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Interoception and Respiratory Sinus Arrhythmia in Gambling Disorder

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Impact Statement

Gambling behaviour has longstanding links with physiological arousal. This study compared individuals with gambling disorder and a healthy control group in interoception, i.e. the ability to detect physiological signals, and on resting-state respiratory sinus arrhythmia (RSA), a marker of parasympathetic function. The groups did not differ significantly across multiple measures of interoception, and a group difference in RSA was driven by individual differences in age and smoking. Our findings provide novel context to theories that emphasize physiological arousal as a reinforcer of gambling behaviour, and highlight the importance of controlling for smoking behaviour in physiological studies of gambling.

Interoception and Respiratory Sinus Arrhythmia in Gambling Disorder

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Running title: Interoception and RSA in gambling disorder

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Abstract

Gambling has long-standing links with excitement and physiological arousal, but prior research has not considered i) gamblers' ability to detect internal physiological signals, or ii) markers of parasympathetic functioning. The present study measured interoception in individuals with gambling disorder, using self-report measures and a heart beat counting task administered at rest. Resting state Respiratory Sinus Arrhythmia (RSA), an index of heart rate variability, was measured as a proxy for parasympathetic control and emotional regulation capacity. In a case-control design, 50 individuals with gambling disorder were compared against 35 controls without gambling problems. Participants completed two self-report measures of bodily awareness and a behavioural test of heart beat counting. A resting state electrocardiogram (five minutes) was used to calculate RSA. There were no significant differences on the self-report or behavioral interoception probes. The group with gambling disorder displayed significantly reduced RSA, which at face value is consistent with reduced parasympathetic control. However, the group difference in RSA did not survive controlling for age and smoking status, as established predictors of heart rate variability. Our findings do not support any changes in interoceptive processing in people with gambling disorder, at least under resting conditions. Our observation that group differences in RSA are partly explained by smoking behavior highlights the importance of controlling for nicotine use in future research characterizing physiological functioning and emotional regulation in disordered gambling.

Keywords: cardiac perception, heart beat counting, respiratory sinus arrhythmia, decision-making, addictions

1. Introduction

Physiological arousal, with excitement as its subjective counterpart, has long been recognized as central to psychological models of gambling and disordered gambling (Baudinet & Blaszczynski, 2013; Rockloff & Greer, 2010; Sharpe, Tarrier, Schotte, & Spence, 1995). A classic study used ambulatory cardiac monitoring to record heart rate as experienced blackjack players gambled in a casino venue (Anderson & Brown, 1984). Heart rate increased by an average of 23 beats per minute above resting baseline. These heart rate changes were greater in naturalistic (i.e. casino) conditions compared to a laboratory condition, and correlated with trait variables including sensation seeking. Heart rate changes and other signs of physiological arousal have been confirmed during engagement in other forms of gambling, including slot machine play (Carroll & Huxley, 1994; Coventry & Constable, 1999) and horse-race betting (Leary & Dickerson, 1985). This arousal may constitute an important source of reinforcement in gambling (Sharpe, 2004; Wulfert, Roland, Hartley, Wang, & Franco, 2005). Effectively, excitement may be "the gambler's drug" (Boyd, 1982). Based on this notion, it is an intuitive prediction that people with gambling disorder should show greater increases in arousal during gambling than non-problematic players. Curiously, there is little compelling support for this arousal hypothesis: although there have been some positive findings (Leary & Dickerson, 1985; Moodie & Finnigan, 2005), other studies have observed no group differences in arousal (Carroll & Huxley, 1994; Diskin & Hodgins, 2003) and even evidence of reduced arousal after gambling (Griffiths, 1993).

To date, this research on arousal in gambling has paid minimal attention to gamblers' abilities to *detect* these physiological signals, focussing instead on the strength of the bodily signals themselves. The term interoception refers to the processes by which physiological signals in the body are transmitted to the brain, to detect and generate awareness of these internal changes (Critchley & Garfinkel, 2017). Relevant interoceptive signals in gambling include pounding heart, sweating of the palms, or gut movements (Wray & Dickerson, 1981). In the general population, substantial individual differences exist in interoceptive abilities at rest, as measured for example by the accuracy of counting heart beats (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015). Heart beat perception is predicted by neuronal density in the anterior insula (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004), a brain region that is widely implicated in interoception (Craig, 2002). Heart beat counting moderates the relationship between physiological signals and the subjective experience of arousal (i.e. excitement), and moderates the relationship between physiological signals and risky decision-making on a modification of the Iowa Gambling Task (Dunn, Galton, et al., 2010). In clinical studies, heightened interoceptive accuracy is seen in patients with panic disorder (Ehlers & Breuer, 1992), whose cardiac signals may become conditioned as threat cues and trigger a vicious cycle that can culminate in full-blown panic attacks. Interoception is impaired in depression (Dunn, Stefanovitch, et al., 2010; Dunn, Dalgleish, Ogilvie, & Lawrence, 2007), a condition that is highly co-morbid with gambling disorder (Fauth-Bühler et al., 2014; Kessler et al., 2008). It is also implicated in substance use disorders, especially in the generation of cravings (Verdejo-Garcia, Clark, & Dunn, 2012), although the construct has received little direct investigation in addictions research.

