

Gambling Dual Disorder: The Rule, Not the Exception

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Faculty Disclosure: Nestor Szerman



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AGENDA

A Roadmap to Understanding and Advancing Care in GDD

01



Gambling Dual Disorder Concept

Definition, scope, and why it matters

02



The Neurobiological Basis of GDD

Brain mechanisms and vulnerability pathways

03



Precision Psychiatry and GDD

Toward personalized assessment and care

04



How to treat GDD

Integrated, multimodal and evidence-informed approaches

05



Conclusions

Key takeaways and future directions



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Part 1: Gambling Dual Disorder (GDD) Concept

*Understanding the intersection of gambling
and other mental health or substance
use disorders.*



FOCUS

Define GDD and
its key components.



PURPOSE

Improve recognition,
assessment, and integrated care.



OUTCOME

Build a shared foundation
for effective treatment.



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THE GAMBLING DUAL DISORDER CONCEPT



From an **EVOLUTIONARY PERSPECTIVE** on mental functioning, **GAMBLING** can be conceptualized as a widespread and historically recurrent human behavior, rooted in cognitive mechanisms related to risk-taking, reward processing, and uncertainty management.



Across cultures and time periods, gambling-like activities have served recreational, social, and adaptive functions, suggesting that **such behaviors may reflect inherent features of the human condition** rather than pathological tendencies.



Most people (70–90%) gamble at some point in their lives, without negative consequences^{**}, ^{***}



^{**} Yan-Hua Xuan et al. Genetic and Environmental influences on Gambling: A Meta-Analysis of twin studies. *Frontiers in Psychology* 2017.

^{***} Potenza MN, Balodis IM, Derevensky J, Grant JE, Petry NM, Verdejo-Garcia A, Yip SW. Gambling disorder. *Nat Rev Dis Primers*. 2019 Jul 25;5(1):51.

Evolutionary Psychiatry Perspective

The Origins of Gambling:

A Window into Human Behavior and Adaptation



Gambling, an activity involving risk, reward, and chance, has been part of human culture across all social classes for centuries.



In the Czech Lands, as early as 1353, the Prague archbishop Arnošt of Pardubice is known to have tried to repress gambling.



The most common games in our territory were based on German-suited playing cards (i.e. with suits of Hearts, Bells, Leaves, and Acorns).



From ancient gambling practices to modern behaviors, *understanding our evolutionary past helps illuminate the neural roots of risk, reward, and decision-making.*



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Gambling Dual Disorder Concept



- Only in some **VULNERABLE PEOPLE** does gambling become a **MENTAL DISORDER** with addictive characteristics.



- This occurs when **GAMBLING** is no longer just recreational and has a negative impact on family, emotional, economic, and academic relationships, as well as behavioural consequences."



- In **some cases**, the impact on individuals is as severe as other serious Mental Disorders."



Szerman N. et al. *Gambling Dual Disorders* Frontiers, 2021. *Yan-Hua Xuan et al. Genetic and Environmental influences on Gambling: A Meta-Analysis of twin studies. *Frontiers in Psychology* 2017. **Potenza MN et al. *Gambling Disorder*. *Nature Reviews. Disease Primers* 2019. 51: 1-21

Gambling Disorder: Dimensional Vision



GAMBLING Behaviour should not be classified as **ADDICTIVE** on the basis of type, frequency, or amount, but rather based on whether the behaviour has a **negative impact** on different areas of the person's life.

THE GAMBLING CONTINUUM



Terms that lie on a continuum, where “gambling addiction” is at one end of the scale and “problem gambling” is a concerning **CONDITION** but may not lead to problems in **all** areas of a person's life.



Griffiths, M. D., Kuss, D. J., Pontes, H. M., & Billieux, J. (2016). Where do gambling and Internet 'addictions' belong? The status of 'other' addictions. In K. Wolff, J. White, & S. Karch (Eds.), *The SAGE Handbook of Drug & Alcohol Studies Biological Approaches* (pp. 446–470). London: SAGE Publications Ltd.



Latent class analysis of gambling subtypes

This analysis was conducted on a non-clinical population of **frequent gamblers**, with the following objectives:*



Analysis of 582 non-treatment-seeking young adults (recruited from 2 US cities) who gambled at least five times in the past year.



(i) **Identify distinct gambling subtypes** using latent class analysis of SCI-GD item responses



(ii) **Examine associations** between these subtypes and clinical and cognitive measures



Three groups emerged:



Recreational gamblers
60.2%



Lower levels of gambling severity, impulsivity, and associated problems



Problem gamblers
29.2%



Moderate levels of gambling-related problems and impulsivity



Pathological gamblers
10.5%



Highest levels of gambling severity, impulsivity, and functional impairment



Chamberlain SR, Stochl J, Redden SA, Odlaug BL, Grant JE. Latent class analysis of gambling subtypes and impulsive/compulsive associations: Addictive Behaviors. 2017;72:79–85.

*Objectives adapted from the study.

Epidemiology of Gambling Dual Disorder



Epidemiological studies show that **Gambling Disorder** frequently co-occurs with other mental disorders (dual disorders).



In people with **GAMBLING DISORDER**, the prevalence of any **OTHER PSYCHIATRIC DISORDER** during the lifespan was

96.3%*



REGARDLESS OF PSYCHOTIC DISORDERS or PERSONALITY TRAITS.*



Prevalence of GD in psychiatric inpatients

6.9%**

* Kessler, R. C. et al. DSM-IV pathological gambling in the National Comorbidity Survey Replication. *Psychol. Med.* 38, 1351–1360 (2008).

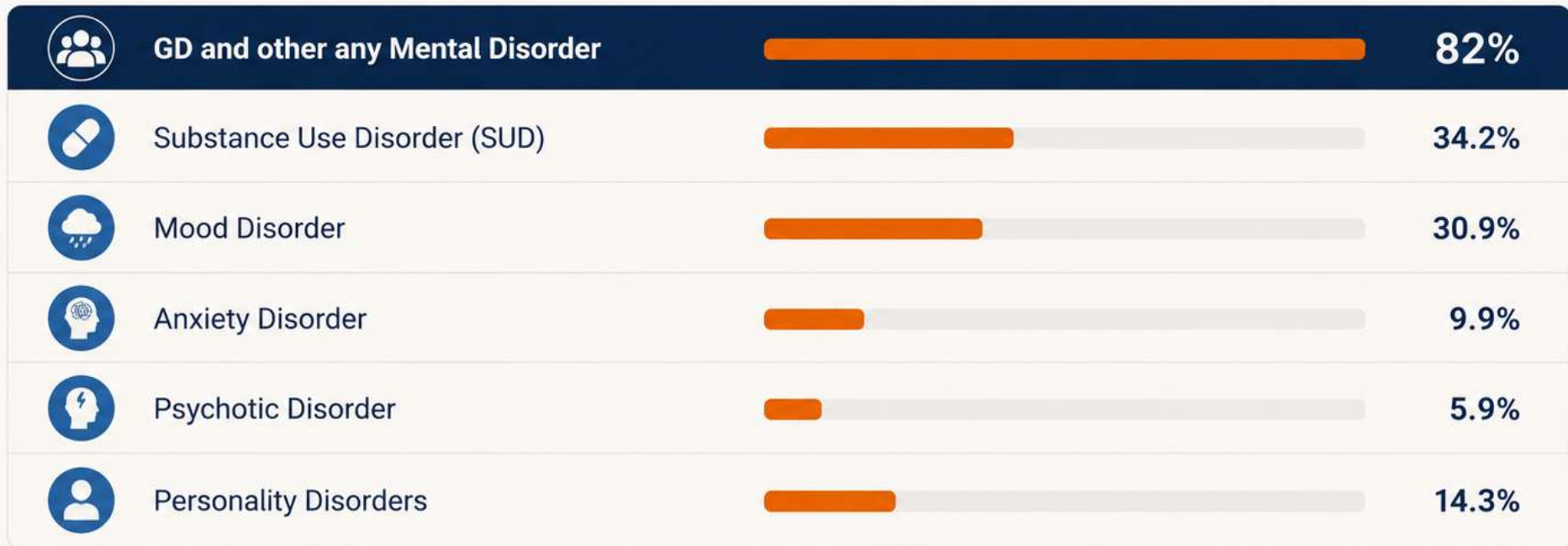
** Cowlshaw, S. & Hakes, J. K. Pathological and problem gambling in substance use treatment: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Am. J. Addict.* 24, 467–474 (2015).





