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Research report

Comfort for uncertainty in pathological gamblers: A fMRI study

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ABSTRACT

This study examined neural anticipation of monetary reward in pathological gamblers (PG) by varying the type of uncertainty associated with the reward. Ten PG and ten controls were scanned while deciding whether to accept ("bet" option, featuring high-uncertain monetary rewards) or reject ("safe" option, featuring low-certain rewards) a bet, within situations of decision-making under risk (probability of the "bet" reward is known) or ambiguity (probability of the "bet" reward is unknown). During decision under risk (as compared to ambiguity), controls exhibited activation in brain areas involved in reward processing (putamen), interoception (insula) and cognitive control (dorsolateral prefrontal cortex; middle frontal gyrus). By contrast, PG exhibited no differential brain activation as a function of the type of uncertainty associated with the "bet" option. Moreover, prior choosing of the "safe" option (as compared to "bet" choices), controls exhibited activation in the posterior insula, dorsolateral prefrontal cortex and middle frontal gyrus. By contrast, PG exhibited higher neural activation during the elaboration of "bet" choices, and in motivational-arousal areas (caudate; putamen; posterior insula). Between-groups contrasts revealed that, as compared to controls, PG showed (i) decreased neural activity in the globus pallidus for decision-making under risk, as opposed to decision under ambiguity, and (ii) increased neural activity within the putamen prior to bet choices, as opposed to safe choices. These findings suggest that (i) unlike control participants, a variation in the level of uncertainty associated with monetary rewards seems to have no significant impact on PGs' decision to gamble and (ii) PG exhibit stronger brain activation while anticipating high-uncertain monetary rewards, as compared with lower-certain rewards.

1. Introduction

Through repetition of gambling behaviors, pathological gamblers (PG) acquire extensive experience in making complex financial decisions involving variable wins, losses, and probabilities. This is likely to bias their neurocognitive approach to decision-making. Furthermore, unlike non-problem gamblers, who shape and maintain their behaviors according to their consequences, PG continue to gamble despite the accumulation of financial losses [1]. One explanation for this stereotyped pattern of decision-making is that response output directed at gambling trigger automated and habit-like processes [2,3].

One key characteristic of habits is that, through the repetition of behaviors, it becomes increasingly estranged from variations in outcome value and reward probability [4]. In this context, addiction-related stimuli may elicit automatic, repetitive and inflexible behavioral sequences [5–7]. In other words, gambling-seeking behaviors may become persistent and ultimately insensitive to devaluation or punishment. For instance, a recent PET study highlighted that, while gambling on a slot machine, ventral striatal dopamine (the mesolimbic dopamine neurotransmitter that plays a major role in reward-driven learning) release in PG was not modulated by gambling outcome [8]. This suggests that, in PG,

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being embedded into gambling-related action is merely sufficient to induce dopaminergic changes independently of its outcome. Moreover, recent fMRI studies showed that PG exhibited higher activation in the brain-reward system during the pre-choice anticipation (i.e., when the subject is pondering potential options before making a decision; [9]) and the post-choice anticipation (i.e., the subject has made a decision and is awaiting the outcome; [10]) of high-uncertain monetary rewards. More specifically, as compared with low-risk decisions, before taking high-risk decisions in a quasi-realistic blackjack scenario [9], PG exhibited enhanced brain responses in the inferior frontal gyrus and lateral orbitofrontal cortex region (OFC; region involved in the integration of emotional and cognitive input; [11]) and in the medial side of the pulvinar nucleus (a relay thalamic nucleus that receives interoceptive input and in turn projects to the insular cortex all of which are brain areas associated with impulsive urges [12]). On the other hand, controls showed a significant signal increase before taking low-risk decisions, as compared to high-risk decisions. With regard to post-choice anticipation, van Holst et al. [10] have observed that, as compared to healthy controls, PG exhibited stronger activation in the ventral striatum (a region involved in reward anticipation and reward processing [13]) and the medial OFC when anticipating a large win (e.g., 5 euros) as opposed to a lower win (e.g., 1 euro). Additionally, several brain imaging studies showed that, in contrast to non-gamblers, there is evidence of a reduction of cerebral activity in the brain reward pathway during the processing of monetary gambling rewards and losses in PG [[14–16], but see [17]]. Together, these findings support the notion that PG exhibit a cue-induced signal increase toward the anticipation of high-uncertain monetary rewards. Nevertheless, a couple of recent imaging studies reported decreased neural activations during the anticipation of monetary gains in PG [18,19]. More specifically, while performing an incentive delay task (which requires an individual to react to a target stimulus presented after an incentive cue to win or to avoid losing the indicated reward), PG exhibited less fronto-striatal activation than controls while anticipating monetary gains [18,19]. One possible explanation for these contradictory findings is the use of different task designs [20–23]. Indeed, experimental paradigms more closely related to gambling (e.g., a blackjack task in [9]; a guessing card game in [10]) may generate increased neural activation in PGs' brain-reward system, as compared with less gambling-related paradigms (such as the incentive delay task [22]), which may be less significant and incentive for gamblers.

