








Increased brain reactivity to gambling unavailability as a marker of problem gambling

Damien Brevers¹  | Chris Baeken^{2,3,4}  | Antoine Bechara⁵ | Qinghua He⁶  |
Pierre Maurage⁷  | Mathieu Petieau⁸ | Guillaume Sescousse⁹  |
Claus Vögele¹  | Joël Billieux^{10,11} 

¹Institute for Health and Behaviour, Department of Behavioural and Cognitive Sciences, University of Luxembourg, Esch-sur-Alzette, Luxembourg

²Department of Psychiatry University Hospital, UZ Brussel, Brussels, Belgium

³Ghent Experimental Psychiatry (GHEP) Lab, Department of Head and Skin, Ghent University Hospital, Ghent University, Ghent, Belgium

⁴Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

⁵Department of Psychology, University of Southern California, Los Angeles, California, USA

⁶Faculty of Psychology, Southwest University, Chongqing, China

⁷Louvain for Experimental Psychopathology Research Group (LEP), Psychological Sciences Research Institute, UCLouvain, Louvain-la-Neuve, Belgium

⁸Laboratory of Neurophysiology and Movement Biomechanics, Faculty of Motor Sciences, Erasme Campus, Université Libre de Bruxelles, Brussels, Belgium

⁹Lyon Neuroscience Research Center—INSERM U1028—CNRS UMR5292, PSYR2 Team, University of Lyon, Lyon, France

¹⁰Institute of Psychology, University of Lausanne, Lausanne, Switzerland

¹¹Centre for Excessive Gambling, Lausanne University Hospitals (CHUV), Lausanne, Switzerland

Correspondence

Brevers Damien, Institute for Health and Behaviour, Department of Behavioural and Cognitive Sciences, University of Luxembourg, Esch-sur-Alzette, Luxembourg.
Email: damien.brevers@uni.lu

Funding information

Luxembourg National Research Fund (CORE Junior Track [BETHAB])

Abstract

The unprecedented development and ubiquity of sports betting constitute an emerging public health concern. It is crucial to provide markers that could help to better identify people experiencing sports betting-related harms. The current study investigated whether problem gambling status, sports betting passion, and trait-self-control modulate brain reactivity to sports betting cues. Sixty-five frequent sports bettors (35 “nonproblem bettors” and 30 “problem bettors”) were exposed to cues representing real upcoming sport events (with varying levels of winning confidence) that were made available or blocked for betting, during functional magnetic resonance imaging (fMRI) recording. Sports betting passion and trait-self-control were assessed using self-report scales. Sport events nonavailable for betting elicited higher insular and striatal activation in problem bettors, as compared with nonproblem bettors. Within a large cluster encompassing the ventral striatum, hippocampus, and amygdala, lower trait-self-control was associated with increased brain reactivity to sport events with high levels of winning confidence that were nonavailable for betting. No significant effect of sports betting passion was observed. These findings suggest that sports bettors' brain reactivity to gambling unavailability might be a relevant marker of sports betting-related harms, as well as of blunted trait-self-control.

KEYWORDS

addiction, cue reactivity, fMRI | gambling disorder, gambling-related harm, reward availability, reward blocking, sports betting

1 | INTRODUCTION

Sports betting has become increasingly embedded into the sport culture, and more globally in the leisure society, which is illustrated by the ubiquity of sports betting advertisements occurring in many countries.^{1,2} With easy access from a computer or mobile apps, it is now possible to gamble on almost every sport event at any time, including when the game is ongoing (i.e., live betting^{3,4}). As nearly all sport events are available for betting, merely viewing such sport events and their related advertisements might act as a powerful incentive cue increasing the desire to gamble. This hypothesis has been tested in a previous functional magnetic resonance imaging (fMRI) study,⁵ showing that the brain processes information about such cues differently, depending on whether sport fans plan to gamble on the sporting event or not. The neural structures recruited when participants have betting intentions include the orbitofrontal cortex (OFC), anterior insula, caudate nucleus, and the hippocampus. These regions represent central brain pathways underlying memory, cognition, and emotion processing associated with addiction-related cue reactivity (for a review, see Brevers et al.⁶).

It remains unclear, however, whether patterns of brain activation vary according to the level of problematic sports betting habits. In the gambling field, previous fMRI studies have shown a positive association between cue-induced ventral striatal activation and problem gambling severity.^{7,8} These findings suggest that brain reactivity to gambling cues constitutes a valid marker of problem gambling. Nevertheless, at a between-group level, fMRI studies on gambling cue reactivity only compared problem gamblers (either active or treatment-seeking) and *nongambling* matched controls,^{7–16} thus failing to identify brain pathways discriminating nonproblematic from problematic gambling. In the present study, we compared two groups of active sports bettors who differed according to their problem gambling status (nonproblem, *NPB* vs. problem sports bettors, *PB*). Specifically, we examined whether brain responses to gambling-related cues could be a marker of the problem gambling status in a nonclinical (i.e., not recruited in addiction treatment centers) sample of sports bettors. This approach has already been adopted in the context of substance use.^{17,18} For instance, brain reactivity to visual alcohol cues distinguishes light from heavy drinkers, with increased blood-oxygen-level-dependent (BOLD) responses in the insula and the ventral striatum in the nonclinical sample of heavy drinkers.¹⁹ Importantly, the fMRI literature on substance use disorders has also shown that situational factors (e.g., reward availability and personalized cues) modulate brain cue reactivity among substance users (consuming cocaine, tobacco, and/or alcohol^{17,18,20,21}).

This study followed a comparable integrative approach in the examination of sports betting cue reactivity. We capitalized on a

neuroimaging paradigm where football bettors view cues representing real sport events (i.e., European soccer matches occurring shortly after the scanning session). To examine the impact of situational factors, we manipulated reward (un)availability and used cues varying in their subjective levels of winning confidence. More specifically, the reward availability component was manipulated through a reward-blocking procedure that made sport events available or nonavailable (i.e., “blocked”) for betting. Reward blocking is an established procedure eliciting frustration or reward-deprivation feelings,^{22–25} and known to trigger insular cortex and amygdala activations, the closer an individual is to achieving a goal (i.e., manipulation of reward proximity^{22,23}). Hence, by implementing both reward availability and reward unavailability conditions, we examined whether *NPB* and *PB* would respond differently to the transient availability and unavailability of betting opportunities. Accordingly, contrasting BOLD responses for available versus nonavailable events allowed to isolate the specific activation related to the available or blocked access to the action of betting, that is, while controlling for more general or confounding processes (e.g., visual activation, cognitive processing of the betting information, and memory-related activation). In the present study, self-report ratings of winning confidence were used to further operationalize reward proximity. Winning confidence ratings were obtained for each sport event presented to examine how brain activity is modulated by the degree of winning confidence towards a distinct sport event. As matches for which participants report “high winning confidence” have been shown to be favored for betting,^{26,27} this should result in higher activity in areas that are related to reward processing if the match is made available for betting. Conversely, we would expect higher activity in areas that are related to frustration or reward-deprivation if the match is made unavailable for betting.

Overall, the current design offers an ecological simulation (i.e., using cues representing real upcoming sport events) of how sports bettors respond to transient availability and unavailability of sport betting opportunities. In other words, this approach allowed to identify the brain regions specifically activated when sports bettors face sport events that turn out to be available or nonavailable for betting. Based on previous fMRI studies on problem gambling^{7,8} and substance use disorder,^{17–21} we hypothesized that, as compared with nonproblem bettors, problem sports bettors would exhibit: (H1) higher cue reactivity in the ventral striatum when viewing sports cues available for betting; (H2) higher levels of brain reactivity in the insular cortex and the amygdala when exposed to sport cues made unavailable for betting. These two hypotheses were also tested by considering the parametric modulation (PM) of self-reported ratings of winning confidence (referred to as “H1_PM” and “H2_PM” across the manuscript).

