NATIONAL CENTER FOR RESPONSIBLE GAMING
Advancing Research, Education and Awareness

INCREASING THE ODDS
A Series Dedicated to Understanding Gambling Disorders

VOLUME 6

Gambling and the Brain: Why Neuroscience Research is Vital to Gambling Research

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TABLE OF CONTENTS

INTRODUCTION

1 ***Gambling and the Brain: Why Neuroscience Research Matters***
by Christine Reilly

RESEARCH SUMMARIES

3 ***Neurobiology and Pathological Gambling***
by Jon E. Grant, M.D., J.D., M.P.H.
A summary of Grant, J.E., Brewer, J.A., & Potenza, M.N. (2006). The neurobiology of substance and behavioral addictions. *CNS Spectrums, 11*(12), 924-930.

9 ***Brain Activity in Pathological Gambling***
by Marc Potenza, M.D., Ph.D.
A summary of Potenza, M.N., Steinberg, M.A., Skudlarski, P., Fulbright, R.K., Lacadie, C.M., Wilber, M.K., Rounsaville, B.J., Gore, J.C., & Wexler, B.E. (2003). Gambling urges in pathological gambling: A functional magnetic resonance imaging study. *Archives of General Psychiatry, 60*(8), 828-836.

14 ***Brain Imaging Studies: A Review***
by Anna E. Goudriaan, Ph.D.
A summary of van Holst, R.J., van den Brink, W., Veltman, D.J. & Goudriaan, A.E. (2010). Brain imaging studies in pathological gambling. *Current Psychiatry Reports, 12*(5), 418-425.

20 ***The Rat Gambling Task: Understanding the Role of Serotonin and Dopamine in Pathological Gambling***
by Catharine A. Winstanley, Ph.D.
A summary of Zeeb, F.D., Robbins, T.W. & Winstanley, C.A. (2009). Serotonergic and dopaminergic modulation of gambling behavior as assessed using a novel rat gambling task. *Neuropsychopharmacology, 34*(1), 1-15.

ADDITIONAL INFORMATION

25 ***Glossary***
A summary of all bolded terms in this publication.

27 ***Resources and Programs***

31 ***About the National Center for Responsible Gaming***

Editor's note: The summaries and information in this publication were compiled with assistance from Nancy Plemens Mayes, a health and science writer.

The first five volumes of *Increasing the Odds* are available via the NCRG's Web site, www.ncrg.org.

INTRODUCTION

GAMBLING AND THE BRAIN: WHY NEUROSCIENCE RESEARCH MATTERS

by Christine Reilly
Senior Research Director, National Center for Responsible Gaming

"Addiction is a brain disease — and it matters," declared Dr. Alan Leshner at the first NCRG Conference in Gambling and Addiction in 1999. The former head of the National Institute on Drug Abuse explained in an earlier article: "Understanding that addiction is, at its core, a consequence of fundamental changes in brain function means that a major goal of treatment must be either to reverse or to compensate for those brain changes" (Leshner, 1997).

Although only three years in operation at that point, the National Center for Responsible Gaming (NCRG) already had heeded this call by supporting several groundbreaking neuroscience projects on gambling disorders. NCRG-funded studies have taken advantage of technological advances in brain imaging, drugs, animal studies and genetics to understand the neurobiology of gambling disorders. Since 1996, the NCRG has awarded more than $2 million for neuroscience research investigations.

Although these technological advances are recent, the recognition that gambling disorders have a neurobiological component is not new. Both scientists and clinicians have previously observed that people diagnosed with pathological gambling experience negative biological consequences (Shaffer & Kidman, 2003). For example, just like individuals with drug dependence who develop tolerance for the drug and, therefore, need higher doses of the drug to experience the desired mood or feeling, those with gambling problems might find that they need to gamble increasing amounts of money to achieve the same level of excitement experienced at lower levels of wagering. When such an individual attempts to reduce or stop gambling, he or she might experience symptoms of withdrawal. This process is called neuroadapation and refers to changes in the structure and function of the brain.

What is new over the past few decades is the research methodology based on advances in the field. This volume of *Increasing the Odds: A Series Dedicated to Understanding Gambling Disorders* focuses on studies representative of this new wave of neuroscience research.

- Biochemical, functional neuroimaging, genetic studies and treatment research have suggested a strong neurobiological link between behavioral addictions and substance use disorders. Given the substantial co-occurrence of these groups of disorders, improved understanding of their relationship has important implications not only for further understanding the neurobiology of both categories of disorders, but also for improving prevention and treatment strategies (Grant, Brewer, & Potenza, 2006). Dr. Jon Grant summarizes a review article in "Neurobiology and Pathological Gambling" that provides a helpful overview of this issue, including a discussion of the various neurotransmitters — chemicals that carry signals — implicated in the development of addiction and other psychiatric disorders.
- Urges to gamble usually precede the self-destructive behaviors observed in individuals with gambling problems (Potenza et al., 2003). Dr. Marc Potenza's article, "Brain Activity in Pathological Gambling," illustrates how the brain

imaging technology known as fMRI can be used to observe brain function in real time and, in this case, better understand the role that urges play in the development and maintenance of a gambling disorder.

- Dr. Anna Goudriaan provides an abridged version of a review essay, "Brain Imaging Studies: A Review," that gives an overview of brain imaging research on gambling disorders. She shows how various types of imaging are used to investigate the role that the reward system, reactivity to cues and impulsivity play in pathological gambling (van Holst et al., 2010).
- Finally, Dr. Catharine Winstanley summarizes an animal research study in "The Rat Gambling Task: Understanding the Role of Serotonin and Dopamine in Pathological Gambling" that not only demonstrates that laboratory rats can play the odds, but also provides evidence that the neurotransmitters dopamine and serotonin play a role in gambling behavior (Zeeb, Robbins, Winstanley, 2009).

Dr. Leshner's admonition to pay attention to the neurobiology of addiction was not intended to narrow our understanding of these disorders as purely biological or medical. Addictive disorders, including pathological gambling, have psychological and social aspects as well. However, the neurobiological research is crucial to understanding the development of, maintenance of and recovery from addiction. As Dr. Howard J. Shaffer observed, "Ultimately, the brain is the final common pathway for subjective experience; the psychosocial features of experience are painted on the backdrop of neurobiology. We must advance our understanding of this pathway" (Shaffer & Kidman, 2003).

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About the author…

Christine Reilly is senior research director of the National Center for Responsible Gaming (NCRG), where she administers the NCRG's research grants program and coordinates educational activities such as the annual NCRG Conference on Gambling and Addiction and EMERGE (Executive, Management, and Employee Responsible Gaming Education). Prior to joining the staff of the NCRG in 1997, Reilly served as executive director of the Missouri Humanities Council for eight years.

RESEARCH SUMMARY

Neurobiology and Pathological Gambling

by Jon E. Grant, M.D., J.D., M.P.H.
University of Minnesota

A summary of the following publication:
Grant, J.E., Brewer, J.A., & Potenza, M.N. (2006). The neurobiology of substance and behavioral addictions. *CNS Spectrums, 11*(12), 924-930.

Over the past decade, the volume and quality of neurobiological research on behavioral addictions such as pathological gambling, kleptomania, pyromania, compulsive buying and compulsive sexual behavior has grown significantly. However, the vast majority of research in behavioral addictions focuses on pathological gambling. Such behavioral addictions are often found in conjunction with one or more other diseases or disorders, and research has suggested possible genetic or neurobiological links between behavioral addictions and substance use disorders.

This review article congregates information from several previously published research studies about how the nervous system responds in regard to behavioral addictions and compares those biological responses to those that are apparent in the study of substance use disorders. The neurobiology of addictions has been predominantly examined in four different realms:

1. Biochemical: studies of the chemical processes that occur in living organisms
2. Functional neuroimaging: technological techniques that allow brain function to be visualized
3. Genetics: studies of genes, variation and heredity patterns to determine markers that may indicate elevated addictive vulnerabilities
4. Treatment research: research that attempts to measure responses and efficacy of psychological and pharmaceutical care

HIGHLIGHTS

- Imbalances within the neurotransmitter system of the brain — serotonin, dopamine, endogenous opiods and hormones — influence both behavioral and substance addictions.
- Neuroimaging studies suggest similarities between behavioral and substance addictions.
- In studies of families with pathological gamblers, a possible shared genetic vulnerability between pathological gambling and other addictions is evident.
- Studies of the use of opioid antagonist drugs and several therapist-driven techniques have proven effective in the treatment of pathological gambling.

