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Psychobiology of gambling-related cognitions in gambling disorder

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The aim of this review is to explore the psychobiological substrates of gambling-related cognitions, and their relationship with motivational and emotional processes, to contribute to the understanding of this important facet of disordered gambling. These cognitions promote gambling initiation and maintenance, and gambling games' structural features are designed to foster them. According to our proposal, individual psychobiological features modulate gambling distortions vulnerability. Abnormal sensitivity to gambling-related rewards promotes the development of unrealistic expectancies, facilitating gambling escalation. As gambling behavior becomes recurrent, gambling cues acquire incentive salience, capable of triggering craving responses. Unsuccessful attempts to control craving generate the perceived inability to stop gambling. A proportion of gamblers use emotion regulation strategies to cope with gambling-related emotions, which fuels cognitive biases.

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Introduction

Gambling disorder (GD) is characterized by excessive and maladaptive gambling behavior, and its prevalence ranges between 0.12 and 3.4% [1,2]. In the fifth Diagnostic and Statistical Manual of Mental Disorders, GD, previously considered as an Impulse Control Disorder, has been reclassified in the new category Substance-Related and Addictive Disorders [3]. This recategorization was driven by evidence highlighting the overlap in neurobiology and symptomatology, and the substantial degree of comorbidity between GD and Substance-Related Disorders [4,5]. Imbalanced reward sensitivity, decision-making alterations, impaired cognitive control and craving, seem to be similarly relevant for compulsive gambling and drug use [6]. In spite of these similarities, the mechanisms driving the transition from recreational to addictive behaviors remain controversial [7,8].

Addictive agents exert their effects by overstimulating the systems involved in learning adaptive responses to probabilistic natural reinforcers. Evidence shows that unexpected rewards evoke dopaminergic prediction error signals [9]. By recurrent association, reward becomes predictable by external cues, and discrepancy between expected and experienced reward eventually disappears [10]. Crucially, drugs of abuse are not only hedonically rewarding, but also activate dopamine (DA) release in the mesolimbic pathway, mimicking prediction error signals, which precludes their attenuation as instrumental learning progresses [11]. By this mechanism, cues associated with drug consumption override the incentive value of natural rewards (i.e. incentive sensitization, IS), and generate a prevailing motivational impulse to use the drug [12]. This approach may help to explain the transition from recreational to compulsive gambling, in the absence of a chemical agent influencing DA activity. Most gambling devices operate under random ratio (RR) schedules [13,14], where reward probability in every single trial is independent from previous trials [15], and uncertainty cannot be reduced. Evidence suggests that reward uncertainty can mimic drug effects by triggering DA release associated with prediction error signals [16–19]. In parallel, animal research has shown that overtraining under similar partial reinforcement schedules facilitates the development of habits [20]. This process seems to depend on a gradual shift in the involvement of the striatum (from its ventral to its dorsal part) in behavior control, and is also likely involved in the generation of compulsive drug use habits [21,22].

Complementarily, gambling games' features facilitate the development of cognitive distortions, by exploiting human sensitivity to detect contingencies in probabilistic environments [23]. When faced with reward uncertainty and randomness of games of chance, gamblers try to make sense of the ambiguity, for instance, by searching patterns [24]. Gambling disorder patients (GDP) are particularly susceptible to experience these cognitive distortions [11,25].

This review is aimed at exploring the psychobiological substrates of gambling-related cognitions. First, these

cognitions are outlined, articulated in the model behind the Gambling-Related Cognitions Scale (GRCS) [26]. Secondly, we analyze these cognitions in terms of neurocognitive components that can be explored using neuroimaging techniques. And finally, we review recent available evidence on how emotion regulation mechanisms contribute to a self-deceptive reasoning style that promotes gambling maintenance.

Gambling cognitions: an overview

Our ability for adaptive decision making rests on the capacity to assess the expected value and to estimate the probability of significant outcomes [27]. Yet, the cognitive literature on gambling has revealed a number of cognitive distortions and pervasive beliefs that affect gambling decision making [24]. These cognitions contribute to the etiology of disordered gambling [23,28••], and predict future gambling involvement [25].

