes (partial η^2) and pairwise comparisons based on estimated marginal means with Bonferroni corrections for multiple comparisons to explore between-subjects effects were conducted. All the dependent variables scores were transformed into Z-scores. Mean (SD) raw scores obtained by the 3 groups on all measures are reported in the Appendix.

Lastly, Go/Nogo task and IGT performances of the 3 samples were analyzed as in Study 1.

4.3.2. Results

4.3.2.1. Differences between groups in self-report and cognitive measures

Multivariate tests revealed a significant effect of group [Pillai's trace $F_{(32,50)}$=1.87; p=.02; partial η^2=.545]. Tests of the between-groups effects are shown in Table 4.6.

Table 4.6. Between-subjects effects tests. Mean (SD) Z-scores obtained by the 3 groups.

		PG	CR	HC	$F_{(2,39)}$	p	partial η^2	Bonferroni post-hoc
PI	**Mental control**	.72(1.43)	-.14(.45)	-.52(.18)	7.39	.002	.275	PG>CR=HC
	Washing	.82(1.14)	-.32(.56)	-.44(.68)	9.84	<.001	.335	PG>CR=HC
	Checking	.55(1.46)	-.07(.49)	-.44(.41)	4.20	.02	.177	PG>HC=CR CR=PG
	Motor Control	.87(2.09)	.69(.99)	-.35(.00)	3.47	.04	.151	PG>HC=CR CR=PG
OBQ-87	**Perf.**	.33(1.16)	.23(.98)	-.39(.69)	2.43	.10	.111	PG=CR=HC
	Resp. Harm	.16(1.32)	-.10(.99)	-.40(.59)	.36	.70	.018	PG=CR=HC
	Overest. threat	.62(1.19)	-.06(.87)	-.39(.59)	4.75	.01	.196	PG>HC=CR CR=PG
	Control thoughts	.31(1.13)	-.14(.80)	-.21(1.04)	1.16	.32	.056	PG=CR=HC
	Resp. Omission	.39(1.35)	.14(.77)	-.46(.55)	3.07	.06	.136	PG=CR=HC
	TAF	.29(1.07)	-.46(.77)	.01(1.07)	1.90	.16	.089	PG=CR=HC
BIS -11	**Total score**	.52(.94)	.22(1.21)	-.63(.50)	6.51	.004	.250	PG=CR>HC
IGT	**Total net score**	-.31(.66)	.05(1.51)	.27(.72)	1.28	.29	.062	PG=CR=HC
Go/Nogo task	**n° omission**	.13(1.14)	-.04(.99)	-.41(.97)	.28	.77	.013	PG=CR=HC
	n° commission	-.20(.84)	.12(1.06)	-.20(.84)	.54	.59	.027	PG=CR=HC
	RTs Go Trials	.20(1.10)	-.37(.93)	.08(87)	1.55	.25	.074	PG=CR=HC
	RTs Nogo Trials	.10(.96)	-.39(.99)	.37(.94)	2.08	.14	.096	PG=CR=HC

Note: CR=croupiers. Mental control=Impaired control over mental activities; Motor control=Impaired control over motor activities; Perf.=Perfectionism; Resp. Harm=Responsibility-Harm; Overest. threat=Overestimation of threat; Control thoughts=Control of thoughts; Resp. Omission=Responsibility-Omission.

As far as concerns differences between groups, pairwise comparisons revealed that:

- PGs had higher scores than both croupiers and HCs in PI subscales Impaired control over mental activities and Washing (all ps<.05);

- PGs scored significantly higher than HCs in PI subscales Checking and Impaired control over motor activities, and in OBQ-87 subscale Overestimation of threat (all ps<.05), whereas croupiers did not differ neither from PGs nor from HCs;

- on the BIS-11 Total score, PGs and croupiers scored similarly and significantly higher than HCs (all ps<.05);

- no differences between groups in the cognitive tasks emerged.

4.3.2.2. Analysis of Go/Nogo task performances

No association between the total number of errors on the Go/Nogo task and mean RTs (on both Go and Nogo trials) was observed in any of the 3 groups (all ps>.05). As far as concern the impulsive errors, none of the correlations between the number of commission errors and mean RTs on Nogo trials was significant (all ps>.05).

4.3.2.3. Analysis of IGT profiles

The mixed model 3(group)×5(IGT blocks 1-5) ANOVA did not detect significant main effects of group [$F_{(2,38)}$=1.28, p=.29] or block [$F_{(1,38)}$=1.18, p=.28], nor a significant Group×Block interaction [$F_{(2,38)}$=.96, p=.39]. Mean IGT partial net-scores and respective standard errors are reported in Table 4.7.