Epidemiology of Gambling Dual Disorder*

People with Gambling Disorder (GD) are at high risk for other mental disorders.



* Galeazzi GM et al. Psychiatric morbidity and gambling disorder:
A systematic review and meta-analysis of population-based surveys
Eur Psychiatry 2025.



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Epidemiology of Gambling Dual Disorder

CONDITION	PREVALENCE	REFERENCE
 ADHD	50%	Szerman N. et al, European Neuropsychopharmacology, 2023
 Impulsivity Traits	71–85%	Ioannidis K, et al. Impulsivity in Gambling Disorder and problem gambling: a meta-analysis. Neuropsychopharmacology. 2019
 Anti-Social Personality Disorder	28.8%	Lorains FK et al Prevalence of comorbid disorders in problem and pathological gambling: systematic review and meta-analysis of population surveys. Addiction. 2011 Mar;106(3):490-8.



European Neuropsychopharmacology 66 (2023) 78-91

Available online at: www.elsevier.com/locate/euroneuro



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

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Beatriz Mesías^c, José Martínez-Raga^d, Francisco Ferre^e,
Celso Arango^e



Check for updates



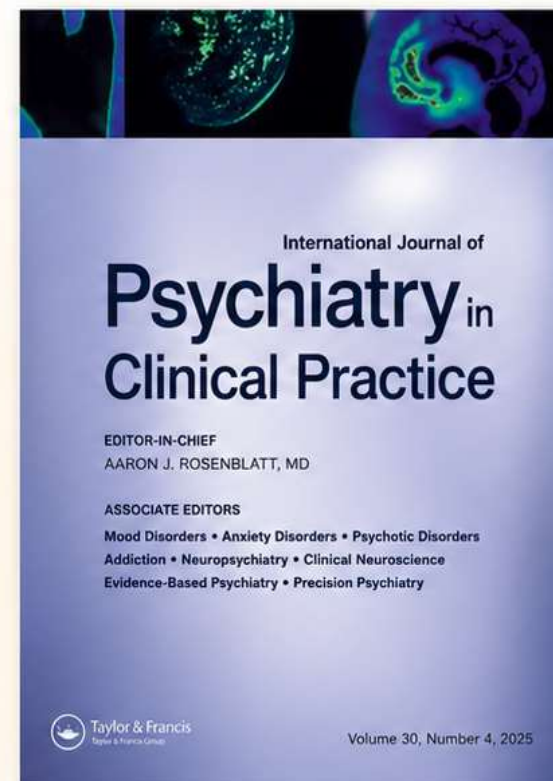
REVIEW ARTICLE

Evidence-based prevention of gambling dual disorder through clinical neuroscience and precision psychiatry



Szerman, N., Ferre, F., Pal Singh Balhara, Y., Waisman, M., Danon, P., Vega, P., ... Baler, R. (2026).

Evidence-based prevention of gambling dual disorder through clinical neuroscience and precision psychiatry.
International Journal of Psychiatry in Clinical Practice, 1–11.



Integrating clinical neuroscience and precision psychiatry to advance prevention strategies in gambling dual disorder.



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International Journal of Methods in Psychiatric Research



ORIGINAL ARTICLE



OPEN ACCESS

Building a Brief Multidomain Questionnaire for Gambling Dual Disorder: Psychometric Validation and RDoC-Based Dimensional Structure



Ignacio Basurte-Villamor | Ismael Gomez-Talal | Pablo Vega | Mana Azizsoltani
Javier Gonzalez-Peñas | Francisco Ferre | Nestor Szerman

Why coin the term “gambling dual disorder”?



1. Clarifies our intention

- We don't intend to include this term as a **new diagnostic category**.



2. Supports clinical practice

- This term is useful in clinical practice to help experts remember to identify **other mental disorders, symptoms or personality traits** that co-occur with Gambling Disorder and require comprehensive treatment.



3. Reflects the current understanding

- We also think it's important to keep in mind that there is likely a shared biological basis for the GD and the other mental disorder.



IMPULSIVITY TRAITS in GDD



We need to consider the centrality of impulsivity to neurobiological models of GDD.
Impulsivity as a **core dimensional trait** of GDD, not merely a symptom.

GAMBLING DISORDER WAS ASSOCIATED WITH SIGNIFICANT IMPAIRMENTS IN IMPULSIVITY



Motor

$g = 0.39-0.48$

Difficulties in motor response control and speed regulation.



Attentional

$g = 0.55$

Problems sustaining attention and resisting distraction.



Inhibition, discounting

$g = 0.66$

Higher impulsive choices and discounting of delayed rewards.



Decision-making

$g = 0.63$

Deficits in evaluating options and making adaptive decisions.



PROBLEM GAMBLING:

Significant impairment versus controls only in

DECISION-MAKING

($g = 0.66$)

- Ioannidis K et al. Impulsivity in Gambling Disorder and problem gambling: a meta-analysis. *Neuropsychopharmacology*. 2019 Jul;44(8):1354–1361. doi: 10.1038/s41386-019-0393-9.
- Mallard TT, et al. Characterizing the Pleiotropic Architecture of Impulsivity and Its Links to Psychopathology and Neurodevelopment. *Am J Psychiatry*. 2025 Oct 29.

Developing a New Paradigm Dual Disorders VULNERABILITY



CLASSIC PARADIGM

“Addiction depends on frequent and intense exposure to substances or situations such as gambling.”



NEW PARADIGM

“Based on individual vulnerability. People with other mental disorders.”



Groups at highest risk



Adolescents and
young adults



Cognitive
impairment



Chronic



Homelessness



Understanding vulnerability
helps us prevent, identify
and treat more effectively.

Part 2:

The Neurobiological Basis of GDD

Understanding the brain mechanisms underlying dual disorders: gambling and other mental disorder.



Brain
Mechanisms



Neurotransmitter
Systems



Neuroplasticity
& Adaptation



Is Gambling Disorder a Behavioural Problem or a Mental Disorder?



> **VICE?**



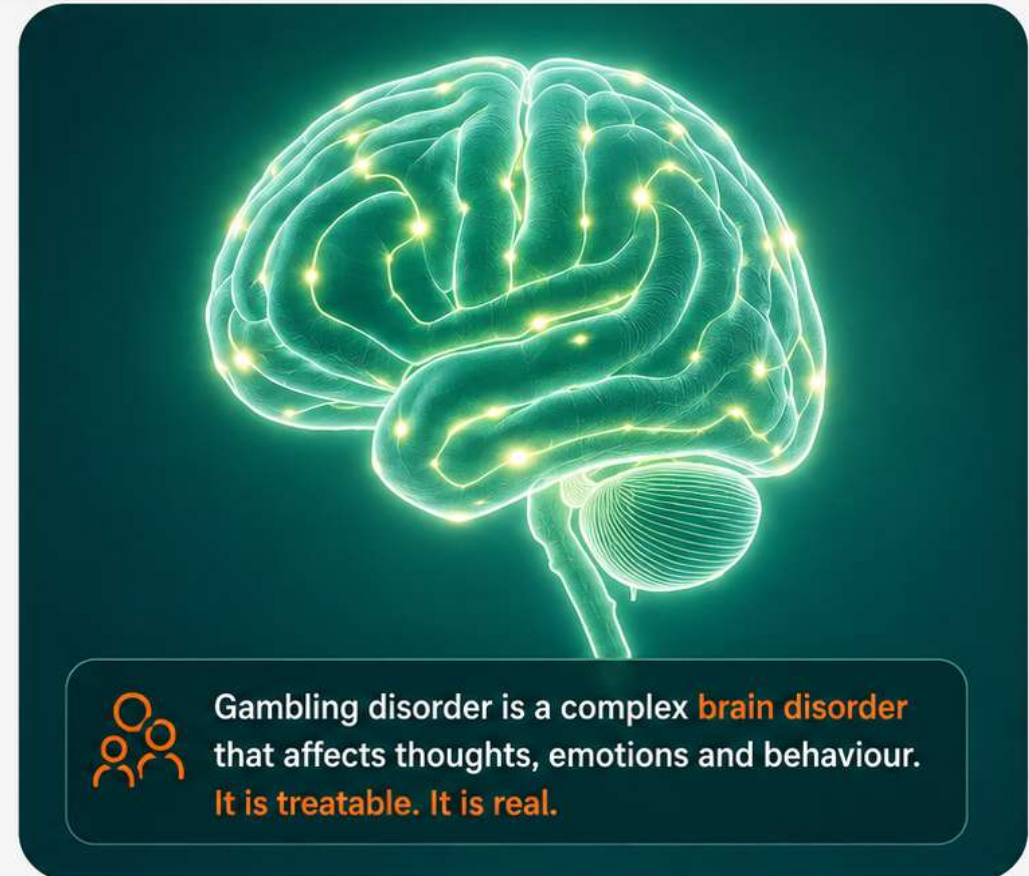
> **PEOPLE WITH WEAK CHARACTERS WHO ALLOW THEMSELVES TO BE TRAPPED BY GAMBLING OFFERS?**