Finally, we also pursued exploratory goals by examining whether sports betting passion and trait-self-control could modulate brain reactivity to sports betting cues. Previous work has distinguished harmonious (i.e., a strong inclination to engage in gambling willingly and with a sense of volition) from obsessive gambling passion (i.e., an uncontrollable urge to engage in the activity^{28,29}). Here, we examined whether sports betting cue reactivity is modulated by levels of harmonious and obsessive passion toward sports betting. Trait-self-control broadly reflects the disposition towards controlled versus impulsive actions,³⁰ and is conceptualized as the ability to promote abstract and distal goals when threatened by competing concrete and proximal ones.^{31,32} This dispositional ability is important for promoting behaviors that are consistent with desirable long-term goals, but also for avoiding inappropriate behaviors producing strong immediate rewards, and are hence difficult to resist.^{33–36} Higher scores in self-reported trait-self-control are associated with lower amygdala reactivity to stimuli triggering negative emotions.³⁷ Accordingly, we expected that trait-self-control would modulate brain cue reactivity when participants faced sport cues that were made unavailable for betting.

2 | METHODS AND MATERIALS

2.1 | Participants

Sixty-five football (i.e., soccer) fans participated in this study (61 males, mean age 26.04 years, standard deviation [*SD*] = 5.63, range: 19–51). All participants gave written informed consent to the experimental procedure, which was approved by the institutional review boards of Ghent University and the University of Luxembourg. All participants were right-handed and had normal or corrected-to-normal vision. We excluded participants who self-reported past or present treatment/therapy for problem gambling. Participants were advised to avoid drinking alcohol in the 24 h prior to participating in the scanning session. Participants received a fixed amount of 50 euros as a compensation for their participation, plus the money actually won in the sports betting game (up to 20 euros).

Participants were recruited via the Internet through advertisements displayed on social media. The ads asked for self-identified football fans (i.e., individuals who like watching European Football) to participate in a neuroimaging study on sports betting. Individuals who were interested were then asked to complete an online survey assessing: (a) the frequency of football game watching, (b) the frequency of football game betting, (c) the knowledge on European Football Leagues, (d), the level of interest for each of the main European Football Leagues. All participants were judged to be physically healthy on the basis of their answers on an MRI screening form, enclosed in the online survey. The prescreening tool was also used to exclude any participant who reported having used mood stabilizers, antidepressants, antipsychotics, sleep medications, morphine, cocaine, heroin, or cannabis (regular use) in the past 12 months. The online prescreening tool is accessible through the following link (in Dutch and French): <http://www.panlablimesurvey.ugent.be/PAN200/index.php/477436/lang-nl>

The screening procedure allowed to identify participants who watch football frequently (6-points Likert scale; all participant scores either “5—frequently” or “6—very frequently”) and maintain a high level of knowledge and interest in European Football Leagues. With regard to the frequency of football betting, participants ranged from nonfrequent to highly-frequent bettors. Specifically, on a 5-points Likert scale, 28 participants reported to bet “3—sometimes” on football, 25 participants reported to bet “4—frequently” on football, and 12 participants reported to bet “5—very frequently” on football.

2.2 | Problem gambling severity

Participants filled out the Problem Gambling Severity Index (PGSI³⁸) while reflecting on their sports betting behaviors. Based on clinical norms provided by the PGSI,³⁹ 35 participants were classified as non-problem bettors (NPB; PGSI < 3), and 30 as moderate to high-risk gamblers (PGSI ≥ 3, labeled problem bettors, PB; see Table 1 for descriptive statistics).

2.3 | Sports betting passion

This adapted Gambling Passion Scale⁴⁰ assesses harmonious and obsessive passion for sports betting. This questionnaire uses a 7-point Likert scale (from “don't agree at all” to “very strongly agree”). It comprises five items indexing harmonious gambling passion (e.g., “Gambling allows me to have memorable experiences”) and five items indexing obsessive gambling passion (e.g., “I couldn't live without gambling”). This instrument was adapted by replacing all occurrences of “gambling” by “sports betting” (e.g., “Sports betting allows me to have memorable experiences”). Scores on the items indexing harmonious and obsessive passion were computed separately, higher scores indicating higher passion levels (see also Table 1 for descriptive statistics, internal reliability of the scales used, and between-groups comparisons).

2.4 | Trait-self-control

Participants completed a French adaptation of the 13-item Brief Self-Control Scale.^{41,42} Items (e.g., “I am good at resisting temptation”) were endorsed on a 5-point scale from (“not like me at all” to “very much like me”). An average score of the 13 items was computed, with higher scores indicating better self-control (see also Table 1).

2.5 | Alcohol consumption

The Alcohol Use Disorders Identification Test (AUDIT⁴³) was included to control for alcohol consumption (see also Table 1).

TABLE 1 Descriptive statistics and group comparisons

	Mean		SD		Min		Max		Cronbach's α	BF10
	NPB	PB	NPB	PB	NPB	PB	NPB	PB		
Age	25.65	26.50	5.65	5.66	20	19	51	39	/	0.22
PGSI	0.53	6.37	0.61	3.18	0	3	2	17	/	>100
Harmonious passion	2.91	3.98	1.23	1.19	1.00	1.40	5.60	6.20	.81	35.71
Obsessive passion	1.17	2.35	0.53	1.46	1.00	1.00	3.60	7.00	.93	>100
Trait-self-control	3.30	3.08	0.62	0.59	2.30	2.15	4.77	4.54	.78	0.49
AUDIT	4.78	8.29	3.36	5.71	0	0	14	20	/	3.07
Posttask ratings available matches	2.72	2.68	0.33	0.34	2.00	2.02	3.48	3.30	.93	0.19
Posttask ratings nonavailable matches	2.65	2.63	0.36	0.35	1.80	1.78	3.34	3.24	.90	0.20

Note: BF10 is a ratio that contrasts the likelihood of the data fitting under the null hypothesis with the likelihood of data fitting under the alternative hypothesis. Bayes factor values below 0.1 indicate substantial support for the null hypothesis, values between 0.1 and 0.33 indicate moderate support for the null hypothesis, values between 0.33 and 3 are considered as inconclusive, values between 3 and 10 indicate moderate support for the alternative, and values greater than 10 indicate strong support for the alternative.

Abbreviations: AUDIT, Alcohol use disorders identification test; BF10, Bayes factor 10; NPB, nonproblem bettors; PB, problem bettors; PGSI, Problem Gambling Severity Index.

A scatter plot matrix with pair-correlations of PGSI, the sports betting passion scales, AUDIT, and Brief Self-Control Scale is reported in Figure S1.

2.6 | Experimental task and MRI procedure

We used a cue-exposure task (adapted from Brevers et al.⁵; see Figure 1) where cues depicting football games appeared on a screen (task length \approx 18 min 40 s). More specifically, each cue depicted a football game from a European league (i.e., English Premier League, German Bundesliga, Italian Calcio, French Ligue 1, Spanish Liga, Portuguese Primeira Liga, Dutch Eredivisie, and Belgian ProLeague) that was about to occur either the same weekend of the scanning session (referred here as “weekend 1”) or the next one (“weekend 2”). We chose games occurring on two consecutive weekends in order to be able to select up to 100 games from the main European leagues. As a consequence, all participants were scanned on a Saturday (9 am–6 pm, 7–10 participants per day), and different games were displayed on each scanning session. Seven Saturday sessions were conducted in total (between April 2019 and September 2019).

