

Pathological gambling and impulsivity: an Italian study

Gioco d'azzardo patologico e impulsività: uno studio italiano

DONATELLA MARAZZITI, MICHELA PICCHETTI, STEFANO BARONI, GIORGIO CONSOLI,
DIANA CERESOLI, GABRIELE MASSIMETTI, MARIO CATENA DELL'OSSO

E-mail: dmarazzi@psico.med.unipi.it

Dipartimento di Medicina Clinica e Sperimentale, Section of Psychiatry, Università di Pisa

SUMMARY. Aim. Although the precise nature of pathological gambling (PG) is still elusive, currently it is considered an impulse-control disorder that shares several features with substance dependence, such as deficit in self-regulation and impaired impulsivity. The aim of this study was to evaluate the impulsivity of PG patients by means of the Barratt Impulsivity Scale, version 11 (BIS-11), as compared with healthy control subjects, and to explore the possible correlations with gambling severity. **Methods.** Thirty-five outpatients (all men) with a diagnosis of PG were recruited at their first psychiatric interview in a psychiatric outpatient ward, and compared with a similar group of healthy control subjects. The severity of PG was assessed by means of the South Oaks Gambling Screen (SOGS). **Results.** The results showed that the BIS-11 total score, as well as the scores of different factors (motor impulsivity and cognitive complexity) and subscales (motor and non-planning impulsivity) were significantly higher in PG patients than in control subjects. In addition, positive correlations were detected between the SOGS and the BIS-11 total scores, and the attention and cognitive instability factor scores, or the attentional and motor impulsivity ($r_s=0.459$, $p=.021$) subscale scores. **Conclusions.** These findings support the notion that impulsivity represents a core element of PG linked to the severity of the clinical picture.

KEY WORDS: pathological gambling, addiction, impulsivity, SOGS, BIS-11.

RIASSUNTO. Scopo. Il gioco d'azzardo patologico (GAP) viene attualmente classificato nell'ambito dei disturbi del controllo degli impulsi e condivide caratteristiche cliniche comuni con il disturbo da uso di sostanze e con i disturbi del controllo degli impulsi. Da un punto di vista clinico e neurobiologico l'impulsività è considerata l'elemento chiave sia dei comportamenti impulsivi sia delle dipendenze. Scopo di questo lavoro è stato quello di valutare l'impulsività mediante la BIS-11, in un gruppo di pazienti drug-free affetti da GAP, rispetto a un gruppo di soggetti sani, e di esplorare le eventuali correlazioni con le caratteristiche cliniche e la gravità del disturbo stesso. **Metodi.** Sono stati inseriti nel nostro studio 35 pazienti (tutti di sesso maschile) affetti da GAP, diagnosticato secondo i criteri del DSM-IV-TR, e confrontati con 35 soggetti sani di controllo. La gravità della sintomatologia è stata valutata mediante il South Oaks Gambling Screen (SOGS). **Risultati.** I risultati ottenuti hanno evidenziato che il punteggio totale della BIS-11, di alcuni fattori (impulsività motoria e complessità cognitiva) e sottoscale (impulsività motoria e senza pianificazione) erano significativamente più alti nei pazienti rispetto ai controlli sani. Sono state inoltre rilevate alcune correlazioni positive tra il punteggio totale della SOGS e quelli della BIS-11, delle scale relative all'impulsività attentiva e all'instabilità cognitiva, e delle sottoscale dell'impulsività attentiva e dell'impulsività motoria. **Discussione.** Questi dati suggeriscono che possa esistere un'associazione tra impulsività e GAP, in accordo con l'ipotesi che l'impulsività rappresenta un elemento chiave del GAP correlato alla gravità del quadro clinico.

PAROLE CHIAVE: gioco d'azzardo patologico, dipendenze, impulsività, SOGS, BIS-11.