> **LACK OF WILLPOWER? SELF-INDULGENCE?**



> **CHANGES IN BRAIN NEUROPLASTICITY CAUSED BY SPENDING TOO MUCH TIME GAMBLING?**



Gambling disorder is a complex **brain disorder** that affects thoughts, emotions and behaviour. **It is treatable. It is real.**

Szerman et al. 2025 under review *International Journal of Psychiatry in Clinical Practice*



National Institutes of Health
Turning Discovery Into Health



INTRODUCING THE BRAIN AT MENTAL HEALTH DISORDERS:

According to the Scientific Community



MENTAL FUNCTIONS ARE BASED ON THE BRAIN.



**MENTAL DYSFUNCTIONS (DISORDERS) ARE
BRAIN DISORDERS.**



They involve brain circuits that support specific
functions of **COGNITION, EMOTION** and **BEHAVIOUR***.



* Cuthbert BN. Research domain criteria: toward future psychiatric nosologies. *Dialogues clin neurosci* (2015).

*** Volkow ND, Boyle M. Neuroscience of addiction: Relevance to prevention and treatment. *Am J Psychiatry* (2018).

*** Kruss DJ, Pontes HM and Griffiths MD (2018) Neurobiological Correlates in Internet Gaming Disorder: A Systematic Literature Review. *Front. Psychiatry* 2018.



HIGH RISK FOR DUAL DISORDERS

“ The factors that determine the risk for most psychiatric disorders (including **Gambling Disorder**) are

PRESENT EARLY IN LIFE



EVEN THOUGH the symptoms of these disorders may not emerge until **later childhood, adolescence, or adulthood.**”



Early-life adversity
and genetics



Increase vulnerability
across development



Contribute to risk for
psychiatric disorders



Include Gambling
Disorder

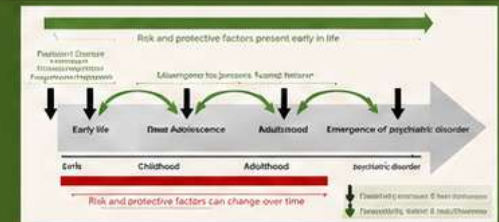


*Kalin NH. Early-life Adversity and Genetics Associated With the Risk to Develop Psychiatric Illnesses. *Am J Psychiatry*. 2023 Aug 1;180(8):525-527.



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The American Journal of Psychiatry



The Devastating Clinical Consequences of Child Abuse
Recalcitrant Agitation in the Psychiatric Setting:
Results From the STAND OUT Study

Overview of Alcohol Use Disorder

A Comprehensive Multilevel Analysis of the Pathways
Linking Internalizing Problems and Suicide in Adolescents

Prenatal Stress Exposure

Causes Underpinning of the Transition From
At-Risk Consumption to Alcohol Use Disorder

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GENETIC Basis of GDD*

Genes shape **risk**, not disorders.



1. GDD is a **HERITABLE** neurodevelopmental condition

and reflects vulnerability rather than gambling specific traits.



2. Genetic risk is highly polygenic (GWAS)

influencing **impulsivity, reward sensitivity, risk taking and neurodevelopmental externalizing traits** that contribute to both gambling disorder and other psychiatric disorders (Gambling Dual Disorders).



3. Environmental exposures

modulate expression, but genetic liability is a major component.



- Lang, M., et al. (2016). Pathological gambling, disordered gambling and genetic association studies: A systematic review. *Addiction Biology*, 22(6), 1610–1626.
- Ioannidis K. et al. (2024). Genetic and neurobiological mechanisms of behavioral addictions.
- Hatoum A.S. et al. (2022). GWAS of risk tolerance and externalizing traits.

*GDD = Gambling Dual Disorder

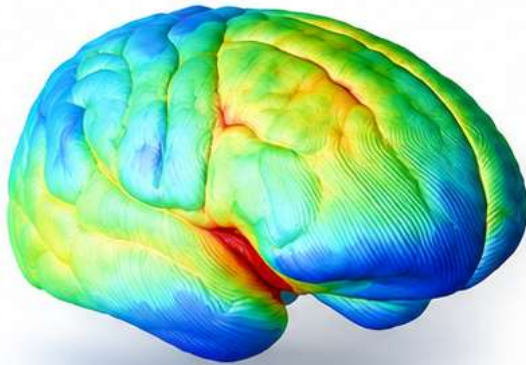
Adolescent Brain and Cognitive Development (ABCD) Study

NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, OBSSR, NINDS

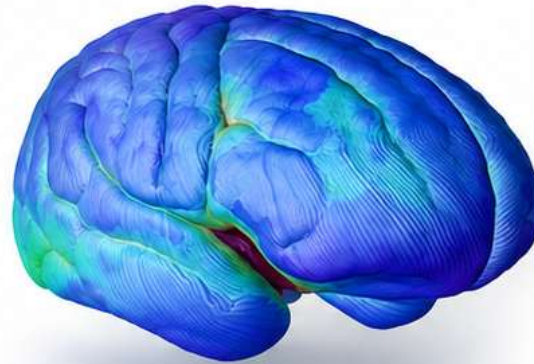


Ten-year longitudinal study of **10,000 children** from **10 to 20 years** to assess effects of drugs (including nicotine, marijuana and alcohol) on individual brain development trajectories and functional outcomes

EARLY ADOLESCENCE (≈10 YEARS)



LATE ADOLESCENCE (≈20 YEARS)



UNDERSTANDING TODAY. IMPROVING TOMORROW.



SEPD



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Research from the Adolescent Brain Cognitive Development (ABCD) Study*

The ABCD study confirmed that highly vulnerable children exhibited early changes in brain structure **before the first contact with any psychoactive substance.**



Structural and functional changes in key brain regions involved in **reward processing**, **impulse control**, and **emotional regulation** are linked to earlier **substance use**.

KEY FINDINGS



1 Altered Volume in Reward-Related Regions

Vulnerable youth show altered brain volume in regions involved in reward processing, including the striatum.



2 Differences in Prefrontal Cortex Maturation

Earlier or delayed maturation of the prefrontal cortex is associated with higher risk of earlier substance use.



3 Stronger Reward Sensitivity and Weaker Cognitive Control

Youth show greater sensitivity to rewards and reduced ability to regulate impulses.



4 Environmental & Genetic Moderators

Family environment, stress, and genetic risk factors can amplify or buffer these brain-related effects.



References

- Chaarani, B., et al. (2019). Baseline brain structure and function predict future substance use in adolescents: *The ABCD Study*. *Nature Neuroscience*, 22, 1793–1804.
- Owens, M. M., et al. (2020). Neuroanatomical correlates of early experimentation with cigarettes and e-cigarettes in the ABCD Study. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 5(7), 636–645.