The best-known approach to study gambling cognitions is Raylu and Oei's five-factor model, materialized in the GRCS [26]. The five dimensions in this model are: *control illusion*, *predictive control*, *interpretative bias*, *gambling expectancies* and *inability to stop*. The first three dimensions, extracted from early analyses of gambling-related misperceptions [29,30], are grouped in the category of causal biases, whereas the remaining dimensions are dysfunctional beliefs adapted from substance addiction research [31]. Control illusion refers to the biased belief that certain strategies or rituals can influence gambling outcomes. Predictive control reflects the belief that gambling outcomes are predictable, based on illusory contingencies between cues and outcomes, or a perceived history of loses followed by wins (e.g. *gambler's fallacy*). Interpretative biases allude to hindsight reformulations of gambling outcomes to attribute success to personal skills, and failure to external influences. Gambling expectancies refer to a variety of motives to gamble, including socializing, coping with negative emotions or excitement-seeking. Lastly, inability to stop gambling denotes the perceived difficulty to control gambling urges.

Among these cognitions, control illusion and predictive control can be considered instances of distorted causal learning, namely an overestimation of the perceived causal link between one's behavior (or environmental cues) and gambling outcomes. This overestimation can be fueled not only by actual rewards, but also by non-rewards that are seen as causally informative. This is the case of near-misses: non-wins that are subjectively perceived as being close to wins, and thus indirectly rewarding and contributing to illusory mastery [28••].

Despite the validated relationships between outcome-related perceptions and beliefs, and general-domain decision making processes, in general (and for gambling-related decision-making in particular) [26,32], the study of their neurobiological bases has received relatively little attention. Hitherto, investigations on brain substrates of cognitive distortions have addressed the illusion of control [28••,33], interpretative biases [34•], the gamblers' fallacy [28••], and *near-miss* effects [33,35–37,38•]. In the next sections, we try to link the neurobiological findings described in these studies to the cognitions described above.

Gambling expectancies – reinforcing properties of gambling

Substance addiction literature has shown that expectations on the potential effects of drugs are relevant in the development of substance-related problems [39–41], and modulate brain reactivity to substance-related cues [42]. Similarly, in gamblers, expectancies about the reinforcing properties of gambling have been associated with gambling-related motivation, problems, and persistence [26,43]. Moreover, an expected reward from placing a bet (compared to passively viewing a competition) triggers increased activity in insular, striatal and prefrontal regions [44]. Thus, although gambling expectations include diverse motives to gamble, psychobiological research has mostly focused on the processing of in-game rewards.

Recently, the emergence of novel gambling opportunities [45] has been accompanied by parallel increases in the number of gambling modalities and games' structural features that facilitate gambling escalation [14,46]. Many of these features are associated with reward delivery and involved in expectancies formation, that is reinforcement schedules [47], frequency of *near-miss* events [48,49], intense sensory feedback as audiovisual stimuli [14], high frequency of betting and reinforcement ratio [50], or superficial features as stop buttons with no real impact on reward probabilities [51].

As a mechanism boosting delusive expectancies, brain response to near-misses has received increasing attention [28••,33,35]. In a seminal article, Clark and collaborators [33] showed that, by recruiting reward system regions (anterior insula and ventral striatum, VS) that mimic win-related responses, near-misses promote gambling motivation. Furthermore, Clark *et al.* [28••] showed that insular lesions abolish the gambler's fallacy and near-miss effects. In regular gamblers, near-misses, when compared to full-misses, were also associated with significant VS response, and higher gambling severity predicted increased responses in the midbrain area to near-misses [35]. Gambling severity was also associated with bilateral connectivity between VS and insula in GDP in response to near-misses [38•]. Similarly, Sescousse *et al.* [52••] compared responses between GDP and controls, showing a heightened striatal response to near-miss outcomes in gamblers. Results from experimental paradigms examining near-miss effects are summarized in Table 1.