INTRODUCTION

According to the previous edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR)¹, pathological gambling (PG) is an impulse-control disorder, characterized by persistent and maladaptive gambling behaviors, that shares similarities with substance abuse disorders. In fact, the core features of PG are craving, tolerance, withdrawal symptoms, frequent relapse, loss of control, and disruption of life, until the point of loss

of job, divorce, deterioration of patrimony or even criminal behavior^{2,3}. Nowadays, a large agreement exists that deficits in self-regulation and impaired impulsivity represent the most salient features of both impulse control disorders, such as PG, and substance dependence⁴. This notion has led to the inclusion of PG amongst substance use disorders in the latest DSM edition (DSM-5)⁵. Therefore, according to several authors, PG should be considered a form of "behavioral or drug-less addiction" characterized by high impulsivity⁶. Nevertheless, an alternative model of

PG considers it related to obsessive-compulsive disorder (OCD), closer to the impulsive pole of an impulsivity-compulsivity dimensional axis^{7,8}. In any case, some studies cast doubt about the significant association between PG and OCD⁹⁻¹¹. Subsequently, impulsivity has been considered mainly as an endophenotype of individuals at risk for both PG and substance use disorder and, not surprisingly, in the next edition of DSM PG will be recategorized into the “addiction and related disorders”¹².

Impulsivity has been variously defined as a swift action without forethought or conscious judgment, behavior without adequate thought, and the tendency to act with less forethought than do most individuals of equal ability and knowledge. The most exhaustive definition of impulsivity is perhaps that given by the International Society for Research on Impulsivity (ISRI), which considers it as “a human behavior without adequate thought, the tendency to act with less forethought than do most individuals of equal ability and knowledge, or a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to negative consequences of these reactions”. Impulsivity may be viewed as a state or a trait, the first referring to a transitory state in response to a peculiar event, while the other refers to a stable personality feature¹³⁻¹⁵. A great bulk of evidence suggests that impulsivity is widely implicated in the development and maintenance of both addictive behaviors and of PG that would arise from an impairment of inhibitory control and self-regulation^{4,15,16}.

When comparing PG patients with control subjects, some studies reported high levels of impulsivity in the first group, or no difference¹⁷⁻²¹. Part of the controversies might be related to the inclusion of heterogeneous samples of PG patients, but also to the use of different instruments for assessing impulsivity, such as neurocognitive tests or self-report questionnaires. Some authors, while using some neurocognitive tests, such as the Stop Signal Task, the Stroop task, the Wisconsin Card Sorting Test, the Tower of London and a few others, described low impulsivity in PG^{21,22}. It should, however, be underlined that these instruments assess state impulsivity. On the contrary, this dimension resulted high on self-report tests, such as the Barratt Impulsivity Scale, version 11 (BIS-11), and the Eysenck Impulsiveness Questionnaires, assessing trait impulsivity²³⁻²⁵. Similar findings were obtained also with neuropsychological measures of trait impulsivity, such as the reaction time and number of errors at Go/No-Go tasks, while highlighting the impact of this dimension in the clinical picture of PG and, perhaps, in the development of the disorder itself^{14,24,26-28}.

Moreover, the combination of both BIS-11 and Iowa Gambling Task in a group of 42 PG patients compared with non gambler subjects showed that the first were more impulsive than the second²⁹.

Given the lack of information in our country, in order to provide a further contribution on this topic, our study aimed to compare impulsivity, by means of the BIS-11 questionnaire, in Italian PG outpatients and healthy control subjects, and to explore the possible correlations between PG severity and impulsivity characteristics.

MATERIALS AND METHODS

Subjects

Thirty-five outpatients (all men, mean age±SD: 46.23±11.6 years) with a diagnosis of PG, as assessed by the structured clinical interview for DSM-IV, patient version 2.0 (SCID-P)³⁰, were recruited at their first psychiatric interview at the outpatient ward of the Dipartimento di Medicina Clinica e Sperimentale, Section of Psychiatry, University of Pisa, Italy. None suffered from any severe physical illness nor had ever taken psychotropic drugs, except for ten patients who had occasionally taken benzodiazepines for difficulty with sleeping or panic attacks. The severity of PG was assessed by means of the South Oaks Gambling Screen (SOGS, normal score <5): the total score (mean±SD) of the patients was 10.9±2.7³¹. The age of onset of the disorder (mean±SD) was 30.8±13.2 years. The majority of the patients used multiple types of gambling: electronic machines²⁵, internet lotteries or casino and bingo¹⁵.

Six patients were suffering also from simple phobia, three from panic disorder, three from bipolar disorder of type II, and two from generalized anxiety disorder. Twelve patients were heavy cigarette smokers (>20/die), three were suffering from cannabis abuse and two from alcohol abuse.

Twenty-three patients were single or divorced, ten married and two were widowed. Twenty-eight patients had completed a high school, four had a university degree and three had completed only the primary school.