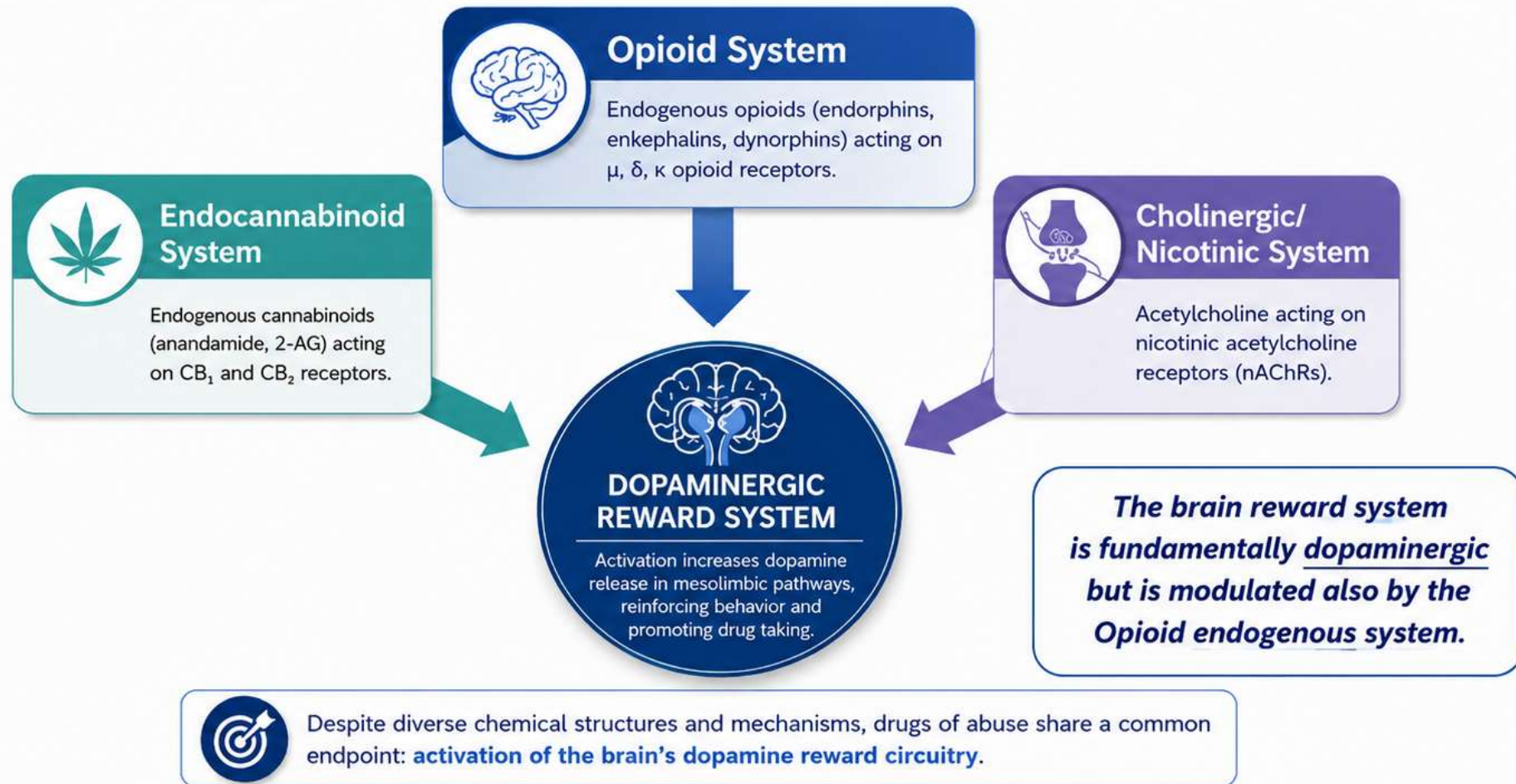
SEPD



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All psychoactive substances with abuse potential bind to some endogenous systems

**Szerman et al, ADTT, 2013*



SEPD



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The role of the opioid system in decision making and cognitive control: A review

Henk van Steenbergen^{1,2} • Marie Eikemo^{3,4} • Siri Leknes⁴



KEY TAKEAWAY

This review proposes that opioids influence decision making and cognitive control by **increasing the subjective value of reward** and **reducing aversive arousal**.



WHAT THIS MEANS

The authors highlight potential mechanisms that might underlie the effects of **mu-opioid signaling** on decision making and cognitive control.

The Endogenous Opioid System regulates dopamine release in the mesolimbic pathway*



Critical role in reward, craving, impulsivity, and compulsive gambling

The Endogenous Opioid System is increasingly recognized as a key modulator of reward processing, craving, impulsivity, and compulsive gambling behavior.



Strong evidence for opioid antagonists

Neuroimaging studies and pharmacological trials show that opioid antagonists—particularly naltrexone and nalmefene—reduce gambling urges.



Current standard of pharmacological care

Opioid antagonists currently represent the most supported pharmacological approach for the treatment of Gambling Disorder.



* Ioannidis K, Del Giovane C, Tzagarakis C, Solly JE, Westwood SJ, Parlatini V, Bowden-Jones H, Grant JE, Cortese S, Chamberlain SR. Pharmacological management of gambling disorder: A systematic review and network meta-analysis. *Compr Psychiatry*. 2025 Feb;137:152566.

Gambling Disorder and Other Mental Disorders Involve Multiple Factors



Genes, Brain Circuits & Development

- Genetic predisposition
- Neurodevelopmental processes
- Brain structure and function
- Early life experiences



Mental Disorders



Drugs–Gambling



Dual Disorders



Environment

- Family relationships
- Peer influence
- School & work
- Socioeconomic factors
- Culture & community



Understanding the interplay of biological, psychological, and environmental factors is key to prevention, treatment, and better outcomes.

PART 3

ADVANCING KNOWLEDGE
FOR BETTER OUTCOMES



Precision Psychiatry and GDD

Integrating precision approaches to improve outcomes in dual disorders



Szerman N, Peris L.

Precision Psychiatry and Dual Disorders.

Journal of Dual Diagnosis. 2018;14(4):237–246.



Journal of Dual Diagnosis

Research and Practice in Substance Abuse Comorbidity

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Precision Psychiatry and Dual Disorders

Nestor Szerman & Lola Peris



www.patologiadual.sepdlab.org



@patologia_dual

Working together
for **better outcomes.**

Precision Psychiatry and Gambling Dual Disorder



Gambling is **especially rewarding** for vulnerable people, **more than** for others, because the effect on the brain is different.



* Szerman & Peris. *Precision Psychiatry and Dual Disorders*. JDD 2018



Precision Psychiatry and Gambling Dual Disorder*



Social acceptance and environments bring people into contact with Gambling (or substances).



Individual factors, genetics, neurobiology and personality traits determine **vulnerability to or resilience against** developing addictive disorders and other mental disorders.

* Yakovenko I and Hodgins DC. A scoping review of comorbidity in individuals with disordered gambling. *International Gambling studies* 2018 vol18; 1: 143-172

Sex Differences in Gambling Dual Disorder

(Precision Psychiatry and Dual Disorders)



PREVALENCE

Men show higher GD prevalence than women. The ratio of males to females with GD is estimated to be anywhere from 3:1 to 9:1.



CLINICAL PATTERNS: DIFFERENT PHENOTYPES

- **Women:** Later onset; higher rates of **Affective disorder**.
- **Men:** Earlier onset; higher **impulsivity, ADHD, ASPD,** and SUD.



IMPLICATION

GD presents differently across sexes, highlighting the need for sex-specific screening, prevention, and treatment strategies.



References

- Merkouris, S. S. et al. (2016). Gender differences in gambling disorder. *Journal of Gambling Studies*, 32, 1001–1014.
- Wong, G., & Zane, N. (2015). Gender differences in gambling behavior and treatment-seeking. *Journal of Gambling Studies*, 31(3), 703–715.
- Blanco C, et al. Sex differences in subclinical and DSM-IV pathological gambling: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol Med*. 2006 Jul;36(7):943–53.