Table 1

Summary of magnetic resonance imaging studies exploring neurocognitive processes associated with gambling cognitions

Cognition category	Neuroimaging paradigm	Summary of results	Studies
Gambling expectancies	Reactivity to near-misses	Consistent hyperactivation of ventral striatum, insula.	Clark *et al.* [33] (↑); Chase and Clark [35] (↑); Habib and Dixon [37] (↑); van Holst, Chase and Clark [38•] (↑); Clark *et al.* [28••] (↑); Dymond *et al.* [36] (↑); Worhunsky *et al.* [101] (↓); Sescousse *et al.* [52••] (↑)
	Reward anticipation	Mixed evidence of hyperactivation and hypoactivation in medial PFC, ventral and dorsal striatum, insula.	Sescousse *et al.* [65] (=); Balodis *et al.* [58] (↓); Choi *et al.* [59] (↓); van Holst *et al.* [57] (↑); Tsurumi *et al.* [62] (↓); Worhunsky *et al.* [101] (↑); Fauth-Bühler *et al.* [105] (=); Romanczuk-Seiferth *et al.* [73] (=); Brevers *et al.* [44] (↑ expectancy bet)
	Reward delivery	Mixed evidence of hyper-activity and hypo-activity in medial and lateral PFC, ventral striatum, insula, OFC.	Reuter *et al.* [61] (↓); de Ruiter *et al.* [60] (↓); Balodis *et al.* [58] (↓); Sescousse *et al.* [65] (↑); Worhunsky *et al.* [101] (=)
Inability to stop	Cue-reactivity and craving induction	Consistent hyperactivation of insula, dorsomedial and dorsolateral PFC, ACC, PCC, parahippocampal gyrus and amygdala, and associations with craving measures.	Crockford *et al.* [83] (↑); Goudriaan *et al.* [80] (↑); Balodis *et al.* [85] (=); van Holst *et al.* [106] (↑); Kober *et al.* [84] (↑); Limbrick-Oldfield *et al.* [72••] (↑)
Causal biases (control illusion, predictive control, interpretative bias)		Interpretative bias predicted reduced dorsal ACC grey matter volume. Personal control modulated neural reactivity and connectivity in response to gambling outcomes.	Clark *et al.* [33]; van Holst *et al.* [38•]; Clark *et al.* [28••]; Ruiz de Lara *et al.* [34•]

(↑) increased reactivity in gambling disorder patients (GDP), compared to controls; (↓) decreased reactivity in GDP, compared to controls; (=) no significant differences in neural reactivity between GDP and controls; PFC, prefrontal cortex; OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; PCC, posterior cingulate cortex.

With regard to actual rewards, etiological theories of addiction can help to explain how exaggerated expectancies emerge. More specifically, according to the reward deficiency syndrome (RDS)[3], the reward system turns increasingly hyposensitive to natural rewards as the addictive process progresses, which can indirectly boost drug-reward-related expectancies [53]. However, in GD research, evidence regarding these putative reward processing anomalies remains inconsistent [54]. The mixed pattern of hyper-responsiveness [52••,55–57] and hypo-responsiveness [58–62] of striatal, medial prefrontal and insular regions found in reward processing research in GD may be due to the intrinsic limitations of case-control studies, as well as samples characteristics and methodological shortcomings [63,64].

Table 1 presents a detailed description of results from studies using reward-processing paradigms in GD with functional Magnetic Resonance Imaging (fMRI). To clarify these discrepancies, Sescousse *et al.* [65] compared sensitivity to monetary and erotic rewards between GDP and healthy controls in non-gambling contexts. GDP showed blunted VS reactivity to cues predicting erotic stimuli, when compared to cues signaling a monetary reward. However, reactivity to monetary cues did not differ between groups. Extending this result, a recent meta-analysis compared brain reactivity to different types of rewards, including natural (food, erotic) and addiction-related (drug, gambling), and found a common network that responds to rewards from different types, including bilateral insula, striatum, frontal and anterior cingulate cortex (ACC) [66•].

Another important methodological distinction regards the focus on reward anticipation or delivery. Reward anticipation, where acquired expected value is central, is specifically involved in coding expectations and motivational processes [67]. Conversely, outcome evaluation is implicated in updating previously learned expected value when confronting novel information [68]. According to this delimitation, a recently published meta-analysis examined brain reward processing during reward anticipation and outcome delivery in GD and substance-use disorder (SUD) patients [69••]. A common pattern of decreased striatal activity during reward anticipation was found for both clinical groups. In contrast, GD and SUD patients showed a distinct response to outcome delivery, with reduced dorsal striatal activity in GDP

[3] Please note that the RDS hypothesis is not incompatible with the IS hypothesis described earlier, as the former predicts hypo-responsivity to natural (non-gambling) rewards, whereas the latter predicts motivational hyper-responsivity to environmental cues that have become associated to gambling rewards. Actually, as discussed below, both processes have received empirical support.

and increased VS activity in SUD patients. Consequently, the pattern of results in GDP was interpreted as evidence supporting the RDS hypothesis in GD.