The patients were compared with a similar group of healthy control subjects (35 men, mean age±SD: 47.19±13.4 years), who had no family or personal history of any major psychiatric disorder, as assessed by a psychiatric interview, carried out by a senior psychiatrist (DM) by means of the SCID. They were recruited amongst medical and nursing staff at the Department of Psychiatry, Neurobiology, Pharmacology, and Biotechnology, University of Pisa, Italy. These subjects were also free of any physical illness, as documented by a general check-up and by the normal blood and urine tests and were completely psychotropic drug-free for about 12 months. None of them were heavy cigarette smokers; none of the participants belonged to a high-risk HIV group, and none took any regular medication. All gave their informed consent to participation in this study, which was approved by the Ethics Committee of Pisa University.

Impulsivity assessment

The impulsivity was assessed by means of the BIS-11 questionnaire validated into Italian³². The BIS-11 is a self-report scale developed to measure impulsivity as a stable characteristic, composed by 30 items, which are answered on a four-point scale; items are scored 1, 2, 3, 4, where 4 indicates the most impulsive response: the higher the total scores for all items, the higher the level of impulsivity. The total score ranges between 30 and 120, with no established cut-off point and is the result of the sum of three different subscales: attentional (rapid shifts of attention and impatience with complexity), motor (impetuous action), and non-planning (lack of future orientation) impulsivity. In addition, the 30 items form six factors determined by principal component analyses: attention, motor impulsivity, self-control, cognitive complexity, perseverance and cognitive instability.

Statistical analyses

The unpaired Student's t test was used to compare parametric variables, such as the age. Since the BIS-11 scales, subscales and

Pathological gambling and impulsivity: an Italian study

factors are not normally distributed, the comparisons between the two independent samples were assessed by the non-parametric Mann-Whitney test, and the relationships between variables by the Spearman's coefficient. All analyses were carried out using the SPSS version 14.0, by means of personal computer programs.

RESULTS

The BIS-11 total score (mean±SD) was significantly higher in PG patients than in control subjects (65.46±12.08 vs 57.34±11.04; Mann-Whitney test: Z=-2.50, p=.012).

As far as the BIS-11 factors were concerned, the “motor impulsivity” and “cognitive complexity” scores were significantly higher in PG patients than in control subjects (16.34±4.84 vs 11.26±3.40, Z=-3.88, p=.001; 13.73±2.75 vs 12.38±2.70, Z=-1.96, p=.050). The same was true for “motor” and “nonplanning” impulsivity subscale scores (23.96±5.17 vs 18.53±3.89, Z=-3.87, p=.001; 18.88±4.00 vs 16.58±4.11; Z=-1.90, p=.047) (Table 1). The comparison of the “self-control” factor scores showed a similar, albeit not significant, trend.

No differences were measured between patients suffering and not suffering from substance abuse, or between those with and without comorbid psychiatric disorders.

A significant and positive correlation was detected between the SOGS and the BIS-11 total scores ($r_s=0.486$, $p=.014$). Statistically significant and positive correlations were also observed between the SOGS total score and the attention ($r_s=0.492$, $p=.012$) and cognitive instability ($r_s=0.461$, $p=.020$) factor scores, or the attentional ($r_s=0.405$,

$p=.045$) and motor impulsivity ($r_s=0.459$, $p=.021$) subscale scores.

DISCUSSION

One of the main results of the present study was that a sample of Italian PG patients showed higher levels of impulsivity, as measured by the BIS-11 total score, than control subjects. This finding is the first of this kind in Italy and supports the existence of the already and widely reported association between impulsivity and PG^{3,5,14,29}. In addition, it is in agreement with the notion that impulsivity may represent a core element of PG, perhaps related to a typical personality trait or structure that may predict the development of addictive and impulsive behaviors^{6,11,12,23,26,33}. Moreover, our findings, while highlighting the positive correlation between gambling severity, as assessed by the SOGS, and BIS-11 total and some factor/subscale scores, would support the assumption that a strict link may exist between PG severity and impulsivity, as already reported by using other questionnaires¹¹. However, some controversies do exist on this topic¹⁹. While comparing the scores of each BIS-11 factor and scale between patients and healthy control subjects, it turned out that PG patients showed higher scores than healthy individuals on the motor impulsivity and cognitive complexity factors, and on the motor and non-planning impulsivity subscales, with no differences either on the attentional impulsivity subscale or attention factor. Similar finding were reported recently in gamblers with different degrees of clinical severity³³, and in strategic and non strategic gamblers assessed by neurocognitive tests³⁴. These data have been generally interpreted along the hypothesis that impulsivity in PG might originate from deficits of executive functions rather than of attention^{23,26,27,35-41}. We would add with cautions that this assumption is indirectly supported by our findings showing that the attention factor and the attentional impulsivity subscale scores were positively related to the severity of PG, as measured by the SOGS total scores.