Recognizing sex differences improves outcomes in precision care for individuals with gambling dual disorders.

Part 4:

How to treat GDD





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Dual Disorders Treatment

Comparing Treatment Models for Co-occurring Mental Illness and Substance Use Disorder



Sequential Model

Patient is offered treatment for either GD or other MD.

- ✗ Separate services sequentially and independently treat GD and other MD
- ✗ Treatment delays, decreased motivations and poorer outcomes.



Parallel Model

Patient receives concurrent treatment for both GD and the MD.

- ✗ Treatment provided by different services.
- ✗ Probable coordination problems and patient drop out.



Integrated Model

The patient benefits from a broader and collaborative approach.

- ✓ Single treatment plan.
- ✓ Multidisciplinary management and follow-up.
- ✓ Enhances continuity of support and improves outcomes.



Kikkert M., et al. (2018). Effectiveness of Integrated Dual Diagnosis Treatment (IDDT) in severe mental illness outpatients with a co-occurring substance use disorder. *Journal of Substance Abuse Treatment*, 95, 35–42.

Treating Gambling Dual Disorder



Before treatment planning can commence, a **comprehensive assessment** is essential.



Psychiatrists need to determine whether the patient has another psychiatric disorder (**DUAL DISORDER**), which is more the rule than the exception.



The **Dual Disorders** perspective involves a **bio-psycho-social approach**.



Treatment should be biological, psychological, and social, **in that order**.



*Jon E Grant. Special Report: Gambling Disorder Not Uncommon but Often Goes Undiagnosed. (2022) Psychiatric News Volume 57, Number 4. <https://doi.org/10.1176/appi.pn.2022.04.4>.



An integrated, patient-centered approach is key to **better outcomes** and long-term recovery.

Precision Psychiatry for GDD Pharmacological Treatment



- ▶ A promising strategy explores the use of **Pharmacotherapies** that target **endophenotypes** associated with **Gambling addiction**.



Using **cognitive enhancers** to improve **impulse control**, **planning**, and **decision making**.



Using **medications** to reduce **stress reactivity** and **dysphoria** to prevent relapses.



Volkow ND, Am J of Psychiatry. NEUROSCIENCE of ADDICTION. 2018

Dual Disorders may help guide Medication selection in treatment



Dual Disorders may help **guide medication selection** in treatment.



Treatment should be not only for GD, but for the **other mental disorders** (ADHD, impulsivity etc).



KEY GAPS REMAIN:



Exploring different gambling subtypes and treatment responses



Explaining high placebo response rates



Lack of longer-term longitudinal information



Limited investigation of neurobiological correlates and dual disorders

COMPREHENSIVE TREATMENT: A MULTIDISCIPLINARY APPROACH



Psychotherapy (CBT, MI, ACT)

Build coping skills, address thinking patterns and improve self-regulation.



Psychosocial Support (e.g., support groups, family involvement)

Enhance motivation, reduce isolation and strengthen recovery networks.



Lifestyle Interventions (physical activity, sleep, nutrition)

Improve mental health, reduce cravings and support overall well-being.



Integrated Care (coordinated, multidisciplinary)

Address co-occurring conditions together for better outcomes.



Mestre-Bach, G., & Potenza, M. N. (2024). Pharmacological management of gambling disorder: an update of the literature. *Expert Review of Neurotherapeutics*, 24(4), 391–407.



Treatment should be individualized, addressing the full spectrum of needs in dual disorders. **Think broader. Treat the whole person.**

Pharmacological Treatment of Gambling Disorder

Cochrane Database Syst Rev 2022



Opioid Antagonists (e.g., naltrexone, nalmefene)

May reduce gambling severity and urge to gamble.



Overall Evidence Quality

Evidence is small, heterogeneous, and often low or very low quality.
Many studies had small sample sizes, short treatment durations, and risk of bias.



Side Effects

Were typically mild to moderate, including nausea, fatigue, and headache.



Conclusion

Possible benefit, but evidence remains uncertain and not strong enough for definitive recommendations.

* Dowling N, et al. Pharmacological interventions for the treatment of disordered and problem gambling. Cochrane Database Syst Rev. 2022 Sep 22;9(9).

Pharmacological Management of Gambling Disorder

A Systematic Review and Network Meta-Analysis*



KEY TAKEAWAY: Moderate-certainty evidence shows that **opioid antagonists** (nalmefene, naltrexone) reduce gambling disorder symptoms more than placebo, but are associated with **higher dropout rates**.



GAMBLING SEVERITY

✓ SIGNIFICANTLY REDUCED

Nalmefene demonstrated greater efficacy than placebo, followed by naltrexone.

Treatment	Effect vs. Placebo (SMD)	95% CI
• Nalmefene	−0.86	−1.32 to −0.41
• Naltrexone	−0.42	−0.85 to 0.01



DROPOUT RATES

HIGHER

Both nalmefene and naltrexone were associated with **significantly higher dropout rates than placebo** due to side effects.

Treatment	Odds Ratio (OR)	95% CI
• Nalmefene	7.55	2.24 to 25.41
• Naltrexone	7.82	1.26 to 48.70



QUALITY OF LIFE

GREATER BENEFIT

In terms of quality of life, naltrexone and nalmefene demonstrated **greater benefit than placebo**.

Treatment	Effect vs. Placebo (SMD)	95% CI
• Naltrexone	−0.50	−0.85 to −0.14

Treatment	Effect vs. Placebo (SMD)	95% CI
• Nalmefene	−0.36	−0.72 to −0.01



Olanzapine and topiramate **did not** show greater efficacy than placebo.

* Ioannidis K, et al. *Comprehensive Psychiatry*. 2025;137:152566.

NALMEFENE ON IMPULSIVITY*



Nalmefene (like Naltrexone) can be prescribed to patients with AUD and, off label, for Gambling Disorder



A single dose impacts “resting-state functional connectivity” (rsFC) and alters the interaction between key nodes of addiction-related neural systems



The effects go beyond AUD

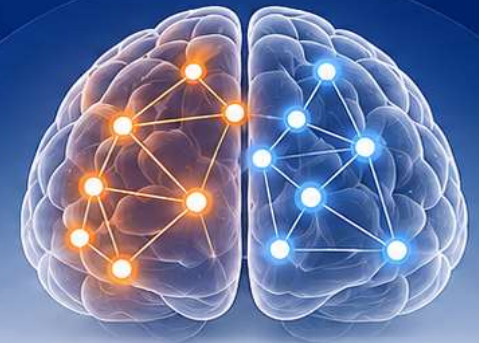


NALMEFENE may normalize rsFC patterns by weakening the **IMPULSIVE SYSTEM** while strengthening the **reflective system**.



*Grundinger N, et al. The effects of nalmefene on the impulsive and reflective system in alcohol use disorder: A resting-state fMRI study. Psychopharmacology (Berl). 2022 Aug;239(8):2471-2489. doi: 10.1007/s00213-022-06137-1. Epub 2022 Apr 15.

**Modulating brain networks.
Improving outcomes.**



— **IMPULSIVE SYSTEM**

Weakened by nalmefene

— **REFLECTIVE SYSTEM**

Strengthened by nalmefene



High Impulsivity Predicts Treatment Response in GDD: *Precision Psychiatry in Treatment*



STUDY DESIGN

Data were pooled from two prior randomized, placebo-controlled pharmacological trials investigating Naltrexone and N-acetylcysteine.



KEY FINDINGS

- Trait impulsivity **significantly accounted** for variability in medication treatment response ($P = 0.026$, $R^2 = 0.26$).
- Greater baseline motor impulsivity was associated with a **stronger treatment response** ($P = 0.009$).



IMPLICATION



Impulsivity, particularly motor impulsivity, may serve as a valuable predictor to guide **personalized treatment strategies** in GDD.