Several lines of evidence indicate that interoceptive processes may be relevant to problem gambling. First, the insula is involved in the representation and awareness of physiological states (Craig, 2002), and insula activation is observed in several aspects of disordered gambling, including subjective cravings (Limbrick-Oldfield et al., 2017), reward anticipation (Tsurumi et al., 2014) and the processing of decision uncertainty (Brevers et al., 2015). In addition, neurological patients with lesions affecting the insula were less susceptible to two gambling-related cognitive distortions, the near-miss effect and the gambler's fallacy (Clark, Studer, Bruss, Tranel, & Bechara, 2014). Second, there is increasing interest in mindfulness-based cognitive therapies in the treatment of gambling disorder (Reid, Di Tirro, & Fong, 2014; Toneatto, Pillai, & Courtice, 2014). One of the main components of mindfulness is to train an inner focus (e.g. on breathing or heart rate) as a means of coping and emotional regulation (Parkin et al., 2014). Reliable alterations in interoceptive processes in people with disordered gambling could influence their ability to harness mindfulness-based treatments. Third, prior studies have documented increases in the related construct of alexithymia in disordered gambling (Bonnaire, Bungener, & Varescon, 2013; Parker, Wood, Bond, & Shaughnessy, 2005), which is characterized by a reduced ability to detect and/or describe emotional feelings. Alexithymia has been related to (poor) interoception (Shah, Hall, Catmur, & Bird, 2016) and changes in risky decision-making, including loss chasing (Bibby, 2016).

In the present study, we assessed interoceptive processing using two established self-report measures, the Body Awareness Scale (Shields, Mallory, & Simon, 1989) and the Body Vigilance Questionnaire (Schmidt, Lerew, & Trakowski, 1997), as well as a behavioural test of cardiac perception (Schandry, 1981). In the behavioural task, participants count their number of heart beats occurring in signalled intervals, and these estimates are compared with the actual number of heart beats recorded on a concurrent electrocardiogram (ECG) trace. As heart rate changes are a robust and well-studied physiological sign of arousal in response to gambling, we reasoned that cardiac perception would be a relevant domain for interoceptive assessment in gambling disorder. As our assessment focussed on interoception at rest (i.e. outside of gambling engagement), we predicted that the group with gambling disorder would show impaired interoception scores, based on the prior evidence of alexithymia, depressive comorbidity, and putative benefits of mindfulness training. Our experiment was not intended to measure interoception *during* gambling engagement, when the stronger bodily signals associated with arousal might lead to distinct predictions.

A second aspect of psychophysiology was analyzed to test a distinct hypothesis in gambling disorder, regarding parasympathetic functioning and cardiac indices of emotional dysregulation. Prior studies of cardiac arousal during gambling have recorded heart rate and blood pressure (Carroll & Huxley, 1994; Diskin & Hodgins, 2003; Griffiths, 1993; Leary & Dickerson, 1985; Moodie & Finnigan, 2005). These parameters can be monitored easily in field studies, but are complex measures under the dual control of the sympathetic and parasympathetic autonomic branches (Berntson et al., 1997). Measures of heart rate *variability* provides a way to extract parasympathetic function more specifically (Allen, Chambers, & Towers, 2007). The parasympathetic branch serves in part to counteract sympathetic, fight-or-flight arousal, in order for the individual to recover from stress and promote homeostasis (Porges, 2007). Conversely, parasympathetic activity drops in response to challenge or stress, termed parasympathetic withdrawal. Parasympathetic control can be captured by the cyclic variability in inter-beat intervals that is specifically linked to respiration, a measure termed Respiratory Sinus Arrhythmia (RSA) (Berntson et al., 1997). A higher level of RSA under resting conditions indicates greater parasympathetic control, and is associated with higher emotion regulation ability on tasks including cognitive reappraisal of emotional stimuli and constructive coping (Appelhans & Luecken, 2006; Holzman & Bridgett, 2017). Substance use disorders, particularly alcohol use disorder, are reliably associated with reductions in RSA (Crowell, Price, Puzia, Yaptangco, & Cheng, 2017; Quintana, McGregor, Guastella, Malhi, & Kemp, 2013). Individuals with disordered gambling tend to show deficient emotional regulation on questionnaire measures (Ciccarelli, Nigro, Griffiths, Cosenza, & D'Olimpio, 2016; Williams, Grisham, Erskine, & Cassedy, 2012) and neuroimaging probes (Navas et al., 2017), but existing work has not examined psychophysiological indicators. In a previous study measuring RSA in a group of students and a group of regular slot machine gamblers, resting RSA was noted to be markedly lower in the regular gamblers, who displayed moderate levels of disordered gambling. However, the two groups in that study were not intended to be demographically balanced (Murch, Chu, & Clark, 2017). In the present study, we predicted that resting state RSA would be reduced in a group of individuals with gambling disorder.