BIOCHEMISTRY OF ADDICTION

A complex system of neurotransmitters, such as serotonin, dopamine, endogenous opioids and hormones, are responsible for what we feel, how we think and what we do. Imbalances within this system have been shown to influence both behavioral and substance addictions.

Serotonin

Several studies of impulse control disorders have provided evidence of **serotonergic dysfunction**. Serotonin is implicated in emotion, mood and cognition. As evidenced by

findings in separate studies, low levels of serotonin, which have been observed in individuals with pathological gambling habits and substance use disorders, may result in increased motivation to satisfy urges, impairment in inhibition or reward processing, or a combination of these factors (Potenza, 2001 and Schlosser et al., 1994). Consequently, individuals with serotonergic dysfunction may have difficulty controlling their desires.

Dopamine

Individuals with impulse control or substance use disorders have shown alterations within the **dopaminergic pathways**, causing them to seek rewards (i.e., gambling or drugs) that trigger dopamine release and result in feelings of pleasure, which reinforces the problematic behaviors. One mechanism of addiction, proposed by Kenneth Blum and colleagues, is "reward deficiency syndrome," a state of chemical imbalance involving multiple genes that causes an individual to crave environmental stimuli to compensate for the inherent imbalance, regardless of the consequences (Blum et al., 1996).

Endogenous Opioids

Endogenous opioids are opiate-like substances, such as endorphins, that function as neurotransmitters. They are produced naturally within the body and contribute to feelings of well-being and lessen feelings of pain. Dackis and O'Brien's research (2005) on the neurobiology of addiction demonstrated that individuals with altered opioidergic systems might have greater difficulty controlling desires to continue an addictive behavior due to intense euphoric feelings experienced after engaging in rewarding behaviors. Clinical studies demonstrating the efficacy in treating impulse control disorders using the opioid antagonists **naltrexone** and **nalmefene**, which prevent the body from responding to opiates and endorphins by blocking receptors, have further substantiated involvement of opioids in both behavioral and substance addictions (Grant & Kim, 2002; Grant et al., 2006; Kim et al., 2001; Mason et al., 1999; and Volpicelli et al., 1992).

Stress and Stress Hormones

Changes in cortisol have been related to impulse control disorders. Significantly higher levels of cortisol, a hormone that helps to regulate stress, and adrenaline have been observed in individuals after participating in gambling activities (Schmitt et al., 1998). Elevated heart rate levels have also been observed in study participants following participation in gambling activity (Krueger et al., 2005). Such findings support the possibility of stress pathway involvement in gambling or may indicate that gambling invokes the stress pathway; however, contradictory findings necessitate cautious interpretation and further study.

…neuroimaging studies of impulse control disorders suggest similarities between behavioral and substance addictions.

NEUROIMAGING

Existing evidence from neuroimaging studies of impulse control disorders suggests similarities between behavioral and substance addictions, as indicated by abnormal function (i.e., decreased activation) of the **ventromedial prefrontal cortex** of the brain, which is located in the frontal lobe and is implicated as a critical component in

the processing of risk and decision making (Potenza, 2006 and Potenza et al., 2004).

The **mesocorticolimbic dopamine system** stimulates the ventral striatium, which is strongly associated with emotional and motivational aspects of behavior. Thus brain imaging data showing diminished ventral striatial activation observed in individuals with gambling and drug addictions suggests that the mesocorticolimbic dopamine system is involved in both substance and behavioral addictions (Reuter et al., 2005).

One brain imaging study measured higher levels of activity in parts of the brain's limbic system and prefrontal cortex when monetary rewards were present versus computer points, suggesting increased sensory and **limbic activation** with increased risks and rewards (Hollander et al., 2005). Other imaging studies have implicated brain regions that are involved in attention processing when comparing non-problem gamblers with pathological gamblers (Crockford et al., 2002).

Collectively, these findings suggest a complex network of brain regions is activated during gambling and related behaviors, and that activity within certain aspects of these regions distinguishes pathological gamblers from non-problem gamblers.

OBSERVED SIMILARITIES BETWEEN BEHAVIORAL AND SUBSTANCE ADDICTIONS:

- Repetitive/compulsive behavior despite adverse consequences
- Diminished control over the problematic behavior
- A state of anticipated pleasure prior to engaging in the problematic behavior
- A positive, satisfying feeling while engaging in the problematic behavior
- Tolerance towards the activity increases over time
- Occurrence of withdrawal symptoms
- Attempts to cut back or stop are often repetitive and unsuccessful
- High usage rates during adolescence and young adulthood
- Rapid rate of progression to problematic behavior in women compared to men

GENETIC VULNERABILITY

Consistently, family studies have demonstrated that pathological gambling subjects have elevated rates of first-degree relatives — parents, children or siblings — with substance use disorders, suggesting a possible shared genetic vulnerability between pathological gambling and other addictions (Shah et al., 2004). Studies suggest that both familial factors and shared genetic vulnerability may account for a portion of the risk for pathological gambling (Comings et al., 1997). However, research has shown that shared genetic contributions are not limited to behavior disorders but also include depression (Potenza et al., 2005).

Investigations into specific genes relating to neorepinephrine, serotonin and dopamine **neurotransmitter systems** involved in pathological gambling have been performed and implicate the specific dopamine-related genes in compulsive/addictive behaviors and disorders, such as pathological gambling, smoking and Tourette's syndrome (Comings et al., 1997; Comings et al., 1999; Diskin & Hodgins, 2000; and Perez de Castro et al., 1997).

DECISION-MAKING AND NEUROCOGNITION

The role of frontal cortical regions and the mesocorticolimbic system in pathological gambling has been supported by findings in the Iowa Gambling Task, a tool developed to investigate decision-making, particularly that involving risk-reward assessment, in which subjects with substance use disorders and behavioral disorders preferred to choose smaller immediate monetary rewards over larger delayed rewards (Petry, 2005). This "delayed discounting" was exacerbated by concurrent substance use disorders in individuals with pathological gambling, strengthening arguments regarding commonality in brain regions with other addictions.

Other studies have shown that individuals with pathological gambling may have a broad range of executive functioning deficits, with individuals exhibiting attention deficits and a lower rate of cognitive control when compared to healthy subjects (Goudriaan et al., 2005 and Kertzman et al., 2006). However, methodological differences resulting in discrepant findings necessitate additional research.

TREATMENT

Pharmacologic

Although still in an early stage, several important factors appear to be emerging in drug treatment of impulse control disorders. Selective serotonin reuptake inhibitors (SSRIs), most commonly referred to antidepressants, have shown mixed results in impulse control disorders (Grant & Potenza, 2004). Studies using **opioid antagonists**, such as naltrexone or nalmefene, have demonstrated efficacy in double-blind trials for pathological gambling (Grant et al., 2006 and Kim et al., 2001).

Psychotherapy

In controlled studies, several therapist-driven techniques, such as cognitive-behavioral therapy, Motivational Interviewing and relapse prevention, modeled on treatments for substance use disorders, have demonstrated efficacy (Shah et al., 2004).

Self-Help Groups

Twelve-step self-help groups patterned after Alcoholics Anonymous seem to be the most widely used treatment for impulse control disorders; however, these groups suffer from high dropout rates, and there is little controlled evidence to support their effectiveness.

FUTURE IMPLICATIONS

Prevention and treatment strategies are expected to improve as increased understanding of different neurobiological disturbances that exist in individuals with impulse control disorders emerges via continued research and correlation to substance use disorders. Evidence-based treatments suggest that specific groups of impulse control disorders respond preferentially to specific treatments, thus step-by-step procedures for diagnosing pathological gambling based on the presence or absence of co-occurring disorders have been proposed to guide clinical treatments (Hollander et al., 2004). Emerging data suggest that pathological gambling co-occurs with disorders more often than not, although further investigation is needed to better understand the relationship of impulse-control disorders to other psychiatric disorders so that more structured, evidence-based screenings and treatments may be created to assist clinicians.