Chamberlain SR, Ionnidis K, Grant JE. *Clinical Neuropharmacology* (2025) 48(9806)

Volume 48 • Number 5 • September–October 2025

Clinical Neuropharmacology

www.clinicalneuropharm.com Full Text
OVID



Wolters Kluwer

GAMBLING DISORDER (GD) AND ADHD:

Shared Mechanisms, Increased Vulnerability, Targeted Treatment



CORE LINK

GD and ADHD share key features: **impulsivity, impaired attention regulation, and increased risk-taking.**



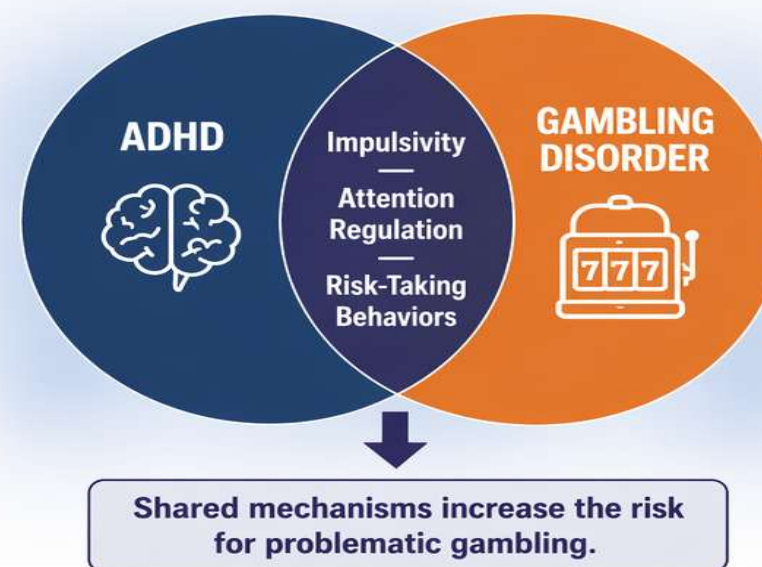
CLINICAL IMPLICATION

This overlap increases vulnerability to **loss of control over gambling behavior.**



TREATMENT APPROACH

- **Pharmacological treatment**
 - **ADHD: Stimulants** (e.g., methylphenidate, amphetamines) or non-stimulants (e.g., atomoxetine, guanfacine)
 - **Gambling Disorder:** Opioid antagonists (e.g., naltrexone, nalmefene)
- **Behavioral interventions**
 - Impulse control training
 - Decision-making skills
 - Cognitive-behavioral strategies



KEY TAKEAWAY

ADHD-related impulsivity significantly contributes to the development and persistence of Gambling Disorder.



REFERENCES

- Grall-Bronnec, M., et al. (2011). Attention deficit hyperactivity disorder among pathological and at-risk gamblers seeking treatment. *Journal of Attention Disorders*, 15(8), 654–662.
- Romo, L., et al. (2015). Gambling disorders and ADHD: Shared vulnerabilities and clinical implications. *Current Addiction Reports*, 2, 267–273.

ADHD + Gambling Dual Disorder

A Precision Psychiatry Approach



EVIDENCE GAP

Very few published studies have tested:

- **ADHD stimulants** (methylphenidate / lisdexamfetamine)
- + **Opioid antagonists**

in people with **both ADHD and gambling disorder**.



CURRENT EVIDENCE

- ✓ Case reports
- ✓ Small clinical studies / observations
- ✓ Pharmacology and interaction data

⚠ **No large** randomized controlled trials (RCTs)



STEPWISE TREATMENT APPROACH

1



START ADHD MEDICATION

Gradual titration over ~3 weeks

2



EVALUATE RESPONSE

- ADHD symptoms
- Impulsivity
- Gambling behavior

3



ADD OPIOID ANTAGONIST

- If response is inadequate
- Introduce and titrate over an additional ~3 weeks



CLINICAL RATIONALE

Opioid antagonists (e.g., naltrexone) may:

- ✓ Reduce reward-seeking and gambling-related behaviors
- ✓ Mitigate stimulant-induced euphoria



KEY TAKEAWAY:

Treat ADHD first, then layer targeted anti-reward therapy if needed.

Spencer TJ, et al.

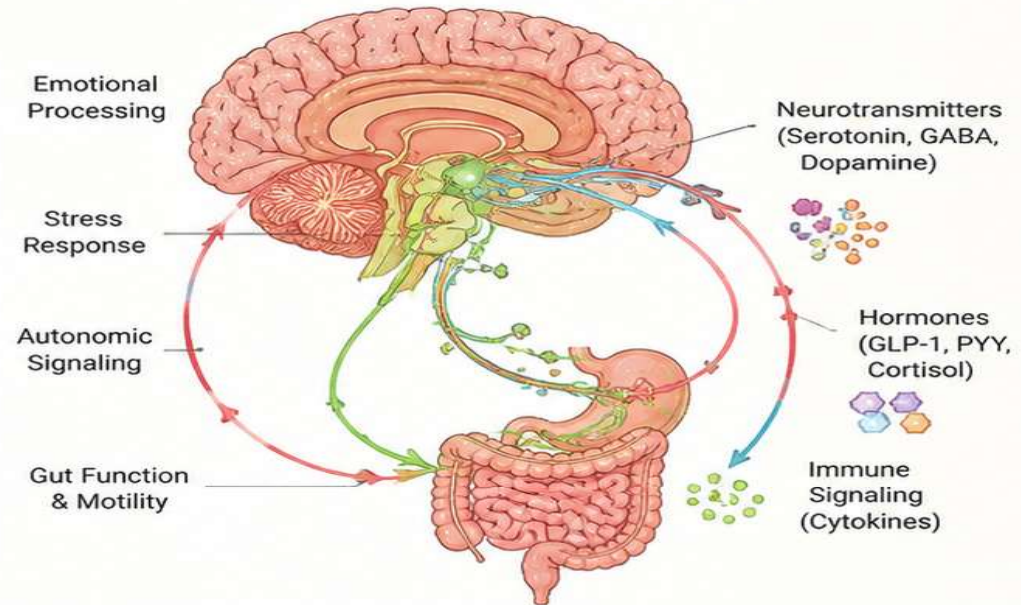
J Clin Psychiatry. 2018;79(2):7m11609.

The GLP-1 Frontier in Psychiatry

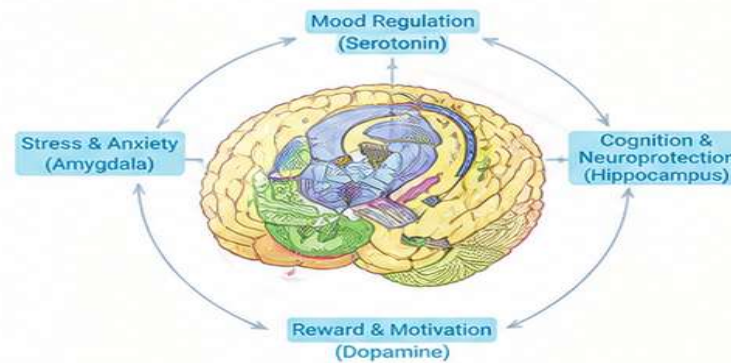
Gut-Brain Revolution in Mental Health



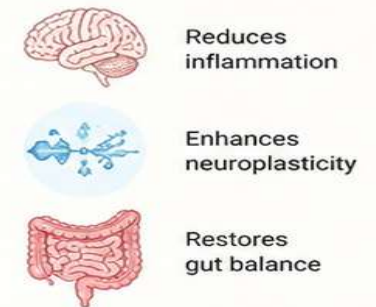
The Brain–Gut Axis A Bidirectional Superhighway



GLP-1: The Multi-System Modulator



GLP-1 in Action



GLP-1 RECEPTOR AGONISTS FOR GDD



- Emerging evidence suggests that **GLP-1 receptor agonists** may have **therapeutic potential** for **Gambling Disorder**, due to their modulation of brain **reward pathways**.



- However, direct randomized trials for **gambling disorder** are still lacking.



- **Arillotta 2024; Klausen 2022; Moosa-Batthey 2025** are the strongest sources for this statement.



GLP-1 receptor agonists represent a promising avenue for GDD, but **high-quality randomized controlled trials** are urgently needed.