Prior to the scanning session, participants received task instructions. They were asked to look attentively at each cue and were informed that the task consists of two types of trials, “available” and “nonavailable.” The games displayed in the “available” condition were available to the participant for betting at the end of a ten-trial block. The games in the “nonavailable” condition were not available for betting. Participants were first presented with those game cues for 1 s (showing the logos of the two teams playing), and after a jittered delay (blank screen, range: 1.7–2.6 s), an “available” cue (green frame and check mark) or “nonavailable” cue (red frame and cross signal) was presented for 4.8 s (see Figure 1). Each block consisted of 10 pseudo-randomized trials (5 “available” and 5 “nonavailable” trials; order

pseudo-randomized with Python's random generation module). Each scanning block terminated with an overview slide (8 s), displaying the five available matches presented during the block (see Figure 1). During this phase, participants orally reported the number of one game and the team that they wanted to bet on (e.g., “One, Chelsea”) via intercom to the experimenter. Participants were informed that they would receive the betting money once the sport event that he bet on had occurred (2 euros for a win; 1 euro for a draw, 0 euro for a loss). Thus, they could win from 0 euro (10 losing bets) up to 20 euros (10 winning bets). Finally, participants were informed that the task consisted of 10 blocks (100 trials in total), and that there were five blocks displaying games occurring during the scanning session weekend (“weekend 1”; indicated by “this weekend” appearing for 2 s at the beginning of the block; see Figure 1), and five blocks displaying games occurring the next weekend (“weekend 2”; indicated by “next weekend” appearing for 2 s at the beginning of the block). The “weekend 1” and “weekend 2” blocks were presented in alternating order (5 s white screen between blocks).

Several specific strategies were employed for preventing participants motion during the MRI session: (a) participants were instructed to relax and to remain still during the entire scanning session; (b) during the task instructions, the experimenters trained the participants on how to express their choice orally (during the overview slide) with a reduced level of mouth movements; and (c) within the head coil, participants head was secured and stabilized with supportive cushions. In addition, participants wore headphones (to facilitate communication with the experimenter), which further prevented (head) motion within the head coil during the MRI session. We also put a rest leg on the scanner table for participants' comfort.

Directly after the scanning session, participants were asked to complete rating scales. For each of the 50 games in the “available” and “nonavailable” conditions, participants were requested to indicate (a) which team they think would win the game (by circling the team;

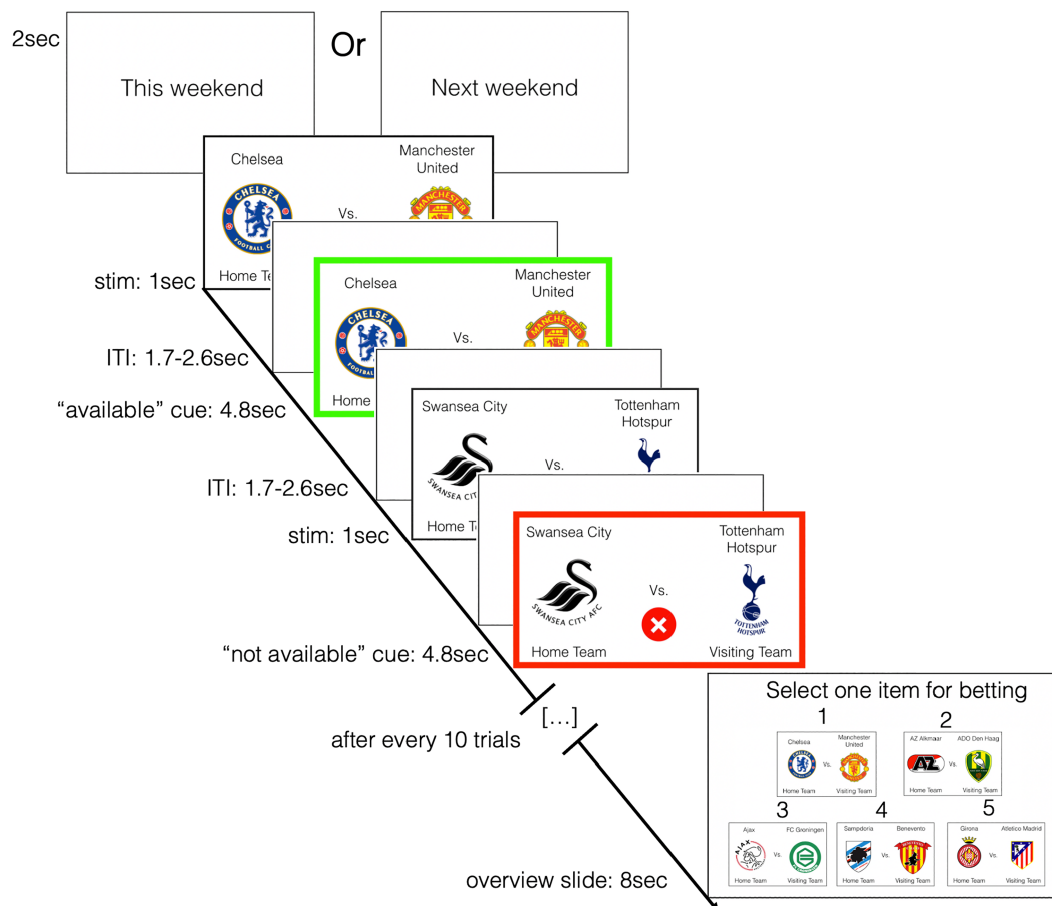


FIGURE 1 The cue-exposure task. Examples of sport cues used and of one overview slide. Participants viewed cues representing real sport events made available or blocked for betting. Participants were instructed to choose, after a run of 10 trials, one team they wanted to bet on. The red frame and the cross signal a trial nonavailable for betting. The green frame with the check mark indicates a trial available for betting. ITI, inter-trial interval [Correction added after first online publication on 23 December 2020: The figure 1 has been updated in this current version.]

there was not the option to choose a draw), and (b) how confident they were about their prediction (1 = *not at all*, 2 = *very little*, 3 = *somewhat*, 4 = *to a great extent*). Then, participants completed the questionnaires (PGSI, Brief Self-Control Scale, Sports Betting Passion Scale, and AUDIT), and indicated their bank account number for receiving the bonus payment from their bets (conducted after week-end 2).

2.7 | Data acquisition

Cues presentation was implemented using Python 2.7.16 and Pygame 1.9.3 on an IBM compatible PC. fMRI imaging was conducted with a 3T Siemens MAGNETOM Prisma scanner at the GfMRI Center, UZ Gent, Gent University. Functional scanning used a z-shim gradient echo EPI sequence with PACE (prospective acquisition correction). This sequence is designed to reduce signal loss in the prefrontal and orbitofrontal areas. The PACE option can help to reduce the impact of head motion during data acquisition. The parameters were: TR = 1720 ms; TE = 27 ms; flip angle = 66°. Fifty-two 2.5 mm axial slices were used to cover the whole cerebral cortex and most of the

cerebellum without gap. The slices were tilted approximately 30° clockwise along the AC-PC plane to improve the signal-to-noise ratio. A 176-slice MPRAGE structural sequence was also acquired (1 mm slice thickness; TI = 900 ms; TR = 2,250 ms; TE = 4.18 ms; flip angle 9°). Prior to the EPI sequence, standard Siemens magnetic field maps were collected with the same slice prescription as the functional scans using a multi-echo gradient echo acquisition (effective EPI echo spacing = 0.52 ms, EPI TE = 27 ms, % signal loss threshold = 10). These field maps were used for correction of geometric distortions in the EPI data caused by magnetic field inhomogeneity.