2. Methods

2.1 Participants

Individuals with gambling disorder (n = 50) were recruited through two routes: i) online advertisements (n = 41), including Craigslist (an online community noticeboard), the University's online paid studies list, or directly contacting the laboratory website, or ii) local gambling treatment groups run by the provincial problem gambling program (n = 9). The gambling disorder participants comprised four subgroups in terms of their treatment profile: 32 gamblers had never sought treatment for gambling problems, 15 were currently receiving treatment, 2 had completed treatment and 1 had discontinued treatment. Upon completion of the study, participants in the gambling disorder group who were not currently in treatment were given information on local resources for problem gambling.

Diagnostic status of the gambling disorder group was confirmed using the Structured Clinical Interview for DSM-IV (First, Spitzer, Gibbon, & Williams, 1996) criteria administered as an interview by a research assistant. The DSM-IV criteria were recoded for DSM-5 to be consistent with the 4 from 9 threshold. Diagnostic status was corroborated by a score ≥ 8 on the Problem Gambling Severity Index (PGSI; Ferris & Wynne, 2001), a 9-item subscale of the Canadian Problem Gambling Inventory. The healthy comparison group (n = 35; henceforth controls) were recruited by advertisements and endorsed no DSM-5 criteria and scored ≤2 on the PGSI, indicating no- or low- risk gambling (26 scored 0, 9 scored 1-2). All participants were aged 19-65 years, in good physical health, able to read and understand fluent English, had normal-to-corrected eyesight and hearing. We excluded participants if they had a history of head injury or neurological illness, previous psychiatric hospitalization, or if psychoactive medications were initiated or changed dose in the past 6 weeks.

Other mental health problems were assessed using 8 of the 13 domains in the DSM-5 Cross Cutting Tool (American Psychiatric Association, 2013), as the SCID-5 Research Version was not released at the time when testing commenced. The 8 domains assessed were: depression, anger, mania, anxiety, somatic symptoms, sleep disturbance, repetitive thoughts and behaviours, and substance use. These questions pertain to symptom severity during the past 2 weeks. In each domain, participants who met the Level 1 screening threshold (Mild for 7/8 domains, Slight for substance use), received the further Level 2 questions to ascertain severity in each domain. For each domain, we report chi-squared analyses on the numbers of gambling disorder and controls meeting the Level 1 screening threshold, followed by t tests on the Level 2 raw severity scores within those subsets of participants. The Cross Cutting Tool has been shown to be have acceptable internal consistency and concurrent validity in adult samples (Bravo, Villarosa-Hurlocker, & Pearson, 2018). We administered the Depression Anxiety and Stress Scale-21 (Lovibond & Lovibond, 1995) to measure subclinical affective symptoms over the previous week, and the Fagerstrom Test for Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) to measure smoking severity in participants who smoked.

The protocol was approved by the Behavioural Research Ethics Board at the University of British Columbia (H15-00165) and all volunteers provided written informed consent. Participants were paid $30 in gift cards, they were reimbursed for transit / parking costs, and there was a bonus payment (also paid in gift cards) based on their performance on two decision-making tasks performed after the interoception test, and reported elsewhere.

2.2 Procedure

Eligibility was confirmed using a pre-screening telephone interview, before scheduling the laboratory appointment for a 2.5 hour assessment. Sessions took place between 10am and 7pm. Following consent, participants completed demographic information and questionnaire measures that included the Body Awareness Questionnaire and the Body Vigilance Scale (see below). Participants removed any wristwatch or cell phone (relevant to the heart beat detection and timing task), and psychophysiology equipment was then affixed to the participant to record an ECG trace. Adhesive Ag/AgCl electrodes (Vermed, Buffalo, New York) were affixed to the chest and abdomen, and the ECG was recorded using a BIOPAC MP150 sampling at 1,000Hz. During the set-up, the participant was shown the detrimental effect of their arm movements on the ECG trace; subsequently, the screen displaying the trace was turned away from the participant. Five minutes of resting heart rate was then recorded for analysis of heart rate variability, during which time the participant sat quietly with their eyes closed. This was followed by the Heart Beat Counting Task.