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Jon E. Grant, M.D., J.D., M.P.H., is a professor of psychiatry at the University of Minnesota and co-directs a clinic for Impulse Control Disorders at the University of Minnesota Medical Center in Minneapolis, Minn. Grant completed a law degree from Cornell University, a medical degree from Brown University, and a master's degree in public health from Harvard University. He is the author of *Stop Me Because I Can't Stop Myself,* a book on impulse control disorders, and co-editor of *Pathological Gambling: A Clinical Guide to Treatment* and *Textbook of Men's Mental Health*. He was honored by the National Center for Responsible Gaming in 2009 with the NCRG Scientific Achievement Award in the Senior Investigator Category. Grant is also the principal investigator of the NCRG's Center of Excellence in Gambling Research at the University of Minnesota.

RESEARCH SUMMARY

Brain Activity in Pathological Gambling

by Marc Potenza, M.D., Ph.D.
Yale University School of Medicine

A summary of the following publication:
Potenza, M.N., Steinberg, M.A., Skudlarski, P., Fulbright, R.K., Lacadie, C.M., Wilber, M.K., Rounsaville, B.J., Gore, J.C., & Wexler, B.E. (2003). Gambling urges in pathological gambling: A functional magnetic resonance imaging study. *Archives of General Psychiatry, 60*(8), 828-836.

INTRODUCTION

Pathological gamblers often experience urges immediately before engagement in self-destructive gambling behaviors, just as individuals suffering from substance use disorders, obsessive-compulsive disorders and other impulse control disorders typically experience urges before engaging in associated self-destructive behaviors.

This study analyzed brain function collected via **echoplanar functional magnetic resonance imaging (fMRI)**, which offers one of the fastest, most efficient means of measuring localized changes in brain activity. Participants viewed videotaped scenarios — with content depicting scenes of happiness, sadness and gambling. Comparisons were then made based on the participants' ratings of the quality and magnitude of their emotional and motivational responses.

HIGHLIGHTS

- Functional MRI (fMRI) technology measures changes in brain activity and is helping researchers understand more about the urges experienced immediately before self-destructive gambling behavior.
- In this study, pathological gamblers showed less activity in the regions of the brain governing emotion regulation, decision-making and impulse control when shown video images of gambling scenarios.
- This study provides additional evidence that pathological gamblers are more impulsive and sensation seeking than comparison subjects.

OBJECTIVE

Other studies of substance use disorders and obsessive-compulsive disorders have identified brain activity related to anticipatory states. By identifying which areas of the brain are actively associated with gambling urges in pathological gamblers, we may better understand the relationship among pathological gambling, substance use disorders and obsessive-compulsive disorders. Better understanding can help direct research to develop effective treatments for pathological gambling.

HYPOTHESES

Based on higher rates of co-occurrence and a greater sense of anticipatory excitement for pathological gambling and substance use disorders than for pathological gambling and obsessive-compulsive disorders, it was hypothesized that brain activity associated with gambling urges would be more similar to cocaine cravings in cocaine dependence than to obsessions in obsessive-compulsive disorder. Specifically, it was hypothesized that the

The **Limbic System** is a set of brain structures that governs emotions and behaviors, and also supports functions including long-term memory and sense of smell. The limbic system is highly interconnected with the nucleus accumbens, a collection of neurons that has been proposed to function as the brain's "pleasure center" and play an important role in reward, pleasure, addiction, aggression and fear.

Cortico-basal-ganglionic-thalamic System is a set of brain structures consisting of the cerebral cortex, basal ganglia and thalamus. Each functional region of the frontal cortex is connected with specific areas of each basal ganglia structure, to which the thalamus is linked. This system is responsible for motivations and related behaviors.

limbic system of the brain would show more activation when gambling cues were presented than would the cortico-basal-ganglionic-thalamic system.

In this examination of cue-elicited reactions over time, the researchers predicted that comparisons of responses to gambling videotape viewing would demonstrate unique correlations related to (1) early responses, before subjective awareness of internal state change; (2) middle responses, linked to onset awareness of state change; and (3) late responses, around the time when the most provocative stimuli were presented.

SAMPLE AND METHODOLOGY

The study included 11 control subjects and 10 pathological gamblers, all of whom were right-handed males between the ages of 18 and 65 who graduated high school and were native English speakers of either Caucasian or African-American descent. The average age of the pathological gamblers (test group) was 36 years; the average age of the control group was 30 years. None of the subjects had a history of neurologic injury or illness, and none showed structural magnetic resonance imaging (MRI) abnormalities. Seventy-two hours prior to testing, the participants denied any psychoactive drug use, except for possibly nicotine and/or caffeine.

The test subjects met the criteria for pathological gambling, as laid out by the latest edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV),* but were free of other mental disorders such as depression, bipolar disorder, anxiety disorders and schizophrenia.

All control subjects reported having gambled, but all scored zeros on the **South Oaks Gambling Screen**. **The Zuckerman-Kuhlman Personality Questionnaire** and the **NEO Personality Inventory-Revised** were administered to all participants as well.

Echoplanar fMRI was used to assess brain functioning as participants viewed videotaped scenarios featuring two young male actors participating in happy, sad and gambling scenarios. The happy scenarios depicted an unexpected visit from a relative and a wedding. The sad scenarios depicted a parental divorce and a relative's death. The gambling scenarios depicted general situational or psychological cues for gambling, such as stress at work or home followed by receipt of an unexpected amount of money, and actors described the excitement and anticipation they felt prior to engaging in commonly problematic gambling forms for men, such as cards or dice. In every scenario, the actors talked directly to the camera, simulating a social interaction between the actor and the viewer.

The happy and sad scenarios were used as active control conditions because anticipatory states, such as gambling urges, share features of emotions — they change over time in an individually independent fashion. For each scenario, participants were asked to push a button at the beginning of each emotional or motivational response to determine the

onset of perceived emotional or motivational responses. Following the viewings, participants were asked to rate the quality and magnitude of these responses.

Changes in the echoplanar imaging signal were evaluated in three pairs of successive periods, including the initial 45 seconds of viewing, the 45 seconds following the push of the button indicating onset of an emotional response and the final 45 seconds of viewing.

The most pronounced differences between the control and test groups were observed during the initial period of viewing the gambling scenarios.

KEY FINDINGS

The Zuckerman-Kuhlman Personality Questionnaire showed that the pathological gamblers were more impulsive and sensation-seeking than the control subjects. The NEO Personality Inventory-Revised showed that the pathological gamblers were overall more neurotic, exhibiting higher scores in areas of anxiety, hostility, depression, self-consciousness, vulnerability and, above all, impulsiveness compared to control subjects.

The groups did not differ significantly in their subjective responses to the happy or sad videotapes. The greatest differences in personal participant responses were observed in reports of gambling urges in response to the gambling scenarios. While no participants described gambling urges when viewing the happy or sad scenarios, all 10 test subjects reported gambling urges when viewing the gambling scenarios, compared to only three of the 11 control subjects.

Although differences in brain activity were observed during the viewing of the sad and happy scenarios, they were distinct from those corresponding to the gambling scenarios. The most pronounced differences between the control and test groups were observed during the initial period of viewing the gambling scenarios.

During the initial viewing of the gambling scenarios (when multiple gambling cues were presented and prior to the participants' awareness of changes in emotional or motivational states), the test subjects demonstrated significantly less brain activity in the frontal cortical, orbitofrontal cortex, caudate/basal ganglia and thalamus compared to controls — areas of the brain associated with emotional and motivational states.

Overall, after subjects indicated an emotional response to the happy, sad or gambling videos, the measure of brain activity observed between the groups indicated that the test subjects showed relatively increased activity compared with control subjects in brain regions implicated in emotional and motivational responses.

No significant differences were observed in brain activity responses to the happy scenarios in the test and control groups during the last 45 seconds of viewing. However, while viewing the

STRUCTURAL MRI (MRI) VS. FUNCTIONAL MRI (FMRI)

Magnetic Resonance Imaging (MRI) offers a non-invasive method of producing images of the brain.