2.8 | Image preprocessing

Image preprocessing was carried out using the fMRI Expert Analysis Tool (version 6.00, part of the FSL package, FMRIB software library, version 5.0.9, www.fmrib.ox.ac.uk/fsl). The first three sets of each participant's functional data were discarded to allow the MR signal to reach a steady state. Functional data for each participant were motion-corrected using rigid-body registration, implemented in FMRIB Software Library (FSL)'s linear registration tool, MCFLIRT.⁴⁴

All participants ($N = 65$) demonstrated less than 1.0 mm of either absolute or relative motion. Hence, head motion did not lead to exclude any participant. After motion correction and temporal high-pass filtering, each time series for geometric distortions caused by magnetic field inhomogeneity was corrected using field maps.^{45,46} Data were spatially smoothed using a 5-mm full-width-half-maximum (FWHM) Gaussian kernel. The data were filtered in the temporal domain using a nonlinear high pass filter with a 90 s cut-off (estimated using FSL's FMRI Export Analysis Tool, FEAT). A two-step registration procedure was used where EPI images were first co-registered to the MPRAGE structural image, and warped to standard (MNI) space, using FLIRT.^{44,47} Registration of MPRAGE structural image to MNI standard space was then further refined using FNIRT nonlinear registration.^{48,49} Statistical analyses were performed in the native image space, with the statistical maps normalized to the standard space prior to higher-level analysis.

2.9 | Brain imaging analyses

We compared BOLD activity during the onset of "available" and "nonavailable" trials (4.8 s; see Figure 1). To this aim, the brain imaging data were modeled using an event-related general linear model (GLM) within FSL's Improved Linear Model (FILM) module. First-level statistical analysis included the following explanatory variables (EV): EV1: onsets for available trials, EV2: parametric modulator (PM) assessing winning confidence for available trials, EV3: onsets for nonavailable trials; EV4: PM assessing winning confidence for nonavailable trials; EV5 (of no-interest): overview slides (i.e., onset with duration of 8 s at the end of each block). The PM regressors were computed by mean centering the post-task confidence ratings for each participant. The event onsets were convolved with canonical hemodynamic response function (HRF; double-gamma) to generate regressors used in the GLM.

For each participant, we computed the following contrasts: (a) available minus nonavailable trials (for testing H1), (b) nonavailable minus available (for testing H2); (c) PM available minus PM nonavailable trials (for testing H1_PM); and (d) PM nonavailable minus PM available trials (for testing H2_PM). These were then included into a random-effect model for group analysis across all participants ($N = 65$) with mean-centered scores of trait-self-control, sports betting passion (harmonious and obsessive) and AUDIT scores as covariates. We computed a random-effect model for between-groups analysis (four two-tailed tests in total) to compare NPB ($n = 35$) with PB ($n = 30$) (i.e., without covariate). We also ran a separate GLM that included "time" as EV (comparing available and unavailable events occurring either on "weekend 1" or on "weekend 2"). These analyses did not reveal any significant differences in the activations related to "weekend 1" and "weekend 2" events. All group analyses were performed using FSL RANDOMIZE (nonparametric permutation analyses, with 10,000 random permutations of the data) and threshold-free cluster enhancement (TFCE) with $p < 0.05$, FWE corrected for multiple comparisons across the whole brain.

3 | RESULTS

3.1 | Behavioral findings on posttask rating questionnaires

The examination of Bayes factors revealed inconclusive evidence regarding a difference on mean scores of winning confidence between the events from the available and nonavailable conditions ($BF_{10} = 1.94$), and moderate support for an absence of group difference in terms of winning confidence (see Table 1 for descriptive statistics and BF_{10} for between-groups comparisons). Moreover, comparisons of the distribution of confidence response types (1 = *not at all*, 2 = *very little*, 3 = *somewhat*, 4 = *to a great extent*) for available and nonavailable matches revealed moderate support for H_0 regarding a between-groups difference (see Table S1). Noteworthy, we observed that the matches related to the highest winning confidence level were most often selected for betting during the task (mean scores of winning confidence for the games selected for betting during the cue reactivity task = 3.22; $SD = 0.18$). Moreover, in each block, we observed that the four other available games for betting (i.e., those not chosen for betting by the participant in the end of each block) were always associated with either lower or equal (but never higher) scores of winning confidence on the posttask rating questionnaires.

3.2 | Brain activation for cues available vs. nonavailable for betting

3.2.1 | Whole group

Across all participants ($N = 65$), for the "available minus nonavailable trials" contrast, we observed a very large cluster of activation (voxel cluster size = 93,491), with peak of activation in the medial frontal gyrus (peak = 26, 42, 24), extending into brain regions encompassing the striatum, the insular cortex, the amygdala, as well as the superior, medial and inferior frontal cortices (see Figure 2A).

For the "nonavailable minus available trials" contrast (see Figure 2B), a significant activation was observed in the frontal medial cortex (voxel cluster size = 3,525, peak = 0, 50, -30), extending into the OFC, and the ventral striatum.

No significant covariate effect of the AUDIT, harmonious sports betting passion, obsessive sports betting passion, and trait-self-control was observed.

3.2.2 | Between-groups

For the "available minus nonavailable trials" contrast, we observed between-groups differences in the right dorsal striatum (voxel cluster size = 721, peak = 24, -8, -2), extending into right posterior insula, right thalamus, and right parahippocampal gyrus (see Figure 3A). No between-group activation was observed for the "nonavailable minus available trials" contrast.

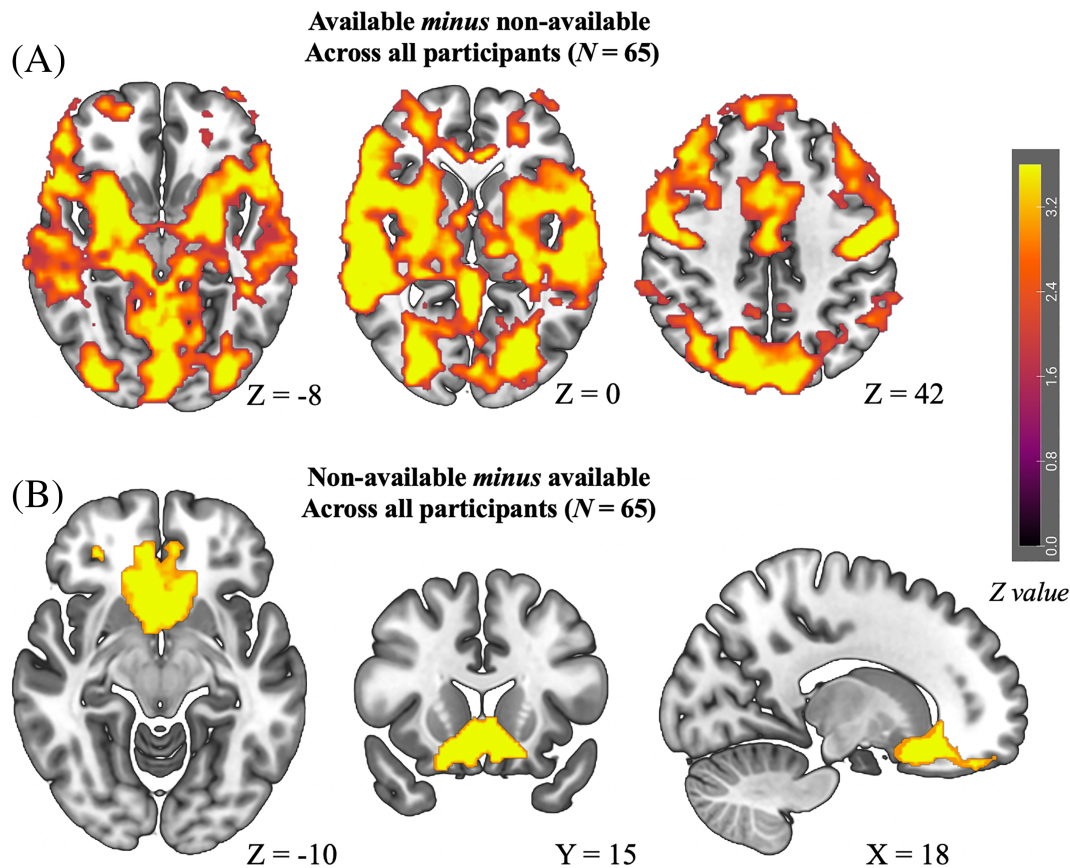


FIGURE 2 Across all participants ($N = 65$), (A) there was an extended pattern of brain activation for the “available minus nonavailable trials” contrast; (B) increased activation in the medial frontal gyrus, the orbitofrontal cortex, and the ventral striatum for the “nonavailable minus available trials” contrast. All images were thresholded using FSL RANDOMIZE (with 10,000 random permutations of the data) and TFCE with $p < 0.05$, FWE corrected for multiple comparisons across the whole brain. Left on Right