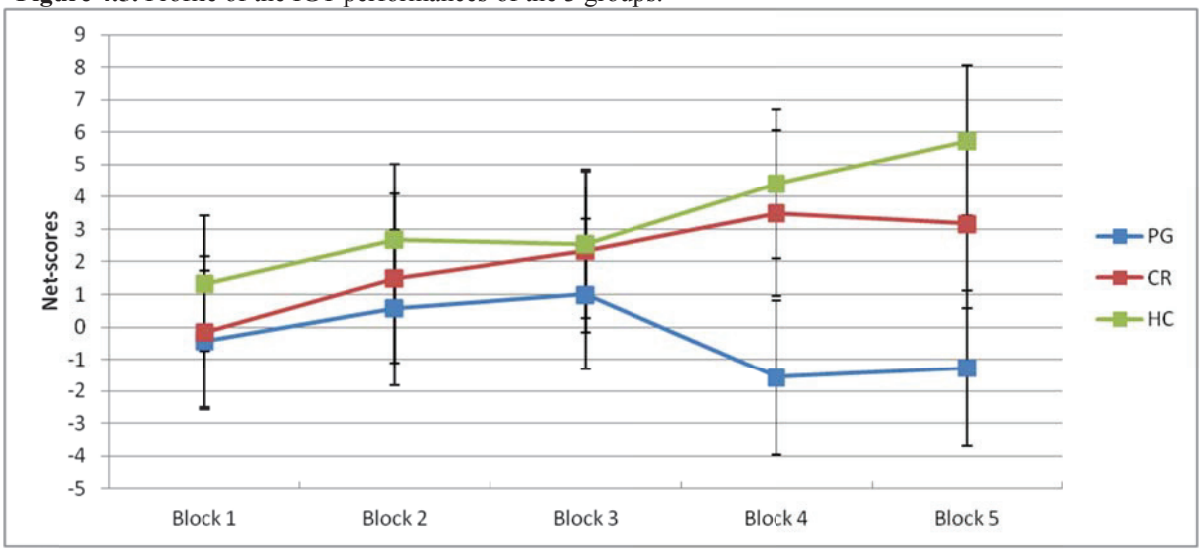
Table 4.7. Mean (with respective standard errors) IGT partial net-scores for the 3 groups.

NET SCORES	PG	CR	HC
Block 1	-.43(2.15)	-.17(2.33)	1.33(2.08)
Block 2	.57(2.41)	1.50(2.61)	2.67(2.33)
Block 3	1.00(2.32)	2.33(2.51)	2.53(2.24)
Block 4	-1.57(2.37)	3.50(2.56)	4.40(2.29)
Block 5	-1.29(2.39)	3.17(2.58)	5.73(2.31)
Total	-.34(1.67)	2.07(1.81)	3.33(1.62)

Note: CR=croupiers.

Nonetheless, the analyses of the IGT learning profiles showed that PGs had a worse performance than the other two groups: they improved over the three blocks but their performance declined on blocks 4 and 5. Their net-scores were overall lower than those obtained by croupiers and HCs. The trend of performance of croupiers and HCs was similar; nonetheless, the former did not improve on block 5 (Figure 4.5).

Figure 4.5. Profile of the IGT performances of the 3 groups.



Note: CR = croupiers.

4.3.3. Summary of results

Study 2 was conducted to preliminary compare compulsive and impulsive features in PGs and in croupiers.

In line with what expected, PGs showed higher levels of self-reported compulsivity than both croupiers and HCs, in particular as regards the fear of losing control over mental activities. Furthermore, PGs and croupiers reported similar levels of impulsivity, significantly higher than those characterizing HCs.

Statistical analyses did not highlight differences between groups in cognitive measures; it is to note that only 45 participants were tested, thus the study was probably underpowered. However, a graphical analyses of the IGT learning profiles suggested that PGs overall performed worse than both croupiers and HCs. Despite the trend of performance of croupiers was similar to that of HCs, the former did not show any improvement on block 5, and obtained overall lower scores than HCs, although differences did not reach significance level. This result, together with the finding of self-reported impulsivity in croupiers, seems to suggest the presence of shared impulsive features in PGs and croupiers.

Chapter 5

General discussion

A large amount of data on the compulsive and impulsive aspects involved in the phenomenology of PG has been gathered during last years. Two main theoretical frameworks based on these dimensions have been proposed for PG categorization in DSM-5: the compulsive-impulsive spectrum hypothesis (Hollander & Wong, 1995a; 1995b; McElroy et al., 1994; Oldham et al., 1996) and the behavioural addiction conceptualization (Frascella et al., 2010; Holden, 2001; Petry, 2006; Potenza, 2006). Both these approaches define compulsivity and impulsivity as crucial features entailing PG. However, the former is based on a dimensional perspective, and attempts to verify the validity of this hypothesis mainly relied on comparisons between PGs and OCD patients on self-report measures. On the other hand, the latter primarily focuses on analogies between PG and SUDs, and identifies impulsivity as the predominant feature of PG, while compulsivity is hypothesized to occur only in later stages of the disorder ("impulsivity-compulsivity shift"; Brewer & Potenza, 2008; Dalley et al., 2011; Everitt & Robbins, 2005; Fineberg et al., 2010; Potenza, 2008); comparisons between PGs and individuals with SUDs, in particular ADs, have been conducted. Evidence supporting one or the other conceptualization are mixed.

Gottesman and Gould (2003) highlighted the importance of using endophenotypic measures in clinical assessment, since such indicators can valuably contribute in clarifying diagnosis and classification issues. In relation to PG,

behavioural tasks assessing motor inhibition and decision making abilities have been used because they evaluate executive functions involved in self-regulating behaviours (Aragues et al., 2011; Bechara, 2003; Dalley et al., 2011; Dawe et al., 2004; de Wit & Richards, 2004; Potenza & Wit, 2010; Yücel & Lubman, 2007). Impairments in these abilities have been observed in PGs, OCD patients and ADs (el-Guebaly et al., 2011; Fineberg et al., 2010).