Response of Gambling Disorder to Semaglutide

Grant, Jon E. JD, MD, MPH¹; Chamberlain, Samuel R. MB/BChir PhD, MRCPsych^{2,3}



BACKGROUND

- Gambling disorder (GD) is a chronic, relapsing condition with limited pharmacological treatment options.
- GLP-1 receptor agonists, such as semaglutide, have shown promise in substance use disorders and may modulate reward circuitry.
- We report the observation of marked improvement in GD symptoms in a patient treated with semaglutide for obesity.



GLP-1 receptor agonists may modulate reward pathways implicated in GD.



CLINICAL OBSERVATION

- A middle-aged man with a longstanding history of GD and obesity was initiated on semaglutide for weight management.
- Within weeks, he reported a marked reduction in urge to gamble, fewer gambling episodes, and improved control.
- These benefits persisted over several months of treatment.



PATIENT OUTCOMES

Outcome Measure	Baseline	3 Months on Semaglutide
Gambling Urge (VAS 0–10)	9	2
Gambling Episodes (per week)	5–7	0–1
Money Spent Gambling (per week)	>\$1,000	\$0–50
PGSI Score (0–27)	19 (Moderate–Severe)	5 (Mild)



This observation suggests that semaglutide may reduce gambling-related thoughts and behaviors.



KEY POINTS

- ✓ This is an observational report and not proof of efficacy.
- ✓ GLP-1 receptor agonists may influence neural circuits involved in reward, impulse control, and decision-making.
- ✓ Further research is needed to evaluate the efficacy and safety of semaglutide for gambling disorder.
- ✓ This case adds to emerging evidence supporting GLP-1R agonists as a promising therapeutic avenue in addiction and impulse-control disorders.



CONCLUSION

Semaglutide may represent a novel treatment approach for gambling disorder. Controlled studies are warranted to confirm these findings and understand underlying mechanisms.



Reference: Grant JE, Chamberlain SR. Response of Gambling Disorder to Semaglutide. J Clin Psychopharmacol. 2025 Dec 19. doi: [10.1097/JCP.0000000000002117](https://doi.org/10.1097/JCP.0000000000002117).

Psychedelic-assisted psychotherapy for Gambling Disorder: **Psilocybin**



A PROMISING NEW FRONTIER

Psychedelic-assisted psychotherapy (PAT), particularly **psilocybin**, has emerged as a promising but still experimental approach for Gambling Disorder (GD).



EARLY STAGE EVIDENCE

Unlike substance use disorders, where evidence is accumulating, research in GD remains at an early stage, with no completed randomized controlled trials published to date.*



ONGOING CLINICAL TRIAL

The PASSENGER Trial is the first registered randomized study evaluating psilocybin-assisted psychotherapy for GD. Participants receive structured psychotherapy combined with either high-dose or low-dose psilocybin.

The study is currently in progress, and efficacy results are not yet available.**



PASSENGER TRIAL AT A GLANCE



STUDY: PASSENGER Trial



AIM: Evaluate the efficacy and safety of psilocybin-assisted psychotherapy for Gambling Disorder



INTERVENTION: Structured psychotherapy + psilocybin (high-dose vs. low-dose)



DESIGN: Randomized, controlled trial



STATUS: Currently in progress



RESULTS: Efficacy results not yet available



* Romero P, Czakó A, van den Brink W, Demetrovics Z. Psychedelic-assisted therapy for people with gambling disorder? J Behav Addict. 2024 Feb 28;13(1):6-11.

** PASSENGER Trial. *Psilocybin-Assisted Psychotherapy for the Treatment of Gambling Disorder*. ClinicalTrials.gov Identifier NCT07391332. 2026.

TMS for Gambling Disorder: State of Evidence



PRELIMINARY EFFICACY

Recent studies (2024–2025) suggest rTMS over prefrontal regions may **reduce gambling craving** and **symptom severity**.



SAFETY

Well-tolerated, with **no serious adverse effects** reported in small cohorts.



MECHANISMS

Theta Burst Stimulation (TBS) targeting control networks (e.g., pre-SMA) may **enhance inhibitory control**.



EVIDENCE GAP

Large **sham-controlled RCTs** with standardized protocols and **long-term follow-up** are still needed.



Conclusion: rTMS shows promise as an adjunctive treatment for gambling disorder, but further rigorous research is essential to establish its clinical value.

* Okechukwu, C. E. (2021). Repetitive Transcranial Magnetic Stimulation (rTMS) for Decreasing Gambling Disorder: A Call for Advanced Clinical Investigations. *NeuroRegulation*, 8(1), 69–71.

** Concerto C et al. High-frequency rTMS as a first-line treatment for gambling disorder – A case report. *Addict Behav Rep*, 2025 Aug 5; 22:100627; Gato K et al. Multitargeted Transcranial Magnetic Stimulation in the Treatment of Gambling Disorder. 2025 Jan 5; 14(1):50405.



Evidence
through 2024–2025



Small studies
to date

Does standard Cognitive Behavioral Therapy work for GDD? (Precision Psychiatry)



Research shows that **impulsive individuals** such as those with **GDD** often find **standard CBT aversive and boring** due to low tolerance for non-stimulating activities and impaired executive function, **increasing the risk of disengagement and dropout**.



THE CHALLENGE FOR THESE INDIVIDUALS

Boredom triggers a **strong physiological stress response**, such as **elevated cortisol**, and acts as a potent **psychological stressor** that can drive **maladaptive, impulsive behavior**.

IN SUMMARY: THE BOREDOM-STRESS-IMPULSIVITY CYCLE



BOREDOM



**ELEVATED
CORTISOL**
(STRESS RESPONSE)



**POTENT
PSYCHOLOGICAL
STRESSOR**



**MALADAPTIVE,
IMPULSIVE
BEHAVIOR**



Boredom:

Under-stimulation
and low engagement



Elevated cortisol:

Physiological stress
response



Psychological stressor:

Emotional discomfort
that amplifies reactivity



Maladaptive, impulsive behavior:

Risky actions used to escape
boredom or stress

* Clay, J. M., Badaricotti, J. I., Kozhushko, N., & Parker, M. O. (2024). HPA activity mediates the link between trait impulsivity and boredom. *Physiology & Behavior*.

Boredom as a Mental State

A neurobiological signal of failed engagement—**not simply** low stimulation



DEFINITION

An aversive state of wanting—**but being unable**—to engage in satisfying activity.

01



Engagement mismatch

The task feels unrewarding, meaningless or poorly matched to available attention.

02



Network reorientation

Attention drifts inward: default-mode activity rises as task-focused control weakens.

03



Motivational reset

Restlessness and variable arousal push the person to seek a better source of engagement.



KEY POINT

**Neural evidence remains limited:
boredom has no single circuit or validated biomarker.**



Impulsivity, Boredom & Stress Shape Clinical Subtypes

Precision Psychiatry Perspective



THREE INTERACTING DIMENSIONS DRIVE PATIENT DIFFERENCES



CLINICAL INSIGHT

These dimensions define clinically meaningful subtypes

Different patients = different dominant drivers



TREATMENT IMPLICATION

Match interventions to subtype → better outcomes



↑ Engagement



↑ Treatment response



↓ Dropout risk



Treat underlying mechanisms, not just diagnoses.

- Conrod, P. J., et al. (2013). Personality-targeted interventions for substance use disorders. *The Lancet Psychiatry*, 1(2), 152–164.
- Verdejo-García, A., et al. (2018). Impulsivity and addiction: A neuroclinical framework. *Nature Reviews Neuroscience*, 19(9), 563–574.
- Mallorquí-Bagué, N., et al. (2018). Trait impulsivity and cognitive domains involving impulsivity and compulsivity as predictors of gambling disorder treatment response. *Addictive Behaviors*, 87, 169–177.



FOR THE BENEFIT OF SOCIETY

WORLD LOTTERY ASSOCIATION

Evidence-Based Alternatives Psychotherapies

for Gambling Disorder (GDD)*



1



Motivational Interviewing / Motivational Enhancement Therapy (MI/MET)

Strong evidence for **standalone efficacy** and **improved engagement**.