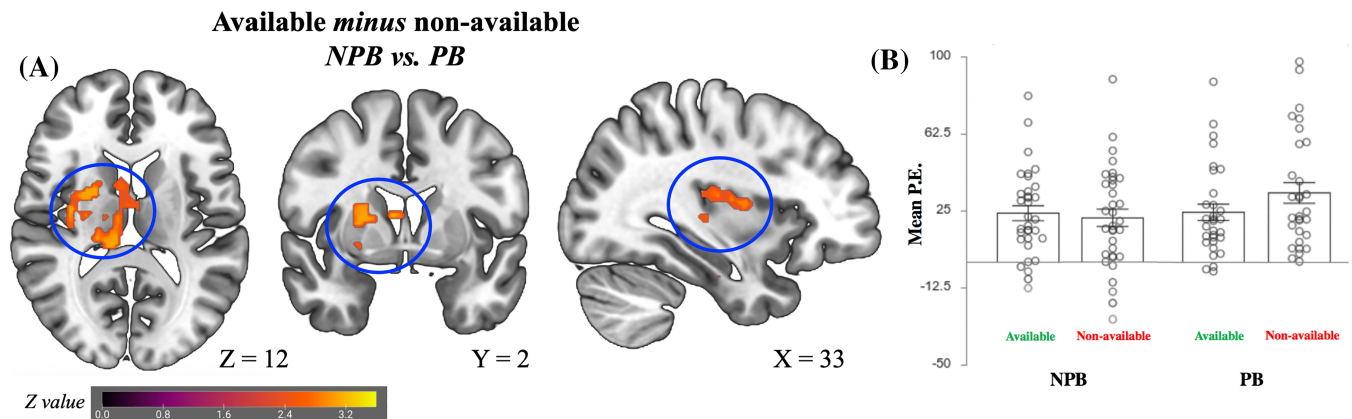


FIGURE 3 Between-group findings. (A) For the “available minus nonavailable trials” contrast, between-groups differences were observed in the right dorsal striatum, right posterior insula, right thalamus, and right parahippocampal gyrus. These images were thresholded using FSL RANDOMIZE (with 10,000 random permutations of the data) and TFCE with $p < 0.05$, FWE corrected for multiple comparisons across the whole brain. Left on Right; (B) increased reactivity of PB to nonavailable trials. These plots represent mean parameter estimate (PE) within the cluster of voxels showing significant activation in the between-group comparisons for the “available minus nonavailable trials” contrast (blue circle). Bidirectional error bars represent standard error

3.2.3 | Supplementary analyses

To determine the direction of the between-group differences for the “available minus nonavailable trials” contrast, we ran two additional simple contrasts: available trials (minus implicit baseline), and nonavailable trials (minus implicit baseline). We then created a region of interest (ROI) from the cluster of voxels with significant activation in the between-group comparison for the “available minus nonavailable trials” contrast (ROI binarized mask available at <https://neurovault.org/collections/6566/>). Using this mask, ROI analyses were performed by extracting parameter estimates (PEs) for each participant and separately for the “available (minus implicit baseline)” and the “nonavailable (minus implicit baseline)” contrasts. We then plotted the mean PEs in each group (NPB; PB) and for each type of events (available; nonavailable). Figure 3B shows that the between-group difference for the “available minus nonavailable trials” contrast is mostly driven by an increased reactivity of PB to nonavailable trials.

3.3 | Parametric contrasts with winning confidence

3.3.1 | Whole group

Figure 4 shows how the relationship between brain activity and winning confidence differs between nonavailable trials and available trials (i.e., the “PM nonavailable minus PM available trials” contrast). This analysis revealed a very large cluster of activation (voxel cluster size = 71,592), with peak of activation in the left superior temporal gyrus (peak = $-66, -4, 2$), extending into the hippocampus, the amygdala, insula, cingulate, parietal, and occipital gyri. Others significant clusters of activation were observed in the left dorsal striatum (voxel cluster size = 107, peak = $-18, 8, 18$), and the left middle frontal gyrus (voxel cluster size = 65, peak = $-24, 58, 16$).

We observed a negative covariate effect of trait-self-control on the “PM nonavailable minus PM available trials” contrast. Hence, the positive correlation between brain activity and confidence in the “nonavailable minus available” PM contrast was higher among participants with lower trait-self-control. This covariate effect was observed in an extended activation cluster (voxel cluster size = 3,799), with a peak in the precuneus cortex (peak = $14, -50, 16$), extending into brain regions encompassing the ventral striatum, left hippocampus, thalamus, amygdala as well as in parahippocampal, middle temporal, angular, cingulate, and middle frontal gyri (see Figure 5). We also run an additional analysis by using activation from the “PM nonavailable minus PM available trials” contrast (from the whole group analyses) as a mask to determine the overlap with the covariate effect of trait-self-control. We observed an overlap within the following regions: lateral occipital cortex, inferior temporal gyrus, superior parietal lobule, middle temporal gyrus, superior frontal gyrus, paracingulate gyrus, frontal pole, and postcentral gyrus (for further details, see Figure S2). There was no covariate effect of the AUDIT, harmonious sports betting passion, and obsessive sports betting passion.

No significant activation or covariate effect was observed for the parametric contrasts “PM available minus PM nonavailable trials.”

3.3.2 | Between-group findings

No between-group effect was observed for the parametric contrasts “PM available minus PM nonavailable trials,” and “PM nonavailable minus PM available trials.”

4 | DISCUSSION

We investigated the brain correlates of sports betting cue exposure as a function of problem gambling severity, sports betting passion and

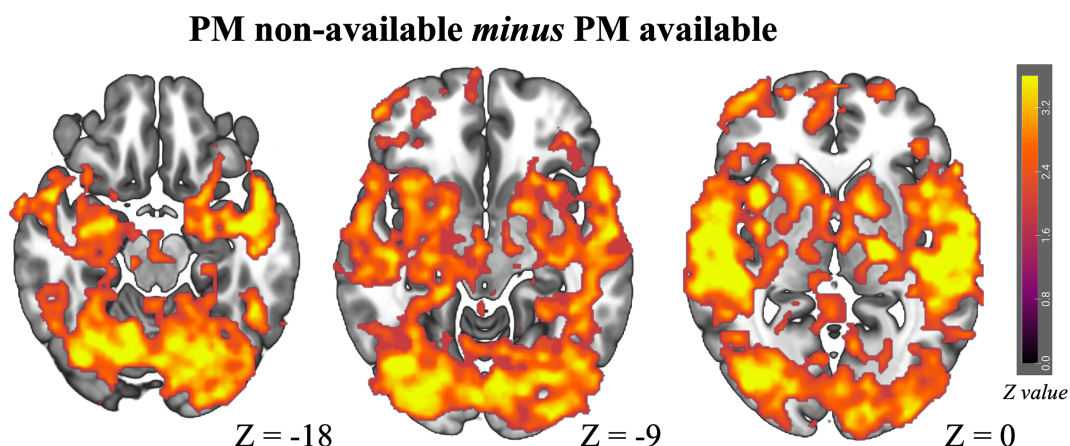


FIGURE 4 Across all participants, there was an increased brain activity for the contrast “PM nonavailable trials minus PM available trials,” in the left occipital pole, bilateral parahippocampal gyrus extending into the hippocampus, the amygdala, posterior insula, posterior cingulate gyrus, and superior temporal gyrus. All images were thresholded using FSL RANDOMIZE (with 10,000 random permutations of the data) and TFCE with $p < 0.05$ FWE corrected for multiple comparisons across the whole brain. Left on Right. PM, parametric modulation