The present dissertation was conducted in the light of these considerations, and following the recommendation that directly comparing PGs with OCD patients and individuals with SUDs can represent a viable way to identify the most suitable classification for PG (Bottesi, 2012; Grant & Potenza 2006).

In regards to self-report measures, PGs showed more compulsive features than healthy individuals. In fact, the former reported significantly higher levels of washing and checking symptoms, as well as more fear of losing control over both mental and motor activities, than the latter. This result is partially in line with findings by Blaszczynski (1999), who observed higher scores on the Impaired control over mental activities and the Impaired control over motor activities subscales of the PI, but not on subscales measuring washing and checking symptoms, in PGs compared to a group of HCs. On the other hand, the present finding is in contrast with results reported by Anholt et al. (2004) and Bottesi et al. (2011a), as they did not find any difference between PGs and healthy individuals on the Padua-R and the OCI-R, respectively. In the present study, PGs also showed higher levels of OC dysfunctional beliefs than HCs, with the only exception of TAF. Similar findings have been reported by Anholt et al. (2004), who made use of the original version of the OBQ-87. Furthermore, higher scores on Perfectionism and Excessive control of thoughts subscales of OBQ-R in PGs

than controls have been observed also by Bottesi et al. (2011a). Lastly, PGs were characterized by more self-reported impulsive features than HCs. In particular, the BIS-11 measures three specific dimensions of impulsivity: the tendency to act without thinking, lack of attention/impulsive decision making, and poor orientation towards future (Patton et al., 1995). The occurrence of these features in the present PG sample is in line with findings from a broad meta-analysis, which highlighted that acting on the spur of the moment and performing behaviours without thinking represent the main impulsive dimensions typical of PG (MacLaren et al., 2011).

PGs, OCD patients and ADs obtained similar scores (higher than HCs) in several self-report measures of both compulsivity and impulsivity. Specifically, all clinical groups referred fears of losing control over their mental activities, checking compulsions, dysfunctional perfectionism and the tendency to overestimate the severity of negative events and their probability of occurrence. These findings are overall consistent with studies suggesting similarities in OC symptoms and cognitions between OCD patients and PGs on one hand (Anholt et al., 2004; Bottesi et al., 2011a) and OCD patients and ADs on the other one (Anton, 2000; Bottesi et al., 2012a; Modell et al., 1992). Interestingly, PGs and ADs reported scores comparable to OCD patients in the OBQ-87 Overestimation of threat subscale. This is in contrast with the result by Anholt et al. (2004), who observed lower levels of this dysfunctional domain in PGs than in OCD patients and commented the finding as "hardly surprising given the very nature of the pathology, and the fact that pathological gambling is correlated with sensation seeking behavior" (p. 535). Nonetheless, the tendency of exaggerating the severity and probability of threats showed by PGs and ADs participating the present study may be related to the ongoing treatment and, therefore, to the recognition of the potentially bad

consequences deriving from the performance of their actions. Furthermore, unmedicated PGs and ADs reported higher sense of responsibility for their actions and higher need of having control over their own thoughts than healthy individuals, whereas OCD patients did not differ from HCs in these domains. This result may also be explained in terms of the re-interpretation, operated by PGs and ADs, of previously rewarding and pleasurable behaviours as potential harms and problems for both themselves and their loved ones. Lastly, clinical groups did not differ in regards to self-reported impulsivity (but only PGs and OCD patients were more impulsive than HCs). This is consistent with the evidence that both PGs and patients with SUDs are generally characterized by high scores in self-report measures of impulsivity (Blaszczynski et al., 1997; Potenza et al., 2003b; 2009), and with studies which pinpointed that also OCD patients may report impulsive features (Ettelt et al., 2007; Potenza, 2007).

In conclusion, results from self-report questionnaires support the co-occurrence of compulsivity and impulsivity in PGs; therefore, both the conceptual frameworks of the compulsive-impulsive spectrum and behavioural addiction appear appropriate. This is particularly true considering that PGs participating the study were all under treatment; thus, the co-occurrence of compulsivity- and impulsivity-related aspects is reasonable both in the light of the compulsive-impulsive spectrum hypothesis, which states that compulsive and impulsive features may occur simultaneously or at different time points within the same individual (Grant & Potenza, 2006), and of the phenomenon of "impulsivity-compulsivity shift", which is typical of addictive behaviours (Brewer & Potenza, 2008; Dalley et al., 2011; Everitt & Robbins, 2005; Fineberg et al., 2010; Potenza, 2008). Independently of the theoretical conceptualization, present results suggest that PGs participating the study were probably in a stage of the disorder

characterized by a shift from egosyntonic novelty driven/impulsive behaviours to egodystonic habit driven/compulsive behaviours.