- *Structural MRI:* produces a high-quality image of the brain's anatomical structure, so that physical manifestations of brain diseases or disorders may be visualized.
- *Functional MRI:* measures localized changes in blood oxygen level dependent signals related to neural activity associated with specific tasks.

…strong evidence that pathological gamblers are more impulsive and sensation-seeking than comparison subjects.

sad scenarios, as compared to the test subjects, the control subjects showed decreased brain activity in the right superior frontal gyrus, which is associated with self-awareness, and an increased activity in the right inferior frontal gyrus, which is associated with risk-aversion. During the viewing of the gambling scenarios, the pathological gambling group showed less activation of the ventral anterior cingulate cortex, a component of the ventromedial prefrontal cortex and one implicated in emotion regulation, decision-making and impulse control.

DISCUSSION

In pathological gamblers, gambling cues elicit gambling urges and lead to a time-dependent, dynamic pattern of brain activity changes in frontal, paralimbic and limbic brain structures. As compared to control subjects, pathological gamblers demonstrate relatively decreased activity in these brain areas implicated in impulse regulation when viewing gambling cues.

The findings from this study (and multiple previous investigations) provide strong evidence that pathological gamblers are more impulsive and sensation-seeking than comparison subjects.

Our hypotheses were supported by the findings that brain activity associated with cue-elicited anticipatory states in pathological gamblers appears to differ significantly from those with obsessive-compulsive disorder as in the existing literature. However, the findings that brain activity in pathological gambling urges was largely not similar to that of subjects experiencing cocaine cravings suggest that pathological gambling may share a closer relationship with nondrug disorders characterized by impaired impulse control.

LIMITATIONS OF STUDY

This investigation, to our knowledge, was the first fMRI study of pathological gambling. One limitation involved the exclusive use of men; future studies should examine female pathological gamblers. A larger sample would allow for examination of effects related to other co-occurring psychiatric disorders.

IMPLICATIONS FOR FUTURE RESEARCH

The comparisons in brain activity indicated in this study warrant additional studies directly comparing pathological gambling, conduct disorders and obsessive-compulsive disorders. Of particular interest is the examination of brain activity in regard to treatment of pathological gambling with medications like selective serotonin reuptake inhibitors — medications typically used to treat depression and anxiety disorders — or opioid antagonists. Data suggest efficacy and tolerability of these drugs (particularly the latter class) in the short-term treatment of pathological gambling.

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About the author…

Marc N. Potenza, M.D., Ph.D., is a professor of psychiatry, child study and neurobiology at the Yale University School of Medicine. Currently, he serves as director of the Problem Gambling Clinic and the Women and Addictive Disorders Core of Women's Health Research at Yale and director of neuroimaging for the VISN1 MIRECC of the VA Connecticut Healthcare System. Potenza is on the editorial boards of eight journals and has received multiple national and international awards for excellence in research and clinical care, including the NCRG's Scientific Achievement Award in 2008. He is principal investigator on the NCRG's Center of Excellence in Gambling Research at Yale University.

RESEARCH SUMMARY

Brain Imaging Studies: A Review

By Anna E. Goudriaan, Ph.D.
University of Amsterdam

A summary of the publication:
van Holst, R.J., van den Brink, W., Veltman, D.J. & Goudriaan, A.E. (2010). Brain imaging studies in pathological gambling. *Current Psychiatry Reports, 12*(5) 418-425.

HIGHLIGHTS

- Studies have shown pathological gamblers demonstrate diminished brain activity and a blunted response to rewards as well as losses, prompting them to continue seeking rewards.
- Pathological gamblers' responses to gambling-related stimuli — such as casino images and emotional descriptions of gambling — indicate increased activity in the region of the brain associated with pleasure processing, mood regulation and risk-taking.
- Studies show pathological gamblers display more risk-taking behavior, impaired decision-making and a hypersensitivity to gambling cues.

INTRODUCTION

Although pathological gambling is classified as an **impulse control disorder**, it is often regarded as a behavioral addiction due to its resemblance to substance dependence. Both show similar patterns of coexisting disorders, genetic vulnerabilities and responses to specific drug treatments.

Given the similarities between substance dependence and pathological gambling, theories regarding pathological gambling and the means of testing those hypotheses have been modeled after similar studies used in research on substance use disorders.

Current addiction theories have identified four important cognitive-emotional processes that are likely to be relevant for pathological gambling:

1. Reward and punishment processing, and its relation to behavioral conditioning
2. Increased sensitivity to gambling cues, which often results in strong urges or cravings for gambling
3. Impulsivity, which has been implicated as both a vulnerability trait for acquiring pathological gambling and as a consequence of gambling problems
4. Continuation of gambling despite severe negative consequences, implicating diminished decision-making abilities

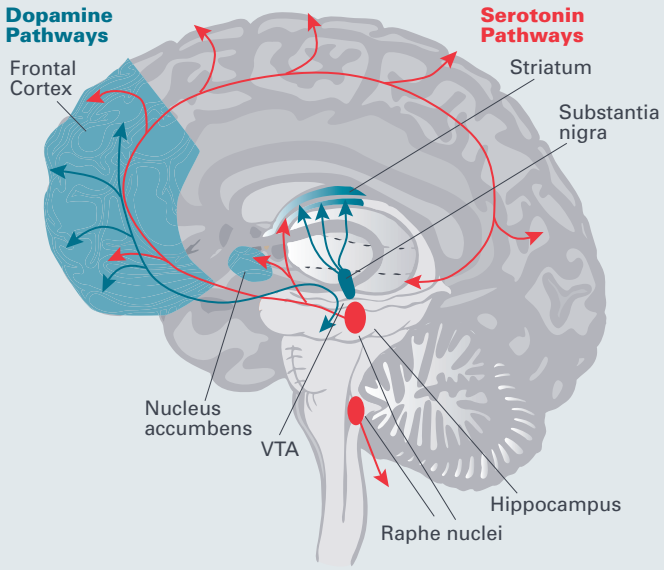
Using these four processes as an organizing principle, this review article congregates information from neuroimaging studies previously published from 2005 to 2010.

Reward and Punishment Sensitivity

Behavioral conditioning is a key process involved in the development of gambling behavior. Differences in behavioral conditioning depend on underlying sensitivity to rewards and punishments, which have been studied in pathological gambling relatively often with neuroimaging techniques.

A review of imaging data from comparable studies (de Ruiter et al., 2009 and Reuter et al., 2005) found that, compared to non-gamblers, pathological gamblers demonstrated a

blunted response to rewards as well as losses, as evidenced by diminished **mesolimbic-prefrontal cortex** activation during nonspecific rewarding and punishing events. Notably, in a study that examined brain functioning associated with risk as problem gamblers participated in a realistic gambling game in which monetary gains and losses were present, such blunted responses were not observed (Miedl et al., 2010). An explanation of this finding may lie in the fact that the realistic gambling game triggered cue reactivity, because higher mesolimbic-prefrontal brain activity patterns were present during high-risk gambles in the problem gamblers.



The **mesolimbic-prefrontal circuit** in the brain is influenced by neurotransmitters such as dopamine and serotonin, and mediates mood and social behavior, pleasure processing, influences motivated behavior related to rewards and risk taking, and thus affects judgment and decision making processes.

Source: National Institutes of Health

Similar findings of diminished brain activity towards rewards have been found in subjects with substance use disorders. Addiction theories state that prior to developing addiction behaviors, there is a pre-existing diminished sensitivity of the brain's reward system associated with dopamine — a neurotransmitter associated with motivation, reward, pleasure and consequently, reinforcement. Dopamine transmission is further reduced with repeated drug use, causing decreased sensitivity to the pleasurable experience of the drug. In consideration of these findings and theories, it has been hypothesized that, similar to substance-dependent individuals, pathological gamblers are more likely to demonstrate insensitivity of the reward system, and therefore more likely to seek rewarding events.

Cue Reactivity

A prominent symptom of pathological gambling is the strong urge to gamble, which often leads to a relapse in gambling behavior. While factors of craving and response to stimuli — or **cue reactivity** — associated with substance use disorders have been studied extensively using neuroimaging techniques, only a few studies in pathological gambling have been published.