Inability to stop – craving control

Recurrent unsuccessful attempts to control gambling cravings foster the belief of inability to stop gambling [70]. Craving, in turn, arises from the repeated association between external cues and rewarding effects of the addictive agent, and progressive neuroadaptations in distinctive brain networks [12,38•,57,60,71,72••,73].

As noted above, most drugs of abuse exert their reinforcing properties by stimulating the DA system [74]. Thereby, ventral tegmental area projections trigger DA release to different regions of mesocorticolimbic system, including nucleus accumbens, VS, insula, hippocampus, amygdala, prefrontal and ACC [75]. The recurrent activation of DA system with repeated drug use or gambling – sensitizes reward circuits and generates increased responses to cues associated with the addictive agent [67].

Sensitization is responsible for cue-triggered urges to gamble, but also causes attentional bias toward gambling cues that gradually generalizes to a variety of contexts [76]. The relocation of attentional resources manifests in the differential recruitment of cognitive control regions in GDP [71], and can generate cognitive control problems in the absence of a substantive alteration on executive functions [77]. Consistent with this hypothesis, structural differences between GDP and controls in cognitive-control areas have been difficult to identify [34•,78•]. Moreover, the insular cortex has been implicated in craving and addiction motivation, as it underpins motivationally relevant interoceptive representations of addiction-related outcomes, and has been shown to divert cognitive resources toward gambling-related goals [79]. Accordingly, insular reactivity to gambling-cues is associated with craving states in GD [72••,80].

In cognitive neuroscience, the most common approach to study neural responses to craving is the cue-reactivity paradigm [81], where participants are exposed to cues previously associated with gambling, and responses are measured using fMRI techniques. These studies have reported an abnormal recruitment of mesocorticolimbic networks [82•], but also of regions devoted to cognitive control (dorsolateral PFC) and salience attribution (insula, ACC) [72••,83,84]. Specifically, the most consistent finding is an increased activation in mesocorticolimbic regions in GDP, including insula, dorsomedial PFC, ACC, posterior cingulate cortex, parahippocampal gyrus and amygdala [72••,80,83,84] (see Table 1 for a summary of main findings from cue-reactivity studies). Interestingly, gambling cue-reactivity studies show an association between cue-related brain activity and craving scores [72••,80,85]. Lastly, in an attempt to integrate available fMRI literature on gambling cue-reactivity, Meng and colleagues [82•] published a meta-analysis reporting an increased activation in putamen and globus pallidus in GD patients.

In summary, available evidence supports the idea that the imperative motivational impulse generated by incentive sensitization defines the development of craving, and perceived inability to stop gambling. This process also marks the initiation of compulsive gambling behavior and detachment of 'wanting' from gambling hedonic properties, and precipitates negative consequences derived from recurrent gambling.

The motivated nature of causal biases

Compared to reward processing and cue-reactivity, psychobiological research on gambling-related cognitive biases (control illusion, predictive control and interpretative bias) has received little attention. It could be tentatively hypothesized that these biases originate in poor reasoning or probabilistic abilities. However, a recent study has shown that gamblers with stronger biases perform better than gamblers with weaker biases in a causal learning task [86]. Moreover, causal biases are unrelated to lack of premeditation and perseverance [87], and stronger cognitive distortions characterize a subgroup of young gamblers with higher education level and preference for skill-based games [88].