The number of similarities between PGs, OCD patients and ADs seems to be in line with the compulsive-impulsive spectrum hypothesis. According to this dimensional approach, OCD is located on the compulsive pole of such a continuum and SUDs lie on the impulsive one; PG is postulated to be closer to the impulsive extreme (van den Heuvel et al., 2010). Compulsivity and impulsivity are supposed to contribute to varying degrees across the disorders, and this would give reason of both similarities and differences among these psychopathologies (Grant & Potenza, 2006). Several phenomenological analogies between OCD and AD have been reported in literature (Anton, 2000; Bottesi, 2012; Lubman et al., 2004; Modell et al., 1992), and the idea of including them in a common category of disorders (i.e. the addictive/reward dependent spectrum) was taken into account but was also controversial (Lochner & Stein, 2006). In the light of the assumptions underlying the compulsive-impulsive spectrum hypothesis and of its dimensional nature, present results from self-report questionnaires support the inclusion of PG, OCD and AD within the same spectrum of disorders.

In regards to motor inhibition ability, PGs, OCD patients and healthy individuals showed similar performances on the Go/Nogo task. This result is in contrast with literature suggesting the presence of motor inhibition deficits in PG (Fuentes et al., 2006; Goudriaan et al., 2005; Kertzman et al., 2008; Ledgerwood et al., 2012; Reena, 2008) and OCD (Abramowitch et al., 2011b; Bannon et al., 2002; 2006; Bottesi et al., 2012a; Chamberlain et al., 2006; 2007; Penadés et al., 2007). Nonetheless, other authors failed in finding impairments in these groups (Bohne et al., 2008; Johannes et al., 2001; Hermann et al., 2003; Kim et al., 2007; Lawrence et al., 2009; Ledgerwood et al., 2009;

Maltby et al., 2005; Ruchsow et al., 2005; 2007). Moreover, a further investigation of Go/Nogo task performances did not highlight any peculiar pattern of response in the clinical groups (whereas a negative correlation between number of commission errors and the associated mean RTs was observed in HCs). Bohne et al. (2008) suggested that the neural processes underlying motor inhibition ability in OCD might be abnormal but not altered enough to result in behavioural deficits. Nonetheless, it is unclear whether, according to the Authors, this explanation is applicable to OCD *per se* or only to OCD patients under treatment. Furthermore, it would be interesting to ascertain whether this argumentation can be applied also to PGs; the neural level of study may be of help in that sense. ADs (in particular those unmedicated) overall performed worse than PGs and HCs, as they made more omission errors and were slower on both Go and Nogo trials. Thus, they did not show motor inhibition deficits, which is in contrast with some previous findings (Goudriaan et al., 2005; 2006; Lawrence et al., 2009). Rather, such a performance may be indicative of attention deficits (Halperin et al., 1991), and can reasonably be attributed to the previous protracted use of alcohol, which may have altered the neural circuits involved in task execution. Lastly, the fact that medicated patients overall did not perform worse than unmedicated ones is in line with evidence suggesting that medication do not affect performance on Go/Nogo task (Bannon et al., 2002; 2006; Harris & Dinn, 2003; Mataix-Cols, Alonso, Pifarre, Menchon & Vallejo, 2002; Penadés et al., 2007; Watkins et al., 2005).

It is important to note that literature on motor inhibition ability makes use of two main paradigms: the Go/Nogo task and the Stop-Signal task (Logan et al., 1984). Comparing results obtained from the administration of the Go/No go task in the present study and research data obtained through the Stop-Signal task may be difficult, as the

specific behavioural indexes of motor inhibition deficits are quite different (i.e. number of commission errors vs SSRTs; Bottesi, 2012). Furthermore, inconsistent results on Go/Nogo task performance can be accounted by the variety of the paradigms adopted in literature: Go/Nogo tasks may differ as regards the nature of stimuli (e.g. geometric figures, strings of letters); the total number of stimuli and the proportion of Go and Nogo stimuli included in each trial; stimuli duration; interstimulus interval duration, which can be fixed or variable (Bottesi, 2012).

Results from the IGT highlighted that PGs and ADs performed worse than HCs, whereas OCD patients performance did not differ from that showed by other participants. These findings are in line with previous ones, which reported a bad performance of PGs (Cavedini et al., 2002b; Goudriaan et al., 2005; Kertzman et al., 2011; Ledgerwood et al., 2012; Linnet et al., 2006) and ADs (Fein et al., 2004; Kim et al., 2011; Miranda et al., 2009; Nöel et al., 2007; Salgado et al., 2009; Tomassini et al., 2012) when compared to healthy subjects. Furthermore, the absence of deficits in decision making ability in OCD patients has been previously observed by several authors (Krishna et al., 2012; Lawrence, 2006; Nielen et al., 2002), despite some reporting impaired performance in OCD patients, hazardously suggesting an analogy between compulsions and immediate rewards (in that they relieve anxiety; Cavedini et al., 2002a).

The analysis of the IGT profiles revealed that ADs did worse than HCs in block 3, PGs performed poorer than HCs in block 4, and both PGs and ADs were more impaired than HCs in block 5. A typical shift to the disadvantageous decks towards the end of the task has been previously observed in PGs (Cavedini et al., 2002b; Forbush et al., 2008; Kertzman et al., 2011) and in ADs (Kim et al., 2011; Nöel et al., 2007;

Tomassini et al., 2012), thus indicating problems in the maintenance of learning. Nonetheless in the present study ADs, differently from PGs, showed a more variable performance, as they improved from block 3 to block 4, and then declined in block 5. This may suggest that ADs are characterized by a delayed, and not completely absent, learning. On the other hand, PGs seemed to be overall impaired, in that they did not learn to shift from high-risk decks to low-risk ones all over the task. Partially similar findings have been reported by Goudriaan et al. (2005): they observed a comparable performance in PGs and ADs, and highlighted that ADs learnt to choose cards from the advantageous decks over time, although they selected less frequently from them than HCs, whereas PG did not.