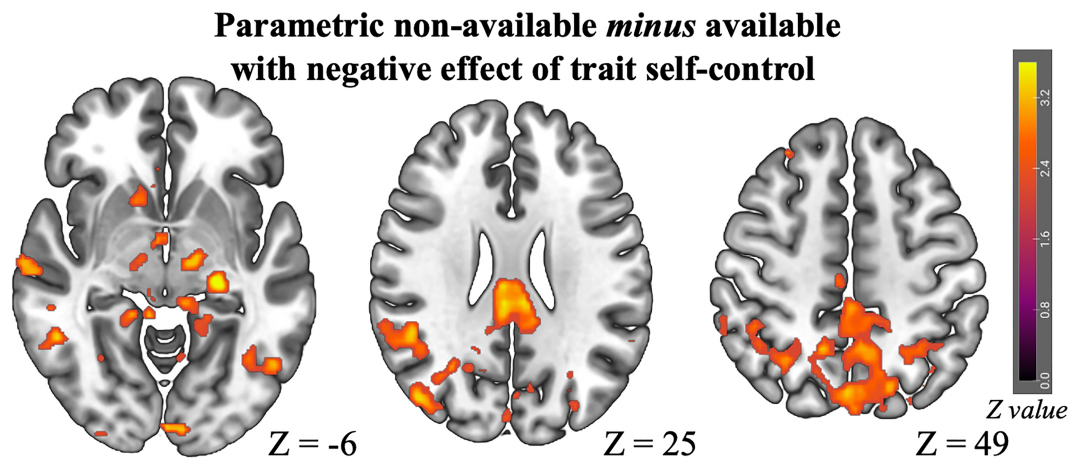


FIGURE 5 Across all participants, lower trait-self-control was associated with a higher parametric modulation (PM) of brain activity with confidence for the “PM nonavailable minus PM available trials” contrast. All images were thresholded using FSL RANDOMIZE (with 10,000 random permutations of the data) and TFCE with $p < 0.05$, FWE corrected for multiple comparisons across the whole brain. Left on Right

trait-self-control. We recruited a sample of sports fans with (PB) or without (NPB) problematic sports betting. We used an ecological fMRI cue exposure task depicting real sport events made available or non-available for betting.

4.1 | Betting (un)availability during sports picture exposure

We observed an extended activation cluster when contrasting cues available for betting against cues nonavailable for betting. This reflects the complex nature of processes induced by cues signaling sports betting availability. More specifically, the exposure to cues available for betting did not only result in activations related to viewing cues (as it would in a pure cue reactivity task¹⁸) but also likely triggered high-order deliberative cognitive processes (i.e., deliberating on whether to select the game for betting at the end of the block).

When comparing nonavailable and available trials, we found higher activation in the OFC and ventral striatum. This result is intriguing as this pattern of activation is commonly observed in paradigms involving the delivery of monetary rewards, where increases are correlated with reward values and predictability.^{50–55} Nevertheless, the OFC is also involved in the processing of a variety of affective states and in the coding of loss and reward outcomes.^{56–61} fMRI studies also identified trial-by-trial changes in the ventral striatum while processing surprise-related signals,⁶² or experiencing differences between expected and gained reward value.⁵⁶ Hence, the unexpected changes that participants experienced during unavailable trials (i.e., reward blocking) may have involved elements related to each of these phenomena.

Importantly, when examining the PM of winning confidence across nonavailable trials minus available trials, we observed activation in an extended cluster that also encompassed fronto-striatal as well as posterior insular and amygdalar activations. These results are

in line with previous brain imaging studies showing that the posterior insula and the amygdala are triggered during reward omission and frustration induction.^{22,23} Surprisingly, no significant cluster of activation was observed for the PM of winning confidence across available trials minus nonavailable trials. One explanation for this result is that the use of a similar amount of money (i.e., 2 euros for a win whatever the winning confidence of the match) might have lowered the impact of parametric increases of winning confidence for available trials. One option for testing this assumption would be to use a more ecological task design featuring win/loss money ratios that are modulated according to the riskiness of the bet. It would also be important to examine the impact of individuals' betting preferences (e.g., to favor high-risk or low-risk matches), which may further modulate brain reactivity to sports betting cues.

4.2 | Problem gambling status

When comparing available trials with nonavailable ones, we first observed between-group differences in the right dorsal striatum, the right posterior insula, and the right parahippocampal gyrus. Supplementary analyses then revealed that this between-group difference was driven by increased reactivity to nonavailable trials in PB. Hence, in line with H2 (but not with H1), PB exhibited enhanced brain reactivity while facing sport cues that were blocked for betting. No significant between-group activation was observed for the other three contrasts: nonavailable minus available, PM available minus PM nonavailable trials, and PM nonavailable minus PM available trials.

Taken together, these findings suggest that PB are more sensitive to the transient inaccessibility of a betting opportunity. This interpretation echoes the incentive sensitization theory⁶³ which posits that wanting (i.e., the motivation to get a particular reward) increases during reward deprivation.⁶⁴ The present data suggest that a key marker

of problem gambling lies in brain reactivity to transient deprivation of sports betting opportunities. It should also be acknowledged that the four between-group contrasts were tested without adjusting the TFCE alpha for multiple comparisons. This aspect highlights the exploratory nature of the present study.

4.3 | Sports betting passion and trait-self-control

We did not find any evidence that self-reported harmonious or obsessive sports betting passion modulates brain reactivity to sports betting cues. This suggests that these self-report constructs did not reflect the brain processes triggered by the cue exposure task. By contrast, we found that self-reported trait-self-control was associated with brain cue reactivity for the parametric contrast comparing the winning confidence in nonavailable trials versus available trials. Specifically, the lower trait-self-control, the higher brain reactivity in trials non-available for betting that were associated with increasing levels of winning confidence. This indicates that sport fans with lower trait-self-control were more reactive to the reward blocking procedure than those with higher trait-self-control. In line with our exploratory expectations and with previous fMRI studies,³⁷ we found that this pattern was partly located in the amygdala, and featured an extended activation cluster encompassing the ventral striatum, superior frontal cortices, and occipital gyri. Overall, these results suggest that trait-self-control, but not harmonious and obsessive passion, could be used for future studies as a sensitive marker of BOLD reactivity to gambling cues.

4.4 | Potential limitations and future directions

Posttask ratings were used to measure winning confidence, but we did not rate participants' levels of frustration related to each blocked trial. The rationale for employing this measure is that every experienced sports fan can express a degree of confidence about the results of forthcoming sport events.^{5,65} This aspect represented a considerable advantage for computing parametric contrasts at each event of our experimental task, which alternated experimental conditions on a trial-per-trial basis. Nevertheless, because we solely focused on confidence ratings, it remains unclear whether participants experienced high frustration levels when facing unavailable matches associated with high degrees of winning confidence. Frustration is usually induced using multitrials²³ or block-design procedures^{13,22} to elicit reward-deprivation feelings the closer an individual is to achieving a goal (i.e., manipulation of reward proximity^{22,23}). Future studies might adapt our cue exposure task with a parametric experimental manipulation of proximity, such as a four-step task where a sport event could turn out to be available or unavailable for betting (e.g., after 2, 4, 6, or 8 s of trial presentation).