Yakovenko, I., & Hodgins, D. C. (2018). *Journal of Consulting and Clinical Psychology*, 77(5), 950–960.

2



Acceptance and Commitment Therapy (ACT)

Has **comparable** or **superior outcomes** to CBT with **better acceptability**.

Dixon, M. R., Wilson, A. N., & Habib, R. (2016).

3



Mindfulness-Based Interventions

Evidence for **craving reduction**, **emotional regulation**, and **relapse prevention**.

Sancho M. (2018). *Journal of Behavioral Addictions*, 7(1), 1–10.

4



Harm Reduction and Non-Abstinence Approaches

Evidence that harm reduction is **effective** and **better accepted**. Supports engagement and improved outcomes.

Overview of harm reduction in addictive behaviors. *Addictive Behaviors*, 23(4), 587–597. (1998)



Dowling, N. A., Merkouris, S. S., Lorains, F. K., et al. (2016). Interventions for problem gambling: A systematic review. *Journal of Gambling Studies*, 32(1), 1–22.

What is Harm Reduction in GDD?*

*“Come as you are”.***

It refers to interventions that aim to **decrease the negative consequences of gambling** without requiring complete abstinence.

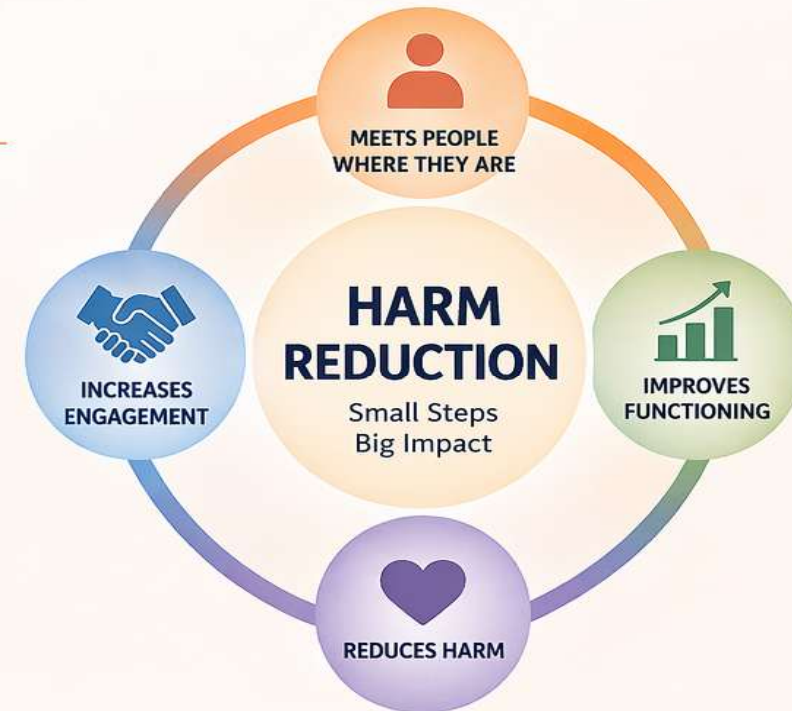
One of the strongest arguments for **Harm Reduction** is treatment acceptability.



- **Instead of focusing solely on stopping gambling**, these approaches prioritize **improved functioning, reduced financial and psychological harm**, and **greater engagement** in treatment.



- Research across addictive behaviors—including gambling—shows that harm reduction can lead to **meaningful improvements even when abstinence is not achieved**.



- * **Hing, N. et al.** Self-Regulatory Strategies Reduce Gambling Spend and Harm in a Randomised Controlled Trial of Electronic Gaming Machine Players. *Int J Ment Health Addiction* 23, 3582–3606 (2025).
- ** **Marlatt, G. A.** (1996). Harm reduction: Come as you are. *Addictive Behaviors*, 21(6), 779–788.

What is the evolution of individuals with GDD?



Longitudinal studies indicate that **two decades** after diagnosis, the disorder has often evolved into **remission**.*



Recovery from “PROBLEM GAMBLING” is common, on average achieved in **only one year**.*



Most people who recover from GDD **continue to gamble** at non-problematic levels.**



However, longitudinal studies indicate that **40–60% of people** with GDD will experience **relapse**.

* Williams RJ, Hann RG, Schopflocher D, West B, McLaughlin P, White N, King K & Flexhaug T (2015). *Quinte Longitudinal Study of Gambling and Problem Gambling*. Report prepared for the Ontario Problem Gambling Research Centre. Guelph, Ontario. February 20, 2015. <http://hdl.handle.net/10133/3641>

** Potenza MN, Balodis IM, Derevensky J, Grant JE, Petry NM, Verdejo-Garcia A, Yip SW. *Gambling disorder*. *Nat Rev Dis Primers*. 2019 Jul 25;5(1):51.



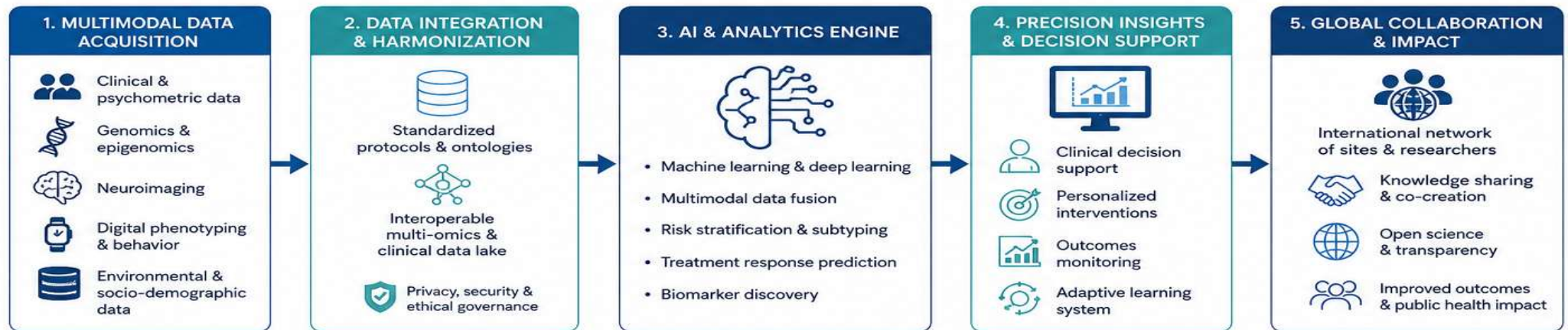
GAMBRAIN

International Precision Psychiatry Platform for Gambling Disorder and Dual Disorders

Scientific White Paper



Figure 1. Overall multimodal architecture of the GAMBRAIN platform.



Document purpose

This document provides the scientific and strategic framework for international collaboration around GAMBRAIN. It is intended as a reference white paper for partners, funders and scientific collaborators. A concise country-specific operational proposal can be derived from this framework for each new partner.



SCIENCE-DRIVEN



INTERNATIONAL & INCLUSIVE



ETHICAL & SECURE



IMPACT-ORIENTED

PART 5

Conclusions

Gambling Dual Disorder

Move beyond one-size-fits-all treatment



Treatment for Gambling Disorder (GD) should move toward **phenotype-informed, multimodal treatment** rather than a one-size-fits-all model.

01



Screen in both directions

Assess Gambling Disorder and other mental disorders together:
Dual Disorders.

02



Define the phenotype

Map impulsivity, reward sensitivity, stress, executive function and the Dual Disorder profile.

03



Treat both disorders

Integrate psychotherapy, indicated pharmacotherapy and treatment of both mental disorders.

04



Individualize the goal

Choose abstinence or harm reduction collaboratively—and revise with outcomes.



PRECISION PSYCHIATRY =
RIGHT COMBINATION • RIGHT PATIENT • RIGHT GOAL

Source: Szerman N. et al. *Frontiers in Psychiatry*. 2020.



Thank you for your attention

Together for better understanding,
care, and support for people
with dual disorders.



WADD

World Association
on Dual Disorders



Knowledge



Collaboration



Impact

Contact



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