Present results suggest that decision making processes in PGs are more similar to those observed in ADs, rather than in OCD patients. From an endophenotype perspective, such deficits are likely to be associated with dysfunctions of the brain circuitry involved in decision making ability. A diminished activation in the vmPFC and in the dopaminergic mesolimbic pathway linking the ventral tegmental area to the nucleus accumbens is supposed to be responsible of impulsive choices and reward-seeking behaviours, and anomalies in these circuits have been observed in both PG and SUDs (Bottesi, 2012; Everitt & Robbins, 2005; Potenza, 2006; 2008; Reuter et al., 2005; Volkow & Fowler, 2000; Williams & Potenza, 2008; Wrase et al., 2007). Therefore, present findings from IGT performances claim analogous cognitive processes in PG and AD, thus suggesting the adequacy of considering PG a behavioural addiction.

A second preliminary study was conducted to investigate compulsive and impulsive symptoms using a dimensional approach, and PGs were compared with a

sample of croupiers. Literature documented that croupiers are individuals at risk for the development of PG (Hing & Gainsbury, 2011; Hu et al., 2012; Lee et al., 2008; Shaffer et al., 1999b; Wu & Wong, 2008); ratios of PG among casino workers vary between 7% (Wu & Wong, 2008) and 14% (Hu et al., 2012). Consistently, 10% of croupiers recruited in the present study obtained a score indicating "some problems with gambling" on the SOGS; therefore, their data were excluded from the analyses.

The comparison on self-report measures revealed that PGs are characterized by more compulsive features than both croupiers and HCs; this result was rather predictable, in the light of the stage of PG characterizing the clinical sample. On the other hand, results suggest that the stereotyped actions frequently endorsed by croupiers because of their job are not related with compulsivity, as measured by the PI and OBQ-87. Conversely, PGs and croupiers showed comparable and higher levels of impulsivity than HCs; this finding is quite interesting, since impulsivity has been considered a probable PG risk factor (Johansson et al., 2009; Vitaro et al., 1997).

No difference between groups in cognitive measures emerged. Nonetheless, a graphical analysis of the IGT profiles highlighted that PGs had a worse performance than both croupiers and HCs. The two healthy groups performed quite similar, except for block 5: HCs continued to improve also at the end of the task, whereas croupiers did not. A typical decline of performance towards the end of the IGT has been observed in PG and AD (Cavedini et al., 2002b; Forbush et al., 2008; Kertzman et al., 2011; Kim et al., 2011; Nöel et al., 2007; Tomassini et al., 2012) and has been previously discussed. Croupiers did not decline, but they did not even increase their net-score, as healthy individuals generally do: studies with larger samples sizes may clarify whether croupiers' performance on the IGT is someway impaired or not.

The current study is characterized by some shortcomings. First of all, the small samples sizes, which imply low power and make difficult drawing generalizable conclusions. Moreover, both PG and OCD groups were heterogeneous: the first in terms of type of gambling, the second as regards symptom subtypes; the heterogeneity increases the generalizability of any results at a diagnostic level but may also cloud individual differences. Furthermore, more than a half of clinical participants were medicated: despite the effects of medication resulted rather limited in the present study, testing medication-free patients would have guaranteed more accurate findings, especially as regards cognitive measures. It is also noteworthy that patients were recruited from different Italian outpatient and inpatient mental health clinics: this entails heterogeneity within the clinical groups, in terms of both typology and duration of treatment. Finally, the inclusion of patients with comorbid Axis-I or Axis-II may have affected results.

The conduction of future studies overcoming the above-mentioned limitations are required. The integration of phenotypic and endophenotypic measures in the assessment of these disorders appears of great promise, thus it should be perpetrated in clinical psychology research; furthermore, studying active and not treatment-seeking gamblers would represent a more suitable way to clarify the best diagnostic classification for PG. Lastly, investigating compulsive and impulsive features among samples at risk for the development of PG, i.e. croupiers, through longitudinal studies is recommended.

To summarize, main findings of the present dissertation suggest that:

a. on the basis of self-reported compulsivity and impulsivity, categorizing PG as a compulsive-impulsive spectrum disorder or as a behavioural addiction is equally

adequate. Nonetheless, the compulsive-impulsive spectrum hypotheses seems to be more appropriate, in the light of the number of similarities observed between PG, OCD, and AD.

b. IGT performances highlighted that PGs and ADs shared similar decision making deficits, whereas OCD patients did not. Thus, from an endophenotype approach PGs is better definable as a behavioural addiction; this is in line with the proposal of including PG ("Gambling Disorder") into the "Substance Use and Addictive Disorders" category in the DSM-5.

c. Croupiers, who can be considered individuals at risk of developing PG, showed levels of self-reported impulsivity comparable to PGs and a potentially impaired performance on the IGT; on the contrary, they did not report any compulsive feature. These preliminary results might further support the notion of PG as a behavioural addiction, in that probable vulnerability factors for addictions seem to occur also in healthy individuals predisposed for PG. Nonetheless, small samples sizes advocate that these findings have to be interpreted cautiously.