A major strength of the present fMRI study is that we compared a group of problem sports bettors to a group of nonproblem frequent sports bettors (i.e., instead of nongambling controls). Groups were

thus matched on gambling type (football betting) and were exposed to ecological sports betting cues. The present sample did not include individuals from addiction treatment centers with a gambling disorder condition. Accordingly, participants' scores for obsessive sports betting passion were quite low. This might explain the absence of significant covariate effects related to (obsessive) sports betting passion. A potential next step for future studies would be to test whether brain *t*-maps from the present study (see <https://neurovault.org/collections/6566/>) could be used as potential diagnostic markers in classification studies,⁶⁶ where a machine learning algorithm would use these brain patterns to distinguish problematic from nonproblematic sport bettors.

4.5 | Conclusion

The present study extends the neuroimaging literature on problem gambling by offering a tenable blueprint on how the interaction between winning confidence and accessibility of sports-betting impact brain activation among people experiencing gambling-related harms.

ACKNOWLEDGEMENTS

D.B. is supported by the Luxembourg National Research Fund (FNR); CORE—Junior Track (BETHAB). P.M. (Senior Research Associate) is funded by the Belgian Fund for Scientific Research (F.R.S.—FNRS, Brussels, Belgium). C.B. was supported by the “Bijzonder Onderzoeksfonds” (grant number BOF 16/GOA/017), and the “Rode Neuzen” funding for scientific research (grant number GOF4617N).

CONFLICT OF INTEREST

All authors declare no conflicts of interest relevant to this manuscript.

AUTHORS CONTRIBUTION

DB, CB, AB, QH, MP, PM, GS, CV, and JB participated to the conception and design of the work. DB and CB were involved in data acquisition. DB undertook the data analysis. DB, CB, AB, QH, MP, PM, GS, CV, and JB participated to data interpretation and on the writing of the manuscript. All authors approve final version of the manuscript prior its submission. The authors would like to thank Jeanette Mumford for her advice on data analyses and the two anonymous reviewers for their insightful suggestions and careful reading of the manuscript.

ORCID

Damien Brevers  <https://orcid.org/0000-0003-4503-0898>

Chris Baeken  <https://orcid.org/0000-0001-9885-3041>

Qinghua He  <https://orcid.org/0000-0001-6396-6273>

Pierre Maurice  <https://orcid.org/0000-0003-0197-0810>

Guillaume Sescousse  <https://orcid.org/0000-0002-8556-3755>

Claus Vögele  <https://orcid.org/0000-0001-8086-0788>

Joël Billieux  <https://orcid.org/0000-0002-7388-6194>

REFERENCES

- Pitt H, Thomas SL, Bestman A, Daub M, Derevensky J. What do children observe and learn from televised sports betting advertisements? A qualitative study among Australian children. *Aust N Z J Public Health*. 2017;41(6):604-610.
- Sharman S, Ferreira CA, Newall PWS. Exposure to gambling and alcohol marketing in soccer matchday programmes. *J Gambl Stud*. 2019;36(3):979-988. <https://doi.org/10.1007/s10899-019-09912-6>
- Newall PWS, Thobhani A, Walasek L, Meyer C. Live-odds gambling advertising and consumer protection. *PLoS ONE*. 2019;14(6):e0216876.
- Thomas SL, Bestman A, Pitt H, et al. Young people's awareness of the timing and placement of gambling advertising on traditional and social media platforms: a study of 11-16-year-olds in Australia. *Harm Reduct J*. 2018;15(1):51.
- Brevers D, Herremans SC, He Q, et al. Facing temptation: the neural correlates of gambling availability during sports picture exposure. *Cogn Affect Behav Neurosci*. 2018;18(4):718-729.
- Brevers D, Sescousse G, Maurage P, Billieux J. Examining neural reactivity to gambling cues in the age of online betting. *Curr Behav Neurosci Rep*. 2019;6(3):59-71.
- Sescousse G, Barbalat G, Domenech P, Dreher JC. Imbalance in the sensitivity to different types of rewards in pathological gambling. *Brain*. 2013;136(Pt 8):2527-2538.
- van Holst RJ, Veltman DJ, Büchel C, van den Brink W, Goudriaan AE. Distorted expectancy coding in problem gambling: is the addictive in the anticipation? *Biol Psychiatry*. 2012;71(8):741-748.
- Balodis IM, Kober H, Worhunsky PD, Stevens MC, Pearson GD, Potenza MN. Diminished frontostriatal activity during processing of monetary rewards and losses in pathological gambling. *Biol Psychiatry*. 2012;71(8):749-757.
- Crockford DN, Goodyear B, Edwards J, Quickfall J, el-Guebaly N. Cue-induced brain activity in pathological gamblers. *Biol Psychiatry*. 2005;58(10):787-795.
- Goudriaan AE, de Ruiter MB, van den Brink W, Oosterlaan J, Veltman J. Brain activation patterns associated with cue reactivity and craving in abstinent problem gamblers, heavy smokers and non-problem controls: an fMRI study. *Addict Biol*. 2010;15(4):491-503.
- Kober H, Lacadie CM, Wexler BE, Malison RT, Sinha R, Potenza MN. Brain Activity During Cocaine Craving and Gambling Urges: An fMRI Study. *Neuropsychopharmacology*. 2016;41(2):628-637.
- Limbrick-Oldfield EH, Mick I, Cocks RE, et al. Neural substrates of cue reactivity and craving in gambling disorder. *Transl Psychiatry*. 2017;7(1):e992.
- Potenza MN, Steinberg MA, Skudlarski P, et al. Gambling urges in pathological gambling: a functional magnetic resonance imaging study. *Arch Gen Psychiatry*. 2003;60(8):828-836.
- Potenza MN. Review. The neurobiology of pathological gambling and drug addiction: an overview and new findings. *Philos Trans R Soc Lond B Biol Sci*. 2008;363(1507):3181-3189.
- van Holst RJ, van Holstein M, van den Brink W, Veltman DJ, Goudriaan AE. Response inhibition during cue reactivity in problem gamblers: an fMRI study. *PLoS ONE*. 2012;7(3):e30909.
- George O, Koob GF. Individual differences in the neuropsychopathology of addiction. *Dialogues Clin Neurosci*. 2017;19(3):217-229.
- Jasinska AJ, Stein EA, Kaiser J, Naumer MJ, Yalachkov Y. Factors modulating neural reactivity to drug cues in addiction: a survey of human neuroimaging studies. *Neurosci Biobehav Rev*. 2014;38:1-16.
- Ihssen N, Cox WM, Wiggert A, Fadardi JS, Linden DEJ. Differentiating heavy from light drinkers by neural responses to visual alcohol cues and other motivational stimuli. *Cereb Cortex*. 2011;21(6):1408-1415.
- Wilson SJ, Sayette MA, Fiez JA. Prefrontal responses to drug cues: a neurocognitive analysis. *Nat Neurosci*. 2004;7(3):211-214.
- Yalachkov Y, Kaiser J, Naumer MJ. Functional neuroimaging studies in addiction: multisensory drug stimuli and neural cue reactivity. *Neurosci Biobehav Rev*. 2012;36(2):825-835.
- Bierzyńska M, Bielecki M, Marchewka A, et al. Effect of frustration on brain activation pattern in subjects with different temperament. *Front Psychol*. 2015;6:1989.
- Yu R, Mobbs D, Seymour B, Rowe JB, Calder AJ. The neural signature of escalating frustration in humans. *Cortex*. 2014;54:165-178.
- Weiss NH, Sullivan TP, Tull MT. Explicating the role of emotion dysregulation in risky behaviors: a review and synthesis of the literature with directions for future research and clinical practice. *Curr Opin Psychol*. 2015;3:22-29.
- Xue G, Lu Z, Levin IP, Bechara A. The impact of prior risk experiences on subsequent risky decision-making: the role of the insula. *Neuroimage*. 2010;50(2):709-716.
- Shapiro AD, Grafton ST. Subjective value then confidence in human ventromedial prefrontal cortex. *PLoS ONE*. 2020;15(2):e0225617.
- Lebreton M, Abitbol R, Daunizeau J, Pessiglione M. Automatic integration of confidence in the brain valuation signal. *Nat Neurosci*. 2015;18(8):1159-1167.
- Rousseau FL, Vallerand RJ, Ratelle CF, Mageau GA, Provencher PJ. Passion and gambling: on the validation of the Gambling Passion Scale (GPS). *J Gambl Stud*. 2002;18:45-66.
- Duarte IC, Afonso S, Jorge H, Cayolla R, Ferreira C, Castelo-Branco M. Tribal love: the neural correlates of passionate engagement in football fans. *Soc Cogn Affect Neurosci*. 2017;12(5):718-728.
- Duckworth AL, Seligman MEP. The science and practice of self-control. *Perspect Psychol Sci*. 2017;12(5):715-718.
- Duckworth AL, Gendler TS, Gross JJ. Situational strategies for self-control. *Perspect Psychol Sci*. 2016;11(1):35-55.
- Fujita K. On conceptualizing self-control as more than the effortful inhibition of impulses. *Pers Soc Psychol Rev*. 2011;15(4):352-366.
- Baumeister RF, Bratslavsky E, Muraven M, Tice DM. Ego depletion: is the active self a limited resource? *J Pers Soc Psychol*. 1998;74(5):1252-1265.
- Brevers D, Turel O. Strategies for self-controlling social media use: Classification and role in preventing social media addiction symptoms. *J Behav Addict*. 2019;8(3):554-563.
- de Ridder DTD, Lensvelt-Mulders G, Finkenauer C, Stok FM, Baumeister RF. Taking stock of self-control: a meta-analysis of how trait self-control relates to a wide range of behaviors. *Pers Soc Psychol Rev*. 2012;16(1):76-99.
- Hagger MS, Chatzisarantis NLD, Alberts H, et al. A Multilab preregistered replication of the ego-depletion effect. *Perspect Psychol Sci*. 2016;11(4):546-573.
- Paschke LM, Dörfel D, Steimke R, et al. Individual differences in self-reported self-control predict successful emotion regulation. *Soc Cogn Affect Neurosci*. 2016;11(8):1193-1204.
- Ferris J, Wynne H. The Canadian Problem Gambling Index: Final report. Ottawa, ON: Canadian Centre on Substance Abuse; 2011.
- Walker M, Blaszczynski A. *Clinical assessment of problem gamblers identified using the Canadian Problem Gambling Index*. Independent Gambling Authority: Adelaide; 2011.
- Vallerand RJ, Blanchard C, Mageau GA, et al. Les passions de l'âme: on obsessive and harmonious passion. *J Pers Soc Psychol*. 2003;85(4):756-767.
- Tangney JP, Baumeister RF, Boone AL. High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. *J Pers*. 2004;72(2):271-324.
- Brevers D, Foucart J, Verbanck P, Turel O. Examination of the validity and reliability of the French version of the Brief Self-Control Scale. *Can J Behav Sci*. 2017;49(4):243-250.
- Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test