The goal of the present study is to further explore the neural correlates of gambling-related choices in PG. More specifically, we aim to examine whether PGs' decision-making is modulated by the type of uncertainty associated with high monetary rewards. Indeed, if PGs' desire to gamble is triggered by the feeling that a large part of money is at stake [9,10], a variation in the type of uncertainty associated with this amount might have a low impact on their decision to gamble. In other words, the type of uncertainty should not significantly modulate risk-taking in PG. In order to test this assumption, we used an adapted version of the Card-Deck paradigm initially developed by Hsu et al. [24]. In this task, participants are asked to choose between a "safe" option, which offers a sure payoff (e.g., $9), and a "bet" option which offers larger (e.g., $25) but uncertain reward. The bet choice carried either some risk (i.e., where probability of reward is known) or some ambiguity (i.e., where probability of reward is unknown). Using this paradigm, Hsu et al. [24] reported differential brain activations according to the type of uncertainty associated with the "bet" option. More specifically, as compared with decision-making under ambiguity, explicit outcome probability during decision-making under risk heightened neural activation within brain region involved in the prediction of reward (i.e., the dorsal striatum [25]). By contrast, decision-making under ambiguity activated a vigilance-evaluative neural network (amygdala and orbitofrontal cortex activations), which suggests that ambiguous choices carry more unknown consequences, and that cognitive and behavioral resources must be mobilized in order to seek out additional information from the environment [24].

In the current study, we hypothesize that, at a behavioral level, the frequency of PGs' "bet" choices will be less modulated by the type of uncertainty (decision-making under risk versus under ambiguity), as compared to non-gambler control participants. At a neural level, we test the hypothesis that, as compared to controls, PG will exhibit less differential brain activation according to the type of uncertainty associated with the "bet" option. Moreover, based on recent findings on pre- [9] and post- [10] decision anticipation in gambling disorder, we expect that PG will exhibit higher brain activation prior taking the "bet" option, as compared to the "safe" one.

2. Methods

2.1. Participants and recruitment

Twelve pathological gamblers (PG) and twelve controls were recruited for this study. All subjects provided informed consent according to the Declaration of Helsinki. The CHU-Brugmann ethics committee approved the study. PG were recruited through advertisements in the casino complex *VIAGE* in Brussels, Belgium. All gamblers had to meet the criteria for DSM-IV-TR Gambling Disorder. Problem gambling severity was assessed using the South Oaks Gambling Screen (SOGS; [26]). All gambler participants scored at least a five on the SOGS, indicative of gambling disorder. Our sample of gamblers was categorized as slot machines gamblers (i.e., the gambling game reported at a higher frequency, by the gambler participants, on the SOGS). We excluded any subject who was (a) over 65 years, or (b) had any substance use disorder during the prior year before enrolling in the study. Participants were judged to be medically healthy on the basis of their medical history. The severity of problems related to substance use and medical history were also examined with items taken from the Addiction Severity Index Short Form ([27]; selection of items undertaken by S.M. and P.V.; CHU-Brugmann board-certified psychotherapists). In addition, we excluded participants who exhibited either excessive motion (i.e., >3 mm and/or >3°, or motion correlated with the task) or BOLD signal instability in a task-independent area (i.e., the occipital cortex), larger than 5%. Based in these thresholds, we excluded two pathological gamblers and two control participants who exhibited BOLD signal instabilities. Hence, our final sample consisted of ten PG and ten controls (see Table 1 for demographics and current clinical status).

Control participants were recruited by word of mouth from the community, excluding psychiatrists, psychologists, and other personnel with previous psychological training. Based on the SOGS, none of the controls gambled frequently (see Table 1).

2.2. Clinical and neuropsychological measures

Current clinical status of depression was rated with the Beck Depression Inventory (BDI; [28]). Alcohol use was estimated through the Alcohol Use Disorder Identification Test (AUDIT; [29]). The number of cigarettes per day was also included in order to control for the effect of nicotine dependence on cognitive processing [30].

2.3. Gambling related craving

All subjects completed the Gambling Craving Scale (GACS; [31]) before and after fMRI scanning. The GACS contains three factors: anticipation (e.g., "Gambling would be fun right now"), desire (e.g.,