Therefore, results from the present dissertation suggest that both the diagnostic classifications may be suitable for PG, but relying on phenotypic or endophenptypic indicators imply different conclusions.

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Appendix

Informativa ex art.13 D. Lgs. 196/2003 per il trattamento di dati sensibili

Gentile Signore/a,
ai sensi del D.Lgs. 196/2003, sulla tutela delle persone e di altri soggetti rispetto al trattamento dei dati personali, il trattamento delle informazioni che La riguardano, sarà improntato ai principi di correttezza, liceità e trasparenza e tutelando la Sua riservatezza e i Suoi diritti.
In particolare, i dati idonei a rivelare l'origine razziale ed etnica, le convinzioni religiose, filosofiche o di altro genere, le opinioni politiche, l'adesione a partiti, sindacati, associazioni od organizzazioni a carattere religioso, filosofico, politico o sindacale, nonché i dati personali idonei a rivelare lo stato di salute e la vita sessuale, possono essere oggetto di trattamento solo con il consenso scritto dell'interessato e previa autorizzazione del Garante per la protezione dei dati personali (articolo 26).
Ai sensi dell'articolo 13 del predetto decreto, La informiamo che, nei limiti dell'Autorizzazione generale del Garante n.2/2004:
i dati sensibili da Lei forniti verranno trattati per la finalità della ricerca denominata "caratteristiche psicologiche e neuropsicologiche in persone con gioco patologico, disturbo ossessivo compulsivo e dipendenza da alcol" e per ricontattarla per via telefonica, fax, posta ordinaria, e-mail, ecc.
2) il trattamento sarà effettuato con le seguenti modalità: elettroniche e cartacee
3) I dati non saranno comunicati a nessuno; garantendone l'anonimato e la riservatezza potranno essere utilizzati solo a fini didattici, di supervisione clinica o di ricerca scientifica
4) Il titolare del trattamento è: …….
5) Il responsabile del trattamento è il Dott…….
6) In ogni momento potrà esercitare i Suoi diritti nei confronti del titolare del trattamento, ai sensi dell'articolo 7 del D.lgs.196/2003, che per Sua comodità riproduciamo integralmente:

Decreto Legislativo n.196/2003, Art. 7 - Diritto di accesso ai dati personali ed altri diritti

1. L'interessato ha diritto di ottenere la conferma dell'esistenza o meno di dati personali che lo riguardano, anche se non ancora registrati, e la loro comunicazione in forma intelligibile.
2. L'interessato ha diritto di ottenere l'indicazione:
   a) dell'origine dei dati personali;
   b) delle finalità e modalità del trattamento;
   c) della logica applicata in caso di trattamento effettuato con l'ausilio di strumenti elettronici;
   d) degli estremi identificativi del titolare, dei responsabili e del rappresentante designato ai sensi dell'articolo 5, comma 2;
   e) dei soggetti o delle categorie di soggetti ai quali i dati personali possono essere comunicati o che possono venirne a conoscenza in qualità di rappresentante designato nel territorio dello Stato, di responsabili o incaricati.
3. L'interessato ha diritto di ottenere:
   a) l'aggiornamento, la rettificazione ovvero, quando vi ha interesse, l'integrazione dei dati;
   b) la cancellazione, la trasformazione in forma anonima o il blocco dei dati trattati in violazione di legge, compresi quelli di cui non è necessaria la conservazione in relazione agli scopi per i quali i dati sono stati raccolti o successivamente trattati;
   c) l'attestazione che le operazioni di cui alle lettere a) e b) sono state portate a conoscenza, anche per quanto riguarda il loro contenuto, di coloro ai quali i dati sono stati comunicati o diffusi, eccettuato il caso in cui tale adempimento si rivela impossibile o comporta un impiego di mezzi manifestamente sproporzionato rispetto al diritto tutelato.
4. L'interessato ha diritto di opporsi, in tutto o in parte:
   a) per motivi legittimi al trattamento dei dati personali che lo riguardano, ancorché pertinenti allo scopo della raccolta;
   b) al trattamento di dati personali che lo riguardano a fini di invio di materiale pubblicitario o di vendita diretta o per il compimento di ricerche di mercato o di comunicazione commerciale.

Formula di acquisizione del consenso per il trattamento di dati sensibili

Luogo……., Data…….

Cognome ..... Nome .....

Il/La sottoscritto/a, acquisite le informazioni fornite dal titolare del trattamento ai sensi dell'art. 13 del D.lgs. n. 196/2003, e consapevole, in particolare, che il trattamento riguarderà i dati "sensibili" di cui all'art.4 comma 1 lett. d), nonché art.26 del D.lgs.196/2003, vale a dire i dati *"idonei a rivelare l'origine razziale ed etnica, le convinzioni religiose, filosofiche o di altro genere, le opinioni politiche, l'adesione a partiti, sindacati, associazioni od organizzazioni a carattere religioso, filosofico, politico o sindacale, nonché i dati personali idonei a rivelare lo stato di salute e la vita sessuale"*;

- presta il suo consenso per il trattamento dei dati necessari allo svolgimento delle operazioni indicate nell'informativa.

Firma leggibile .....

- presta il suo consenso per la comunicazione dei dati ai soggetti indicati nell'informativa.

Firma leggibile .....