Moreover, the perseverance factor was not different between the groups. This last aspect could be considered as consistent with some studies reporting no link with OCD or obsessional personality, as perseverance is a feature typical of these two conditions²⁶. However, recently, Blanco et al.²⁵ observed that, although PG patients exhibit characteristics of both obsessiveness/compulsiveness and impulsiveness, impulsiveness is prevalent, and changes in gambling severity are paralleled by those in impulsiveness. The results of the present study should be interpreted while keeping in mind some limitations. First, we utilized one instrument only, in particular the BIS-11, to assess impulsiveness. It is noteworthy to keep in mind that the BIS-11 is a self-report scale that was developed to measure impulsiveness as a stable characteristic or trait. A second limitation is the small sample size, so that it was not possible to perform subgroup analyses aimed at investigating the possible correlation between the BIS-11 factors /scales and the severity of PG. Third, a relevant bias is represented

Table 1. BIS-11 total, factor, and subscale scores (mean±SD) in PG patients and healthy control subjects

	PG patients	Control subjects
BIS-11 total score	65.46 ± 12.08	57.34 ± 11.04*
BIS-11 factor score		
attention	8.88 ± 3.01	9.85 ± 2.92
motor impulsivity	16.34 ± 4.84	11.26 ± 3.40**
self-control	13.73 ± 3.53	11.81 ± 3.74
cognitive complexity	13.73 ± 2.75	12.38 ± 2.70***
perseverance	7.62 ± 2.00	7.27 ± 1.66
cognitive instability	5.15 ± 1.57	4.77 ± 1.63
BIS-11 subscale score		
attentional	22.61 ± 4.73	22.23 ± 5.01
motor	23.96 ± 5.17	18.54 ± 3.89****
nonplanning	18.88 ± 4.00	16.58 ± 4.11*****

* significant: $z=-2.50$, $p=.012$; **significant: $z=-3.88$, $p=.001$.
 *** significant: $z=-1.96$, $p=.050$.
 **** significant: $z=-3.87$, $p=.001$.
 ***** nearly significant: $z=-1.90$, $p=.057$.

by the fact that 14 patients were suffering from different comorbid psychiatric disorders and 17 from substance abuse, conditions that are all characterized by high levels of impulsivity⁴². Interestingly, disinhibition, that often equates impulsivity, is considered an endophenotype of subjects at high risk for PG and substance abuse¹². Fourth, the gambling severity was assessed by the SOGS only. This scale was chosen because it is the most used in our country and can be useful for comparing the results deriving from different centers. Fourth, our sample was composed almost entirely by men, so that we cannot exclude a gender effect on impulsivity, although literature findings on this topic are controversial⁴³.

CONCLUSIONS

Taken together, the findings of the present study support the notion that impulsivity represents a core element of PG perhaps linked to the severity of the clinical picture. However, further studies, carried out in larger samples of PG patients of both sexes with and without comorbid psychiatric disorders, and assessed by means of multiple neurocognitive tests and neuroimaging techniques, such as those used recently⁴⁴⁻⁴⁷, are necessary to explore the possible relationships between impulsivity and PG.