Three of four neuroimaging studies in pathological gamblers showed that when exposed to gambling-related stimuli, such as dramatic portrayals of gambling, casino images and descriptions of emotions when gambling, pathological gamblers demonstrate increased activity in the mesolimbic-prefrontal cortex (Crockford et al., 2005; Goudriaan et al., 2010; and Miedl et al., 2010). While contrasting results were found in another study, they were ultimately difficult to interpret due to the complexities of the test (Potenza et al., 2003).

Differences in the way cue reactivity experiments are conducted and how the brain processes complex information may affect outcomes. For example, some studies required participants to calculate a win or loss, while others displayed gambling related photos. As compared to substance use disorder studies, where cue reactivity is specific to a targeted substance, the diversity of gambling activities may limit the ability to detect differences in cue reactivity in pathological gambling studies.

Impulsivity in Pathological Gambling

Impulsivity is often equated with an overall lack of restraint, in which an individual has difficulty suppressing responses. An aspect of impulsivity frequently addressed in neurocognitive studies is delay discounting, in which choices between immediate, smaller rewards and larger, delayed rewards are made. A large number of neurocognitive studies have indicated that pathological gamblers are impaired in several inhibitory processes, including delay discounting and response inhibition, but, to date, there is only one neuroimaging study that investigates the brain activity associated with impulsivity.

A functional MRI (fMRI) study on the Stroop interference in pathological gamblers has been published (Potenza, Leung et al., 2003). The Stroop interference uses a color-word association task in which a participant is asked to name the color that a word is printed in rather than read the word. This activity is used to measure inhibition of an automatic response, which would be to read the word. The study found that when compared to controls, pathological gamblers showed lower prefrontal brain activity.

Similar to substance use disorder patients, pathological gamblers exhibit a pattern of decision-making in which long-term negative consequences are ignored in order to obtain immediate gratification.

Decision-Making in Pathological Gambling

Similar to substance use disorder patients, pathological gamblers exhibit a pattern of decision-making in which long-term negative consequences are ignored in order to obtain immediate gratification (Goudriaan, 2004). The decision-making process is multifaceted and involves impulsivity as well as risk-taking, and experiencing and evaluating immediate and delayed wins and losses. Neurocognitive studies regarding decision-making in pathological gambling have implicated impaired decision-making among pathological gamblers (Hewig et al., 2010 and Tanabe et al., 2007).

A recent study that measured brain response in correlation to decision-making found that problem gamblers displayed more risk-taking behavior while gambling and experienced a stronger neural response to infrequent, successful outcomes compared to non-problem gamblers (Hewig et al., 2010). Similarly, an fMRI study that measured cerebral blood flow as related to real-life decision-making by using a modified version of the Iowa Gambling Task, which uses choice behavior for card decks related to different rewards and losses over time, found that subjects with both substance use disorders and pathological gambling showed lower brain activity in areas associated with risk, fear and decision-making than control subjects; and compared to substance use disorder subjects, pathological gamblers reflected a hypersensitivity to gambling cues (Tanabe et al., 2007).

KEY FINDINGS

Although the overall number of neuroimaging studies in pathological gamblers is still modest, fMRI studies have consistently shown diminished activity in the mesolimbic-prefrontal cortex of pathological gamblers when dealing with reward and loss processing, but not when they are in a gambling situation. Instead, when problem gamblers are confronted with gambling-related cues, increased activity is present in areas of the brain associated with reward and motivation. Ultimately, changes in dopamine transmission may contribute to the overall functioning of these areas of the brain, which play an important role in integrating emotional processing and behavioral consequences in healthy individuals. However, many other neurotransmitter systems also influence the reward and motivation circuit in the brain.

When problem gamblers are confronted with gambling-related cues, increased activity is present in areas of the brain associated with reward and motivation.

CLINICAL IMPLICATIONS

Several pharmacological agents have been demonstrated in clinical trials to be effective in the treatment of pathological gambling. Opioid antagonists, such as naltrexone and nalmefene, which decrease dopamine release in the brain, have been found to reduce reward sensitivity and therefore may be effective in battling the urges that pathological gamblers experience. Other drugs that regulate function of the neurotransmitter glutamate have also been effective in reducing gambling behavior in pathological gamblers.

Selective serotonin reuptake inhibitors (SSRIs) — commonly used as antidepressants or anxiety medication — have targeted impulsivity and impulse control, but careful consideration of co-existing disorders must be given before prescribing such treatments. While the effectiveness of cognitive enhancing medication is not yet proven, cognitive-behavioral therapy has been found to be effective in treating pathological gambling.

IMPLICATIONS FOR FUTURE RESEARCH

More research is needed regarding the neurological basis of impulsivity and decision-making in pathological gambling. Neurocognitive similarities and comparable responses to pharmaceutical drugs in pathological gambling and substance use disorders suggest common underlying pathological pathways. This observation is used to support the rationale for changing the classification of pathological gambling from an impulse control disorder to a behavioral addiction, as proposed by the DSM-5 Task Force for the next edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders.* (For more information, visit http://www.dsm5.org.)

Implementation of novel neuroimaging techniques may inform us about brain functions critically involved in addictive behavior, and by using neuromodulation research, eventually new treatment options for pathological gambling may evolve. For example, by using real-time displays of neural activity to measure brain waves and to train individuals to change specific brain activity patterns, we can test how this affects gambling behavior.

The neurophysiologic factors predisposing individuals to addictive behaviors may be further explored by looking at dopamine impairment and interactions with genetic variations in patients with Parkinson's disease with and without pathological gambling. This may contribute to our understanding of neurological factors that make individuals vulnerable to addictive behaviors.

Cue reactivity studies in pathological gambling have reported conflicting results thus far; therefore, future research should focus on the type of stimuli that elicit the most powerful cue reactivity, such as pictures versus movies and active versus passive gambling situations. Additional research is also necessary to understand the transition of gambling to problem gambling. Regarding the addictive potential of certain game characteristics in problem gamblers and gamblers without problems, a recent study indicates that near misses — losses that are proximal to a win or payout — involve reward-related brain circuitry. In addition, problematic gambling was related to higher recruitment of these brain areas, indicating that near misses are processed as rewards in the brains of problem gamblers (Clark, 2009).

Because only one neuroimaging study on inhibition has been published, additional neuroimaging studies on impulsivity are warranted, preferably examining a large variety of impulsivity measures in pathological gamblers.

Finally, future research on the treatment of pathological gambling should clarify whether a combination of medication and psychological treatment will lead to more sustained remission rates than either of these treatments alone.

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About the author…

Anna E. Goudriaan, Ph.D., is a senior researcher in the department of psychiatry at the Academic Medical Center, University of Amsterdam, the Netherlands. She specializes in the study of neurobiological mechanisms of behavioral addictions and substance related disorders and in the neurocognition and epidemiology of problem gambling. Currently, she is heading neuroimaging studies in pathological gamblers and alcohol dependent patients, studying cognitive and motivational processes through functional MRI (fMRI). Her interests also lie in studying the effects of neuromodulation and psychopharmacological interventions on abnormal motivational and cognitive functions in addictive disorders. Goudriaan was the 2009 recipient of the NCRG Scientific Achievement Award in the Young Investigator category. Currently she is a principal investigator on grants sponsored by the Dutch Organisation for Health Research, Dutch Scientific Society and the international program of the National Institute on Drug Abuse.

RESEARCH SUMMARY

The Rat Gambling Task: Understanding the Role of Serotonin and Dopamine in Pathological Gambling

By Catharine A. Winstanley, Ph.D.
University of British Columbia

A summary of the publication:
Zeeb, F.D., Robbins, T.W. & Winstanley, C.A. (2009). Serotonergic and dopaminergic modulation of gambling behavior as assessed using a novel rat gambling task. *Neuropsychopharmacology, 34*(1), 1-15.