- presta il suo consenso per la diffusione dei dati nell'ambito indicato nell'informativa.

Firma leggibile .....

- Il/la sottoscritto/a dichiara inoltre: (1) di non essere stato/a in alcun modo forzato/a alla partecipazione, (2) di essere stato/a informato/a sulla possibilità di abbandonare in qualsiasi momento la ricerca stessa senza penalizzazione alcuna

Firma leggibile .....

SCHEDA INFORMATIVA

Di seguito troverà dei questionari che riguardano alcuni atteggiamenti o comportamenti che le persone possono avere. La preghiamo di rispondere alle domande contenute nei questionari, nel modo più sincero possibile, tenendo presente che ogni persona è diversa da un'altra per cui non ci sono risposte giuste o sbagliate, cerchi semplicemente di ricordare come lei è (o come pensa) la maggior parte delle volte.

Grazie

DATA_____

ETÁ: _____ SESSO: □ Maschio □ Femmina

STATO CIVILE: 1____Celibe/Nubile
2____Sposato/Convivente
3____Separato/Divorziato
4____Vedovo/a

NUMERO DI ANNI DI FREQUENZA SCOLASTICA _____
(In base al titolo di studio di grado più alto conseguito. Per esempio, diploma superiore = 13 anni; scuola media = 8 anni)

OCCUPAZIONE: 1___Studente 2____Occupato a tempo pieno
3___Part-Time 4____Casalinga
5___Disoccupato 6____Pensionato/a
7___Non in grado di lavorare per disabilità
8___Altro

FARMACI: □ Sì □ No
Se sì, indichi il tipo di farmaco assunto ed il dosaggio _____

Mean (SD) raw scores obtained by the PG, OCD, AD, and HC groups on self-report and cognitive measures.

		Medication	PG	OCD	AD	HC
PI	**Mental control**	no	15.20(13.26)	12.25(9.64)	16.33(13.35)	3.00(3.14)
		yes	15.85(14.63)	27.92(16.60)	14.26(9.31)	
		total	15.45(13.59)	24.00(16.42)	14.55(9.76)	
	Washing	no	11.80(8.95)	22.00(19.17)	10.40(9.32)	4.10(4.54)
		yes	9.85(8.56)	18.92(16.80)	8.13(5.90)	
		total	11.03(8.72)	19.69(16.80)	8.44(6.35)	
	Checking	no	6.85(7.97)	4.00(4.97)	9.00(12.10)	1.98(1.98)
		yes	8.85(7.65)	12.92(8.26)	7.48(7.42)	
		total	7.64(7.79)	10.69(8.42)	7.69(8.01)	
	Motor Control	no	1.21(1.68)	.00(.00)	.34(.47)	.10(.33)
		yes	1.20(1.69)	2.00(2.23)	.85(1.48)	
		total	1.21(1.66)	1.50(2.11)	.78(1.39)	
OBQ-87	**Perf.**	no	40.85(13.99)	49.75(24.31)	54.00(12.83)	28.98(10.80)
		yes	46.01(22.96)	45.47(14.47)	40.72(17.04)	
		total	42.88(17.90)	46.54(16.59)	42.56(17.01)	
	Resp. Harm	no	54.65(9.74)	40.85(9.78)	64.43(8.64)	45.03(12.91)
		yes	57.14(23.01)	56.77(15.17)	56.06(12.27)	
		total	55.63(16.01)	52.79(15.44)	57.22(12.09)	
	Overest. threat	no	28.68(11.22)	26.82(14.48)	38.93(9.03)	16.93(5.86)
		yes	31.08(16.29)	36.95(14.26)	29.56(11.72)	
		total	29.63(13.25)	34.41(14.54)	30.86(11.74)	
	Control thoughts	no	49.47(15.15)	28.25(13.38)	56.20(12.48)	35.16(15.95)
		yes	53.69(22.92)	56.23(15.43)	50.56(15.78)	
		total	51.14(18.38)	49.24(19.16)	51.35(15.33)	
	Resp. Omission	no	14.72(6.87)	9.75(6.85)	25.16(3.72)	10.64(3.65)
		yes	19.77(11.34)	18.70(9.14)	15.77(7.20)	
		total	16.71(9.09)	16.46(9.31)	17.08(7.54)	
	TAF	no	17.45(6.39)	14.50(11.27)	15.60(4.83)	14.19(6.75)
		yes	18.34(8.88)	14.17(8.92)	16.99(8.67)	
		total	17.80(7.35)	14.25(9.15)	16.79(8.21)	
BIS-11	**Total score**	no	65.62(9.75)	62.25(11.32)	59.78(8,74)	56.58(6.22)
		yes	70.72(7.49)	66.72(9.82)	64.89(9,35)	
		total	67.63(9.16)	65.61(10.02)	64.18(9.32)	
IGT	**Total net score**	no	-.30(18.71)	3.50(9.57)	9.20(12.21)	17.64(24.87)
		yes	-.77(15.89)	4.67(10.79)	2.77(9.19)	
		total	-.48(17.39)	4.38(10.20)	3.67(9.72)	
Go/Nogo task	**n° omission**	no	5.40(5.78)	1.50(1.73)	24.00(20.60)	4.64(5.75)
		yes	8.62(6.95)	18.25(19.85)	13.58(17.85)	
		total	6.67(6.36)	14.06(18.59)	15.03(18.31)	
	n° commission	no	9.10(8.48)	6.00(3.74)	15.20(14.29)	9.91(6.26)
		yes	12.00(7.92)	16.00(14.57)	10.71(8.55)	
		total	10.24(8.26)	13.50(13.36)	11.33(9.41)	
	RTs Go Trials	no	334.41(49.63)	318.60(31.61)	389.00(56.88)	318.26(39.43)
		yes	337.93(45.12)	348.61(46.15)	356.32(46.36)	
		total	335.79(47.21)	341.10(44.06)	360.85(48.40)	
	RTs Nogo Trials	no	274.54(41.78)	256.30(22.76)	341.74(66.52)	270.26(46.11)
		yes	276.60(45.02)	295.56(55.48)	299.18(53.89)	
		total	275.35(42.40)	285.75(51.67)	305.09(56.72)	