REFERENCES

- American Psychiatric Association. DSM-IV: Diagnostic and Statistical Manual of Mental Disorders (4th ed.). Washington, DC: American Psychiatric Press, 1994.
- Blum K, Braverman ER, Holder JM, et al. Reward deficiency syndrome: a biogenetic model for the diagnosis and treatment of impulsive, addictive, and compulsive behaviors. *J Psychoactive Drugs* 2000; 32: 1-112.
- Blaszczynski A, Nower L. A pathways model of problem and pathological gambling. *Addiction* 2002; 97: 487-99.
- Goldstein RZ, Volkow ND. Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. *Am J Psychiatry* 2002; 159: 1642-52.
- American Psychiatric Association. DSM-5: Diagnostic and Statistical Manual of Mental Disorders (5th ed.). Washington, DC: American Psychiatric Press, 2013.
- Potenza MN. The neurobiology of pathological gambling and drug addiction: an overview and new findings. *Philos Trans R Soc Lond B Biol Sci* 2008; 363: 3181-9.
- Stein DJ, Hollander E. The spectrum of obsessive-compulsive related disorders. In: Hollander E (ed). *Obsessive-compulsive related disorders*. Washington, DC: American Psychiatric Press, 1993.
- Blaszczynski A. Pathological gambling and obsessive-compulsive spectrum of disorders. *Psychol Rep* 1999; 84: 107-13.
- Black DW, Shaw M, Blum N. Pathological gambling and compulsive buying: do they fall within an obsessive-compulsive spectrum? *Dialogues Clin Neurosci* 2010; 12: 175-85.
- Bienvenu OJ, Samuels JF, Riddle MA, et al. The relationship of obsessive-compulsive disorder to possible spectrum disorders: results from a family study. *Biol Psychiatry* 2000; 48: 287-93.
- Tavares H, Gentil V. Pathological gambling and obsessive-compulsive disorder: towards a spectrum of disorders of volition. *Rev Bras Psiquiatr* 2007; 29: 107-17.
- Verdejo-García A, Lawrence AJ, Clark L. Impulsivity has a vulnerability marker for substance-use disorder: review of findings from high-risk research, problem gamblers and genetic association studies. *Neurosci Biobehav Rev* 2008; 32: 777-810.
- Swann AC, Lijffijt M, Lane SD, Steinberg JL, Moeller FG. Trait impulsivity and response inhibition in antisocial personality disorder. *J Psychiatr Res* 2009; 43: 1057-63.
- Lai FDM, Ip AKY, Lee TMC. Impulsivity and pathological gambling: Is it a state or a trait problem? *BMC Research Notes* 2011; 4: 492.
- Petry NM. Pathological gamblers, with and without substance use disorders, discount delayed rewards at high rates. *J Abnorm Psychol* 2001; 110: 482-7.
- Aron AR, Monsell S, Sahakian BJ, Robbins TW. A componential analysis of task-switching deficits associated with lesions of left and right frontal cortex. *Brain* 2004; 127: 1561-73.
- Clark L, Roiser JP, Cools R, Rubinsztein DC, Sahakian BJ, Robbins TW. Stop signal response inhibition is not modulated by tryptophan depletion or the serotonin transporter polymorphism in healthy volunteers: implications for the 5-HT theory of impulsivity. *Psychopharmacol* 2005; 182: 570-8.
- Forbush KT, Shaw M, Graeber MA, et al. Neuropsychological characteristics and personality traits in pathological gambling. *CNS Spectr* 2008; 13: 306-15.
- Sáez-Abad C, Bertolin-Guillén JM. Personality traits and disorders in pathological gamblers versus normal controls. *J Addict Dis* 2008; 27: 33-40.
- Lawrence AJ, Luty J, Bogdan NA, Sahakian BJ, Clark L. Impulsivity and response inhibition in alcohol dependence and problem gambling. *Psychopharmacol* 2009; 207: 163-72.
- Dannon PN, Shoenfeld N, Rosenberg O, Kertzman S, Kotler M. Pathological gambling: an impulse control disorder? Measurement of impulsivity using neurocognitive tests. *Isr Med Assoc J* 2010; 12: 243-8.
- Conversano C, Marazziti D, Carmassi C, Baldini S, Barnabei G, Dell'Osso L. Pathological gambling. A systematic review of biochemical, neuroimaging and neuropsychological findings. *Harv Rev Psychiatry* 2012; 20: 130-48.
- Alessi SM, Petry NM. Pathological gambling severity is associated with impulsivity in a delay discounting procedure. *Behav Processes* 2003; 64: 345-54.
- Fuentes D, Tavares H, Artes R, Gorenstein, C. Self-reported and neuropsychological measures of impulsivity in pathological gambling. *J Int Neuropsychol Soc* 2006; 12: 907-12.
- Blanco C, Potenza MN, Kim SW, et al. A pilot study of impulsivity and compulsivity in pathological gambling. *Psychiatry Res* 2009; 167: 161-8.
- Steel Z, Blaszczynski A. Impulsivity, personality disorders and pathological gambling severity. *Addiction* 1998; 93: 895-905.
- Goudriaan AE, Oosterlaan J, De Beurs E, Van Den Brink W. The role of self-reported impulsivity and reward sensitivity versus neurocognitive measures of disinhibition and decision-making in the prediction of relapse in pathological gamblers. *Psychol Med* 2007; 14: 1-11.
- Kertzman S, Lowengrub K, Aizer A, Vainder M, Kotler M, Dannon PM. Go-no-go performance in pathological gamblers. *Psychiatry Res* 2008; 161: 1-10.
- Glicksohn J, Zilberman N. Gambling on individual differences in decision making. *Pers Indiv Differ* 2010; 48: 557-62.
- First MB, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P, Version 2.0, 4 97 revision)*. New York: Biometrics Research, New York State Psychiatric Institute, 1997.
- Lesieur HR, Blume SB. The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. *Am J Psychiatry* 1987; 144: 1184-8.
- Fossati A, Di Ceglie A, Acquarini E, Barratt ES. Psychometric properties of an Italian version of the Barratt Impulsiveness Scale-11 (BIS-11) in nonclinical subjects. *J Clin Psychology* 2001; 57: 815-28.
- Odlaug BL, Chamberlain SR, Kim SW, Schreiber LR, Grant JE. A neurocognitive comparison of cognitive flexibility and response inhibition in gamblers with varying degrees of clinical severity. *Psychol Med* 2011; 41: 2111-9.
- Grant JE, Chamberlain SR, Schreiber LR, Odlaug BL. Neurocognitive deficits associated with shoplifting in young adults. *Compr Psychiatry* 2012; 53: 1049-55.