Consequently, it has been recently proposed that causal biases have a motivational basis. In other words, gambling-related biases can reflect an attempt to justify gambling motivation, or temper negative emotions resulting from adverse gambling outcomes. Although cognitive biases are often depicted as automatic or mindless [89], people can also elaborate on them, and they can result from overthinking rather than 'underthinking' [90]. In accordance with a reflective view of gambling biases, the dispositional use of intentional emotion regulation strategies customarily considered as adaptive (*putting into perspective*, *reappraisal*), has been associated with stronger gambling-related cognitive distortions [91,92,93]. According to the recently proposed Gambling Space Model [11], this association is mostly driven by a specific subtype of gamblers characterized by a self-serving reasoning style, oriented towards deluding themselves about their higher gambling abilities. This proposal could account for the inconsistent results regarding executive dysfunction in GDP [77]. Although the understanding of neurocognitive bases of emotion regulation in GD is preliminary [94,95], their study in the general population is reasonably well-developed, with dominant models distinguishing between incidental (model-free) and intentional (model-based) emotional regulation mechanisms, anatomically associated with, respectively, lateral prefrontal/parietal, and ventral/medial prefrontal cortices [96–98]. Further research on the possible involvement

of the former in gambling-related cognitive distortions is warranted.

Summary and conclusions

The development of distorted cognitions contributes to gambling behavior initiation, and is associated with gambling escalation and development of gambling problems [25,28••,99,100]. In this review, we outlined how structural features of gambling games interact with human bounded rationality to develop these distorted gambling-related cognitions, and explore the psychobiological basis of this interaction.

Gambling expectancies are associated with how the gambler processes the rewarding properties of gambling outcomes. However, evidence regarding reward processing in GDP is mixed, which precludes any simple interpretation. Although compelling preliminary evidence supports striatal hyporesponsivity in GDP [69••], consistent with the RDS hypothesis, studies using simulated gambling have also revealed an increased anticipatory activity to gambling rewards in mesocorticolimbic regions, including striatum and medial PFC [52••,55,57,101]. A plausible interpretation of this pattern of results is the potential complementary roles of reward deficiency and incentive sensitization in distinct phases of disorder progression. According to the RDS framework, initially blunted activity of the reward system and the ensuing less pleasurable experience from natural rewards may turn the individual vulnerable to gambling [54]. Subsequently, incentive sensitization caused by repeated exposure to gambling opportunities may render the reward system hypersensitive to gambling-related cues, which contributes to gambling expectancies, that are however detached from actual hedonic value [102•].

Research on the brain responses to near-misses in GDP has yielded more consistent results, showing an augmented response in VS and insula [28••,33,35,38•,52••] associated with an increased motivation to gamble. The rewarding properties of near-misses in GDP have a direct effect on gambling expectancies, and can function as information on skill acquisition or strategy improvement, thus also contributing to illusory control [28••].

The perceived inability to stop gambling is proposed to originate from repeated unsuccessful attempts to control craving. The incentive sensitization hypothesis holds that craving is mostly cue-triggered, and results from learning-driven neuroadaptations. More specifically, repeated exposure to environmental cues associated with gambling reinforcement endows initially neutral stimuli with incentive salience, detaching 'wanting' from gambling hedonic properties, and diverting attention towards them.

Research on gambling craving using the cue-reactivity paradigm supports the incentive sensitization hypothesis. Augmented response to gambling-related stimuli has been reported in the insula, ACC, dorsomedial PFC, posterior cingulate cortex, parahippocampal gyrus and amygdala [72••,80,83,84]. Notably, the consistent association between gambling cue-reactivity and craving measures [85,72••,80], emphasizes the potential role of cue-reactivity as an indicator of gambling craving and inability to stop gambling. Complementarily, diverted attentional resources towards gambling-related stimuli can generate cognitive-control problems, in the absence of manifest alterations on executive functions [77,103,104].

Further, the attempts to explore the psychobiological underpinnings of cognitive biases have been scarce. However, (a) the unsuccessful attempts to find an association between causal biases and poor probabilistic or general reasoning [86,88] and (b) the association between gambling biases and supposedly adaptive emotion regulation strategies suggest that these biases can be motivated by the desire to continue gambling or the attempts to cope with negative gambling outcomes [91,92,93]. If this hypothesis is correct, it could also help to elucidate the seemingly puzzling results on executive dysfunction in GDP [77]. More importantly, it could redirect psychobiological research on gambling biases towards the structures and networks involved in emotion regulation [97,98].

Conflict of interest statement

Nothing declared.

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associated with reduced connectivity between right ventral striatum and anterior cingulate cortex. However, in the personal control condition, higher gambling severity predicted increased connectivity between ventral striatum and right insula. Lastly, in response to near-misses, gambling severity was associated with bilateral connectivity between ventral striatum and insula in gamblers.

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