Note: Mental control=Impaired control over mental activities; Motor control=Impaired control over motor activities; Perf.=Perfectionism; Resp. Harm=Responsibility-Harm; Overest. threat=Overestimation of threat; Control thoughts=Control of thoughts; Resp. Omission=Responsibility-Omission. RTs on Go and Nogo trials are reported in ms.

Pearson's correlations between self-report and cognitive measures (total sample).

		PI					OBQ-87				BIS-11	IGT	Go/Nogo task			
		Washing	Checking	Motor control	Perf.	Resp. Harm	Overest. threat	Control thoughts	Resp. Omission	TAF	Total score	Total net-score	n° omission	n° commission	RTs Go trials	RTs Nogo trials
PI	Mental control	.572**	.700**	.417**	.656**	.466**	.809**	.578**	.525**	.344**	.401**	-.138	.247**	.315**	.125	.067
	Washing		.571**	.213**	.453**	.313**	.496**	.299**	.329**	.167*	.138	-.176*	.196*	.102	.214**	.138
	Checking			.373**	.512**	.459**	.644**	.511**	.491**	.269**	.224**	-.148	.274**	.186*	.211*	.133
	Motor control				.117	.091	.286**	.158	.105	.027	.118	.011	-.057	.078	-.069	-.057
	Perf.					.695**	.700**	.692**	.692**	.507**	.188*	-.152	.208*	.249**	.164*	.192*
	Resp. Harm						.611**	.784**	.705**	.607**	.060	-.108	.220**	.305**	.089	.163
OBQ-87	Overest. threat							.683**	.695**	.482**	.393**	-.222**	.239**	.256**	.146	.118
	Control thoughts								.651**	.663**	.198*	-.096	.191*	.222**	.080	.175*
	Resp. Omission									.494**	.192*	-.160	.308**	.322**	.123	.178*
	TAF										.031	.055	-.012	.008	.073	.061
BIS-11	Total score											-.267**	.189*	.133	.082	.027
IGT	Total net score												-.099	-.124	-.109	-.074
Go/Nogo task	n° omission													.305**	.408**	.370**
	n° commission														-.264**	-.161
	RTs Go trials															.711**

Note: * = p<.05; ** = p<.01. Mental control=Impaired control over mental activities; Motor control=Impaired control over motor activities; Perf.=Perfectionism; Resp. Harm=Responsibility-Harm; Overest. threat=Overestimation of threat; Control thoughts=Control of thoughts; Resp. Omission=Responsibility-Omission.

Mean (SD) raw scores obtained by PGs, croupiers and HCs on self-report and cognitive measures.

		PG	CR	HC
PI	**Mental control**	16.47(16.50)	5.93(4.80)	2.27(2.12)
	Washing	13.53(8.61)	4.53(4.03)	4.07(5.12)
	Checking	8.00(8.64)	4.20(3.14)	2.13(2.42)
	Motor Control	1.91(2.06)	.64(.85)	.06(.22)
OBQ-87	**Perf.**	40.60(16.14)	36.71(14.10)	30.53(9.64)
	Resp. Harm	51.94(16.94)	49.42(12.17)	48.18(8.43)
	Overest. threat	28.85(12.90)	19.64(9.22)	17.82(6.34)
	Control thoughts	46.07(17.91)	39.47(12.47)	37.73(16.55)
	Resp. Omission	16.93(9.32)	14.73(5.34)	11.07(3.77)
	TAF	16.89(7.25)	12.87(5.37)	15.00(7.24)
BIS-11	**Total score**	66.50(9.80)	62.30(11.74)	54.48(5.22)
IGT	**Total net score**	-0.53(19.77)	10.33(45.09)	16.67(21.54)
Go/Nogo task	**n° omission**	5.67(6.22)	5.07(5.02)	4.20(5.27)
	n° commission	7.53(5.94)	11.80(8.50)	7.60(5.95)
	RTs Go Trials	325.25(44.84)	299.49(35.82)	315.90(33.44)
	RTs Nogo Trials	274.40(44.79)	249.46(42.24)	286.82(50.55)

Note: Mental control=Impaired control over mental activities; Motor control=Impaired control over motor activities; Perf.=Perfectionism; Resp. Harm=Responsibility-Harm; Overest. threat=Overestimation of threat; Control thoughts=Control of thoughts; Resp. Omission=Responsibility-Omission. RTs on Go and Nogo trials are reported in ms.