Pathological gambling and impulsivity: an Italian study

35. Brevers D, Cleeremans A, Bechara A, et al. Time course of attentional bias for gambling information in problem gambling. *Psychol Addict Behav* 2011; 25: 675-582.
36. Spinella M. Evolutionary mismatch, neural reward circuits, and pathological gambling. *Int J Neurosci* 2003; 113: 503-12.
37. Kertzman S, Lowengrub K, Aizer A, Nahum ZB, Kotler M, Dannon PN. Stroop performance in pathological gamblers. *Psychiatry Res* 2006; 142: 1-10.
38. Tamminga CA, Nestler EJ. Pathological gambling: focusing on the addiction, not the activity. *Am J Psychiatry* 2006; 163: 180-1.
39. Marazziti D, Catena Dell'Osso M, et al. Executive function abnormalities in pathological gamblers. *Clinl Pract Epidemiol Ment Health* 2008; 27: 4-7.
40. Marazziti D, Golia F, Picchetti M, et al. Decreased density of the platelet serotonin transporter in pathological gamblers. *Neuropsychobiology* 2008; 57: 38-43.
41. Takano Y, Takahashi N, Tanaka D, Hironaka N. Big losses lead to irrational decision-making in gambling situations: relationship between deliberation and impulsivity. *PLoS One* 2010; 5: e9368.
42. von Diemen L, Bassani DG, Fuchs SC, Szobot CM, Pechansky F. Impulsivity, age of first alcohol use and substance use disorders among male adolescents: a population based case-control study. *Addiction* 2008; 103: 1198-205.
43. Marazziti D, Baroni S, Masala I, et al. Impulsivity, gender and the platelet serotonin transporter in healthy subjects. *Neuropsychiat Dis Treat* 2010; 6: 9-15.
44. Potenza MN, Leung HC, Blumberg HP, et al. An FMRI Stroop study of ventromedial prefrontal cortical function in pathological gamblers. *Am J Psychiatry* 2003; 160: 1990-4.
45. van Holst RJ, van den Brink W, Veltman DJ, Goudriaan AE. Brain imaging studies in pathological gambling. *Curr Psychiatry Rep* 2010; 12: 418-25.
46. Dannon PN, Kushnir T, Aizer A, Gross-Isseroff R, Kotler M, Manor D. Alternation learning in pathological gamblers: an fMRI Study. *Brain Imaging Behav* 2011; 5: 45-51.
47. van Holst RJ, van Holstein M, van den Brink W, Veltman DJ, Goudriaan AE. Response inhibition during cue reactivity in problem gamblers: an fMRI study. *PLoS One* 2012; 7: e30909.