HIGHLIGHTS

- This study used rats and reward vs. punishment scenarios to better understand the neurotransmitters serotonin and dopamine and their roles in relation to impulsivity and addiction.
- The rats' ability to perform the gambling task proved that they are sensitive to drugs that regulate serotonin and dopamine.
- Patterns were observed in the rats' decision-making relative to the size of the expected reward and both the probability and magnitude of the expected punishment.
- Drugs that regulate serotonin and dopamine are considered therapeutically relevant drug treatment options for gambling-related disorders. This study's results provide more insight into the most effective drug options.

INTRODUCTION

The neurotransmitters serotonin and dopamine play important roles in impulsivity and addiction, and current data suggest that they also contribute to pathological gambling. Better understanding of the mechanisms through which dopamine and serotonin regulate gambling could, therefore, contribute to better treatments for pathological gambling.

This study was based, in part, on the **Iowa Gambling Task (IGT)** (Bechara et al., 1994), which was designed to simulate real-life decision-making in laboratory experiments. During this task, participants choose cards from four decks and either win or lose money. Individuals diagnosed with pathological gambling will consistently choose the larger rewards regardless of the penalties, which is indicative of risky decision-making.

In all areas of science, animal studies provide information that is useful in understanding human problems, including pathological gambling. This study uses an animal model similar to the IGT, in which rats chose among four different options to earn as many sugar pellets as possible within 30 minutes. Each option is not only associated with the delivery of a different amount of reward, but also with a different probability and duration of punishing timeout periods during which a reward cannot be earned. Similar to human subjects performing the IGT, if the rats consistently choose larger rewards, they end up earning less reward overall.

This study analyzed the effects of dopamine and serotonin drugs on rats in relation to their ability to maximize their earnings.

OBJECTIVE AND HYPOTHESES

By examining the behavioral habits of rats in regards to reward and punishment sensitivity and drawing comparisons to gambling behaviors seen in humans, and then assessing how rat behavior is affected by pharmaceutical drugs that impact the brain's serotonin and

dopamine systems, we can improve our understanding of the neural and neurochemical basis of gambling and the treatment of pathological gambling. This study hypothesized:

1. Drugs that enhance dopamine function will impair performance.
2. Drugs that inhibit dopamine function may improve optimal behavior.
3. Drugs that inhibit serotonin release will impair performance.

SAMPLE AND METHODOLGY

The subjects were 32 male Long-Evans rats of similar weights, feeding habits and environmental habitats. Long-Evans rats represent a species strain that is typically used in behavioral research. Prior to testing, the subjects were acclimated to the testing apparatus and trained to ensure that all animals had equal experience with all of the four reinforcement possibilities. This training step was designed to prevent simple biases toward a particular hole from developing due to inadequate sampling of all the options.

In this rat gambling task, subjects have a limited amount of time to maximize the number of sugar pellets obtained, and loss is signaled by punishing timeouts during which a reward cannot be earned. On each trial, animals choose from four options, each associated with different numbers of sugar pellets. The animal then receives either the associated reward or a punishing timeout.

For this task, the reward versus punishment contingencies were set as follows in Table 1:

TABLE 1

	P1	P2	P3	P4
Reward – sugar pellets	1 (p= 0.9)	2 (p= 0.8)	3 (p= 0.5)	4 (p= 0.4)
Punishment – timeout	5 seconds (p=0.1)	10 seconds (p= 0.2)	30 seconds (p= 0.5)	40 seconds (p= 0.6)

(p=probability)

The schedules were designed so that persistent choice of options linked with larger rewards resulted in fewer pellets earned over time. The best option in this task, P2, provides a greater probability of a reward of two sugar pellets versus a smaller probability of a 10-second time out. Larger rewards are associated with a high chance of longer timeouts, resulting in less reward earned overall per session.

In order to determine how important punishment signals were in determining choice, two groups of rats were used as the control. For one group, the probability of punishment remained constant at 0.2, and for another group, the punishment duration remained constant at 10 seconds.

To determine their baseline behavior, the rats were first tested without any drugs in their system. Then all subjects received equal dosages of drugs. The drugs were either: 1) dopamine or serotonin agonists, which bind to corresponding receptors to trigger a specific response or action; or 2) dopamine or serotonin antagonists, which bind to corresponding receptors in order to inhibit a specific response or action. See Table 2 for results.

TABLE 2: KEY FINDINGS	
Baseline	The rats significantly favored the best option P2, followed by P4, P1, and P3. Ranking P4 highly suggests that rats, like humans, find larger reward options tempting despite the associated heavier punishments.
	Choice does not depend solely on either the probability of punishment or the punishment duration, but an integration of both variables with the value of the reward.
DOPAMINE AGONISTS	
SKF 81297	Only the highest dose increased the choice of the largest reward with the largest probability of punishment.
Bromocriptine	Behavior was not altered in any of the three groups.
Quinpirole	At the highest dose, the drug only affected preference for the different options in the control groups. When compared to the similar effects of SKF 81297, these findings highlight the difference between decision-making processes based solely on differences in reward probability and those incorporating more complex punishment signals.
Amphetamine	This drug shifted preference towards smaller rewards with smaller punishments by reducing rats' tolerance for both increased probability and duration of the punishing timeouts. The shift may have occurred because the animals became hypersensitive to the punishment signal and became risk averse.
DOPAMINE ANTAGONISTS	
Eticlopride	At the lowest dose, optimal choice significantly improved. However, there was no change in choice behavior in the control groups, suggesting that the dopamine receptor inhibited by this drug is particularly important when the task requires greater cognitive effort or conflict resolution.
SCH 23390	When the probability of the punishments was held constant, and at a particular dose of this drug, there was a small decrease in the largest reward option.
SEROTONIN AGONIST	
8-OH-DPAT	Performance was significantly impaired, decreasing choice of the best option and increasing choice of the non-optimal options. However, when punishment duration was constant, there was no effect on behavior, which may reflect increased sensitivity to punishment magnitude rather than punishment probability.
SEROTONIN ANTAGONIST	
WAY 100635	Choice behavior was not significantly altered in any group.

DISCUSSION

This study demonstrated that rats are capable of "playing the odds" when choosing between multiple options differing in the probability and magnitude of gain and loss; they learn to avoid options associated with larger rewards but heavier long-term losses and prefer more advantageous options associated with smaller rewards but greater net gain.

…rats are capable of "playing the odds" when choosing between multiple options differing in the probability and magnitude of gain and loss…

Furthermore, the rats' ability to perform the gambling task is sensitive to drugs that regulate serotonin and dopamine levels, which clinical studies have implicated in the regulation of gambling behavior. Therefore, this rat gambling task may be a useful tool for investigating the neurochemical regulation of gambling.

Different patterns of choice preference were observed when either the probability of punishment or the duration of the punishing timeouts was held constant, suggesting that choice in the rat gambling task is guided by an integration of the size of the expected reward with both the probability and the magnitude of the expected punishment.

This cognitive process shares key features with the decision-making process involved in gambling. Therefore, the rat gambling task may provide new, important and timely data in relation to the neurobiological basis of gambling that can be used to identify therapeutically relevant drug options for such gambling-related disorders.

LIMITATIONS OF STUDY

From this study, we see that rats can solve discriminations on the basis of the probability of reward and loss; however, this only simulates part of the gambling process. Other factors, such as the natural tendency to chase losses, sensitivity to previous outcomes and the amount wagered, are critically important when considering the motivation to gamble.

It can be argued that the rats are relying on memory for the position of the different options to solve the task, rather than basing their preferences on the different reinforcement circumstances. Theoretically, the possibility that the rats' performance in this gambling task relies on memory could be completely abolished if the location of the different options was altered randomly between sessions; however, this would make the task exceedingly complex and it is doubtful that the rats would reliably perform such a task.

IMPLICATIONS FOR FUTURE RESEARCH

The findings do suggest that the rat gambling task or IGT will be a useful tool to study the biological basis for gambling, but more research is needed.

The effect of dopaminergic drugs could depend on both the body's natural levels of dopamine and gambling-induced changes in dopamine release that may vary according to the type of gambling, causing individual differences in dopamine function to regulate the motivation to gamble. Further research should examine the conditions under which dopamine antagonists may improve or worsen gambling behavior, and their relation to the type of gambling patterns in which individuals are engaged. The importance of punishment and punishment-related signals in models of gambling also warrants further investigation.