- (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addiction*. 1993;88(6):791-804.
44. Jenkinson M, Bannister P, Brady M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage*. 17(2):825-841.
 45. Jenkinson M. (2003): A fast, automated, n-dimensional phase unwrapping algorithm. *Magn Reson Med*. 2002;49:193-197.
 46. Jenkinson M. Improving the registration of B0-disorted EPI images using calculated cost function weights. Paper presented at Tenth International Conference on Functional Mapping of the Human Brain, Budapest, Hungary; 2004.
 47. Jenkinson M, Smith S. A global optimisation method for robust affine registration of brain images. *Med Image Anal*. 2001;5(2):143-156.
 48. Andersson JLR, Jenkinson M, Smith S. Non-linear optimisation (FMRIB Technical Report TR07JA1). Oxford, UK: FMRIB Analysis Group Retrieved from www.fmrib.ox.ac.uk/datasets/techrep;2007
 49. Andersson JLR, Jenkinson M, Smith S. Non-linear registration, aka spatial normalisation (FMRIB Technical Report TR07JA2). Oxford, UK: FMRIB Analysis Group. Retrieved from. www.fmrib.ox.ac.uk/datasets/techrep;2007
 50. Daniel R, Pollmann S. A universal role of the ventral striatum in reward-based learning: evidence from human studies. *Neurobiol Learn Mem*. 2014;114:90-100.
 51. Delgado MR, Locke HM, Stenger VA, Fiez JA. Dorsal striatum responses to reward and punishment: effects of valence and magnitude manipulations. *Cogn Affect Behav Neurosci*. 2003;3(1):27-38.
 52. Fouragnan E, Retzler C, Philiastides MG. Separate neural representations of prediction error valence and surprise: evidence from an fMRI meta-analysis. *Hum Brain Mapp*. 2018;39(7):2887-2906.
 53. Galvan A. Adolescent Development of the Reward System. *Front Hum Neurosci*. 2010;4:6.
 54. Heekeren HR, Wartenburger I, Marschner A, Mell T, Villringer A, Reischies FM. Role of ventral striatum in reward-based decision making. *Neuroreport*. 2007;18(10):951-955.
 55. Knutson B, Fong GW, Adams CM, Varner JL, Hommer D. Dissociation of reward anticipation and outcome with event-related fMRI. *Neuroreport*. 2001;12(17):3683-3687.
 56. O'Doherty J, Critchley H, Deichmann R, Dolan RJ. Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. *J Neurosci*. 2003;23(21):7931-7939.
 57. Howard JD, Kahnt T. Identity-specific reward representations in orbitofrontal cortex are modulated by selective devaluation. *J Neurosci*. 2017;37(10):2627-2638.
 58. Howard JD, Kahnt T. Identity prediction errors in the human midbrain update reward-identity expectations in the orbitofrontal cortex. *Nat Commun*. 2018;9:1611.
 59. Lopatina N, McDannald MA, Styer CV, Sadacca BF, Cheer JF, Schoenbaum G. Lateral orbitofrontal neurons acquire responses to upshifted, downshifted, or blocked cues during unblocking. *Elife*. 2015;4:e11299.
 60. McDannald MA, Esber GR, Wegener MA, et al. Orbitofrontal neurons acquire responses to 'valueless' Pavlovian cues during unblocking. *Elife*. 2014;3:e02653.
 61. Stalnaker TA, Cooch NK, Schoenbaum G. What the orbitofrontal cortex does not do. *Nat Neurosci*. 2015;18(5):620-627.
 62. Chumbley JR, Burke CJ, Stephan KE, Friston KJ, Tobler PN, Fehr E. Surprise beyond prediction error. *Hum Brain Mapp*. 2014;35(9):4805-4814.
 63. Robinson TE, Berridge KC. The neural basis of drug craving: an incentive-sensitization theory of addiction. *Brain Res Brain Res Rev*. 1993;18(3):247-291.
 64. Epstein LH, Truesdale R, Wojcik A, Paluch RA, Raynor HA. (2003) Effects of deprivation on hedonics and reinforcing value of food. *Physiol Behav*. 2003;78:221-227.
 65. Brevers D. "When viewing is already gambling"—the need for eye-tracking research to examine sports betting cue reactivity. *Addiction*. 2020;115(6):1139-1140. <https://doi.org/10.1111/add.14952>
 66. Wen D, Wei Z, Zhou Y, Li G, Zhang X, Han W. Deep Learning Methods to Process fMRI Data and Their Application in the Diagnosis of Cognitive Impairment: A Brief Overview and Our Opinion. *Front Neuroinform*. 2018;26:12-23.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Brevers D, Baeken C, Bechara A, et al. Increased brain reactivity to gambling unavailability as a marker of problem gambling. *Addiction Biology*. 2021;26:e12996. <https://doi.org/10.1111/adb.12996>