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About the author…

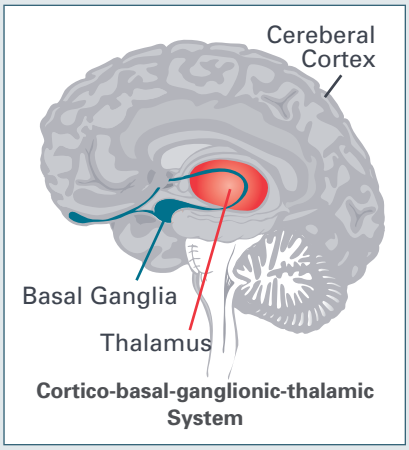
Catharine Winstanley, Ph.D., is an assistant professor of psychology at the University of British Columbia (UBC). Winstanley received a first class honours degree in psychology and physiology from Oxford University in 2000, after which she completed her doctorate in the psychology department of the University of Cambridge. Winstanley then worked as a post-doctoral fellow at the University of Texas Southwestern Medical Center in Dallas for nearly three years before taking up a faculty position at UBC. She now directs the Laboratory of Molecular and Behavioural Neuroscience, which studies the neural, neurochemical and molecular basis of cognitive processes such as impulsivity, attention and gambling-related decision-making.

GLOSSARY

Behavioral addiction is a term that refers to addictive disorders in which a behavior or activity, such as gambling, is the object of addiction rather than a substance such as alcohol or drugs. The term is not used in the current *Diagnostic and Statistical Manual of Mental Health Disorders (DSM)* but has been proposed for the next edition of the DSM to characterize a gambling disorder.

Cortico-basal-ganglionic-thalamic System is defined as three areas of the brain (the cerebral cortex, the basal ganglia and the thalamus) that work together to influence motivation and behaviors related to motivation.

Cue reactivity is the study of the environmental factors or stimuli that trigger an addictive craving or impulse response.



Cortico-basal-ganglionic-thalamic System

Dopaminergic pathways are neurological pathways in the brain through which the neurotransmitter dopamine transmits.

Echoplanar functional magnetic resonance imaging (fMRI) is a fast magnetic resonance imaging (MRI) technique that depicts changes in brain activity or function.

Endogenous opioids are natural chemicals the body produces in the central nervous system that can induce pain relief and euphoria, as well as certain behaviors, such as alcohol consumption.

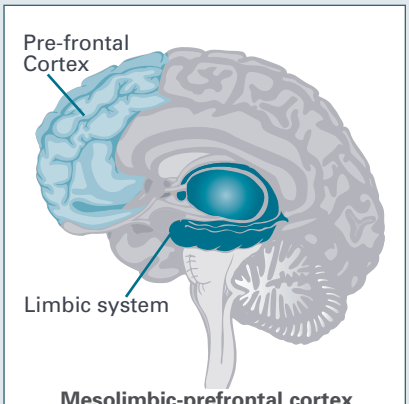
Impulse control disorder is characterized by impulsive engagement in harmful or potentially harmful behavior despite likely consequences to one's self or others.

Iowa Gambling Task is a tool for simulating real-life decision-making in the laboratory and is widely used in the research of cognitive and emotional functioning. During the simulation, participants play a card game and must assess the risks of continuing to draw from a deck of cards when the card may either win them money or lose them money.

Limbic activation is responsiveness in the areas of the brain that are responsible for memory and emotions.

Limbic System is considered to be a set of brain structures that govern emotions and motivation, as well as long-term memory and a sense of smell.

Mesolimbic-prefrontal cortex are the areas of the brain, specifically the limbic system and prefrontal cortex, that work together to affect judgment and decision making processes, as well as mediate mood and social behaviors. It is sensitive to changes in the neurotransmitters dopamine and serotonin.



Mesolimbic-prefrontal cortex

Mesocorticolimbic dopamine system consists of parts of the brain that use the neurotransmitter dopamine to signal emotional and cognitive functions.

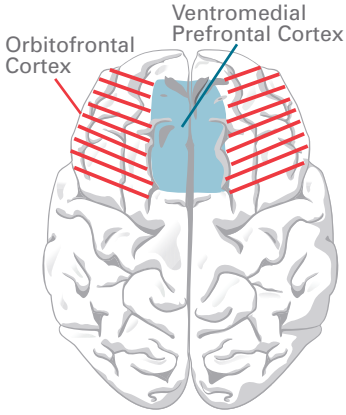
Nalmefene and naltrexone are commonly used drugs to prevent the body from responding to opioids, a class of chemicals that can block pain and create a feeling of euphoria.

NEO Personality Inventory-Revised is a personality assessment tool that measures five personality traits: neuroticism, extraversion, openness to experience, agreeableness and conscientiousness.

Neuroadapation is the ability of the brain to change how it responds or functions in the presence or absence of different stimuli (i.e., changes associated with withdrawal from an addictive substance).

Neurotransmitter systems are different classes of chemicals that carry signals to perform the varying functions of the central nervous system.

Opioid antagonists are drugs that prevent the body from responding to opioids, a class of chemicals that can block pain and create a feeling of euphoria.



Ventromedial Prefrontal Cortex

Serotonergic dysfunction is the occurrence of low levels of the neurotransmitter serotonin, a chemical that carries signals for mood, emotion and cognitive functioning.

South Oaks Gambling Screen (SOGS) is a questionnaire used to screen for pathological gambling.

Ventromedial prefrontal cortex is the area in the frontal lobe part of the brain that is responsible for processing risk and fear for decision-making.

Ventral striatium is a part of the limbic system that is strongly associated with emotional and motivational aspects of behavior.

Zuckerman-Kuhlman Personality Questionnaire is a true/false questionnaire used to assess personality traits in the following areas: neuroticism-anxiety, activity, sociability, impulsive sensation-seeking, aggression-hostility and infrequency (or inattention).

REFERENCES

In addition to the studies summarized in this monograph publication, the editors used the following sources to compile this glossary of terms and images:

American Psychiatric Association Committee on Nomenclature and Statistics. (2000). *DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders,* (Fourth ed., text revision). Washington, DC: American Psychiatric Association.

Canadian Institutes of Health Research: Institute of Neurosciences, Mental Health and Addiction
www.cihr-irsc.gc.ca

Merriam-Webster
www.merriam-webster.com

National Institutes of Health
www.nih.gov

Radiological Society of North America
www.rsna.org

RESOURCES AND PROGRAMS

While research on gambling disorders is still a relatively young field of study, it already is yielding valuable information and guiding practical applications. The NCRG and the American Gaming Association (AGA) offer a variety of programs and tools to increase awareness of gambling disorders and implement responsible gaming practices and programs. A few examples are listed below.

NCRG RESOURCES AND PROGRAMS

NCRG Conference on Gambling and Addiction

Since 1999, the annual NCRG Conference on Gambling and Addiction has brought together researchers, health care providers, regulators, policy makers and gaming industry representatives from around the world. The conference provides a unique forum for these audiences to discuss the latest research advances in the field of gambling and related disorders, and how these findings can be incorporated into practical, real-world applications. Each year, the conference explores a different theme, presenting the most current topics from scientific, clinical, government and industry perspectives. Since 2002, the NCRG has also annually recognized outstanding contributions to the field of gambling studies with the NCRG Scientific Achievement Award presented at the conference. The NCRG conference is held each October in conjunction with Global Gaming Expo, the gaming industry's largest international trade show and conference.

More information about the NCRG Conference on Gambling and Addiction is available at www.ncrg.org/conference. Summaries of key sessions from past conferences and upcoming conference details are available on the NCRG's blog, Gambling Disorders 360°, at http://blog.ncrg.org.

Research and Resources Guide

Research & Resources: A Guide to Gambling Disorders and Responsible Gaming allows quick and easy access to a library of the most significant research findings now available in the field of gambling disorders, providing an overview of key studies by leading researchers. Also included is a guide to the NCRG's and the industry's major responsible gaming education and outreach initiatives, a glossary of commonly used research terms, and helpful online publications and resources. You also will find a list of experts in the field of gambling disorders, organized by subject category, who can provide additional information about specific areas of research on gambling disorders. To view the guide, visit www.ncrg.org/press_room/res-guide.cfm.

Gambling Disorders 360° and Other Social Media

Gambling Disorders 360° is the blog for the NCRG that explores the latest news, issues and research relating to gambling disorders and responsible gaming. The blog is also a forum where researchers, clinicians, regulators, policymakers and industry representatives can come together to share knowledge and best practices and discuss the field's most pressing and vital issues. To subscribe to Gambling Disorders 360°, visit http://blog.ncrg.org.

The NCRG is also active on Facebook and Twitter. To connect with the organization on Facebook, visit www.facebook.com/theNCRG. To follow the NCRG on Twitter, visit www.twitter.com/theNCRG.

PEER and EMERGE Programs

The Partnership for Excellence in Education and Responsible Gaming (PEER) is a dynamic, one-of-a-kind program created by the NCRG to provide gaming entities with the tools and resources needed to develop a comprehensive and world-class responsible gaming program. The PEER program offers members full access to the blueprint needed to implement the NCRG Code of Conduct for Responsible Gaming, best practices and in-depth, how-to instructions to put these words into action. PEER program members also have access to unique employee training opportunities, on-call implementation assistance and an annual report card to demonstrate progress on their initiatives. To learn more about the PEER program and how it can help your organization, visit www.ncrg.org/peerprogram.

The Executive, Management and Employee Responsible Gaming Education (EMERGE) program is a science-based, online training program for gaming industry employees developed by Harvard Medical School faculty with support from the NCRG. EMERGE is the only program of its kind grounded in scientific research but designed for a lay audience. The self-paced program teaches employees about the nature of addiction, how gambling can become an addiction and the specific responsible gaming policies and practices of their organization. EMERGE is an important component of the PEER program. For more information, download the brochure at www.ncrg.org/public_education/emerge.cfm.

A Call to Action: Addressing College Gambling: Recommendations for Science-Based Policies and Programs

The *Call to Action* report consists of science-based policy recommendations about gambling that help higher education institutions inform their students about the risks of excessive gambling, mitigate gambling-related harms and offer rehabilitative programs that can help reduce addictive behaviors. The publication was developed by the Task Force on College Gambling Policies, which was established in 2008 by NCRG and the Division on Addictions at the Cambridge Health Alliance, a teaching affiliate of Harvard Medical School. Task force members combined scientific research findings with real-world experiences in student health and university policy issues to craft the recommendations, which provide schools with a roadmap for reducing gambling among students and enabling those who are struggling with addiction to participate more fully in college life. To download the full report, visit http://www.ncrg.org/assets/files/college%20task%20force/A_Call_to_Action_Full_Report_92909.pdf.

CollegeGambling.org

Building upon the recommendations of the Task Force on College Gambling Policies, the NCRG developed www.CollegeGambling.org as a tool to help current and prospective students, campus administrators, campus health professionals and parents address gambling and gambling-related harms on campus. The first site of its kind, CollegeGambling.org brings together the latest research and best practices in responsible gaming and the field of addiction awareness and prevention in order to provide a substantive and versatile resource that will help schools and their students address this important issue in the way that best fits each school's needs.

Talking With Children About Gambling

"Talking with Children about Gambling" is a research-based guide designed to help parents, as well as others who work with youth, deter children from gambling and recognize possible warning signs of problem gambling and other risky behaviors. The guide was developed in consultation with the Division on Addictions at Cambridge Health Alliance, a teaching affiliate of Harvard Medical School. For more information, download the brochure at www.ncrg.org/public_education/talking-with-children.cfm.

Your First Step to Change

Your First Step to Change is a self-help guide for individuals thinking about changing their gambling behavior. Originally developed as a booklet in 2002 for callers to the Massachusetts Council on Compulsive Gambling's help line, the guide is available in Spanish, Chinese, Khmer and Vietnamese.

Your First Step to Change was developed by the Division on Addictions and the Massachusetts Council on Compulsive Gambling with support from the Massachusetts Department of Public Health and the NCRG. To view the guide, visit www.basisonline.org/self-help_tools.html.

The Brief Biosocial Gambling Screen (BBGS)

The Division on Addictions at Cambridge Health Alliance released the Brief Biosocial Gambling Screen (BBGS) to help people decide on their own whether to seek a formal evaluation of their gambling behavior. Released in 2011, this 3-item survey is based on the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* criteria for pathological gambling. The researchers' objective was to develop a concise screening instrument that would correctly identify the largest proportion of current pathological gamblers and exclude non-pathological gamblers (i.e., reduce the number of false positives). The development of this screen was funded by the NCRG, and it is available online on the Division of Addictions website (www.divisiononaddictions.org/bbgs_new/).

AGA RESOURCES AND PROGRAMS

The American Gaming Association Code of Conduct for Responsible Gaming

The American Gaming Association (AGA) and its members pledge to their employees and patrons to make responsible gaming an integral part of our daily operations across the United States. This pledge encompasses all aspects of our business, from employee assistance and training to alcohol service, advertising and marketing. The AGA Code of Conduct for Responsible Gaming also covers the commitment of our members to continue support for research initiatives and public awareness surrounding responsible gaming and underage gambling. The brochure, which details how the pledge is fulfilled, can be found at www.americangaming.org/social-responsibility/responsible-gaming/code-conduct.

The American Gaming Association *Responsible Gaming Statutes and Regulations*

The AGA developed a publication that contains a compilation of statutes and regulations regarding responsible gaming in the 20 states that had commercial casinos or racetrack casinos, also known as "racinos," as of February 2008. The content in each section is divided into seven general categories, including Alcohol Service, Credit/Cash Access, Funding/Revenue Sharing (treatment funding), Self-exclusion, Signage/Help Line/Advertising, Training/Education (employee training, employee responsible gaming prevention, public awareness) and Miscellaneous (loss limits/limited stakes, direct mail/marketing). To view the publication, visit www.americangaming.org/industry-resources/research/responsible-gaming-statutes-and-regulations.

The House Advantage: A Guide to Understanding the Odds

This publication, which fulfills a provision of the AGA Code of Conduct for Responsible Gaming, explains the house advantage, providing typical ranges for specific games, along with other factors that should be taken into account when betting on casino games, such as the amount wagered, the length of time played and, to a degree, a player's skill level. It also debunks common myths about gambling and provides an explanation of regulatory procedures in place to ensure all the games in a casino are fair. This publication can be purchased in packs of 100 by visiting www.americangaming.org/files/aga/uploads/docs/rgew/odds_brochure_2011_final.pdf.

Taking the Mystery Out of the Machine: A Guide to Understanding Slot Machines

While a significant majority of gamblers say slot machines are their favorite form of casino entertainment, most people know very little about how slots are developed or how they work. Since educating employees and patrons about the odds of casino games and how they work is a key priority of the gaming industry and an important part of responsible gaming, the AGA developed "Taking the Mystery Out of the Machine: A Guide to Understanding Slot Machines." The brochure provides digestible information about how slots are operated, developed and regulated and uses common language to debunk many players' most widely held myths about slot machines. The resource has been made available to patrons and employees as an important part of many casinos' standard responsible gaming education efforts. To download a free copy of the brochure, visit www.americangaming.org/files/aga/uploads/docs/taking_the_mystery_out_of_the_machine_brochure_final.pdf.

ABOUT THE NCRG

The National Center for Responsible Gaming (NCRG) is the only national organization exclusively devoted to public education and funding research that will help increase understanding of pathological and youth gambling and find effective methods of treatment for the disorder. The NCRG is the American Gaming Association's (AGA) affiliated charity.

Founded in 1996 as a separate 501(c)3 charitable organization, the NCRG's mission is to help individuals and families affected by gambling disorders by supporting the finest peer-reviewed, scientific research into pathological and youth gambling; encouraging the application of new research findings to improve prevention, diagnostic, intervention and treatment strategies; and advancing public education about gambling disorders and responsible gaming.

More than $22 million has been committed to the NCRG through contributions from the casino gaming industry, equipment manufacturers, vendors, related organizations and individuals. Since its founding, the NCRG has mandated stringent firewalls to separate the gaming industry's contributions from the research it funds.

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