The Body Awareness Questionnaire (Shields et al., 1989) is an 18-point questionnaire ($\alpha = 0.843$) assessing the ability to sense bodily changes (i.e. “I notice differences in the way my body reacts to various foods). Items are rated using a Likert scale ranging from 1 (Not at all true of me) to 7 (Very true of me). The BAQ total score is the sum of the items, with item 10 reverse-scored, such that scores can range from 18-126. The total scores were negatively skewed, and this skew remained after square root transformation, hence data were analyzed using non-parametric tests.

The Body Vigilance Scale (Schmidt et al., 1997) is an 18-point scale ($\alpha = 0.952$) that measures how sensitive a person is to internal bodily sensations, based on feelings in the past week. Item 4 comprises 15 sub-items referring to the degree of attention paid to various specific sensations including heart palpitations, dizziness, stomach upset; each scored from 0 (None) to 10 (Extreme). If the participant had not experienced the symptom in the last week, they marked that items as zero. The BVS total is the sum of the first 3 questions divided by 10, plus the average of the scores on item 4.

On the Heart Beat Detection task (Schandry, 1981), participants were instructed to count their heart beats over six timed periods of 20 – 60s. Participants wore headphones and time intervals were signalled by an initial warning beep, followed by further beeps to indicate the onset and offset of the timed window. Participants were not permitted to use any tools or strategies (e.g. feeling pulse on the neck) that could assist heart beat counting. The six trials were interleaved with a control block of three time periods that assessed time estimation ability as a possible confound (i.e. estimate simply the elapsed time between the beeps, in seconds) (Dunn, Stefanovitch, et al., 2010; Ring & Brener, 1996). After each timing period, the participant was asked to enter the number of heart beats detected (or elapsed time) into an input box, as well as a rating of their confidence in their judgment. The actual number of heart beats was recorded via the ECG trace and calculated using a custom script in Matlab. Interoceptive accuracy was calculated from the absolute difference between the estimated and actual number of heart beats ($|nbeats_{real} - nbeats_{reported}|$), using the equation by Garfinkle et al (2015) of $1 - (|nbeats_{real} - nbeats_{reported}|) / ((nbeats_{real} + nbeats_{reported})/2)$, such that perfect heart beat tracking is represented by a score of 1, and poor interoception by scores closer to zero. By using the absolute difference, this formula does not differentiate under- and over- estimation of the number of heart beats, and so a secondary analysis recoded the interoceptive accuracy with the same equation coded bi-directionally.

2.3 Statistical Analysis

For statistical tests on the interoception measures, independent-samples t tests were run on continuous variables that were normally distributed, and for non-normal variables, group comparisons were run using Mann Whitney U tests. On the DSM-5 Cross Cutting Tool, the domain severity scores were tested using Mann-Whitney U tests due to the unequal sample sizes, and in some cases, low cell counts for participants screening positive. Categorical variables (e.g. gender, education, participants screening positive on DSM-5 Cross Cutting Tool) were compared using chi-squared. Data for three participants (one control, two gambling disorder) could not be analyzed on the heart beat detection task, due to synchronization failure between the BIOPAC and the task. HRV data could not be estimated for one participant with gambling disorder, due to excessive movement leading to insufficient data. Tests were considered significant at $p < .05$ two-tailed. For the interoception and HRV measures, effect sizes are reported for parametric tests using partial eta-squared (η_p^2) (small effect 0.01, medium effect 0.06, large effect 0.14 according to Cohen, 1988) and we report unstandardized betas for effect size in the linear regression models.

RSA was calculated from the ECG trace for the resting baseline, using QRSTool (Allen et al., 2007) to visualize and clean any movement artefacts in the time series of inter-beat intervals, and automatically mark the R-wave peak of each beat. Each full time series was manually inspected for movements, which can distort estimates of heart rate variability to a greater extent than the effect sizes typical for psychology experiments (Berntson et al., 1997). Movement artefacts lasting less than 2 (assumed) heart beats were corrected by interposition. For movement artefacts that extended across several heart beats, if the artefact was early or late in the time series, the time series was cropped to exclude the artefactual section. Participants were retained if the clean time series was over three minutes. The CMetX software was then used to calculate RSA from the cleaned inter-beat interval time series, as the natural log of the

0.12-0.40 Hz band-limited variance of inter-beat-intervals (Allen et al., 2007). We also report heart rate (beats per minute) for the same period, following recommendations (de Geus, Gianaros, Brindle, Jennings, & Berntson, 2018).

3. Results

3.1 Demographics and other mental health measures

The group with gambling disorder (n = 50) and the control group (n = 35) did not differ significantly in terms of age or the ratio of male to female participants (see Table 1). The gambling disorder group had an overall mean PGSI score of 16.7 (SD = 4.89), and the control group had a mean PGSI score of 0.31 (SD = 0.58). The gambling disorder participants reported slot machines as the most common preferred form of gambling (50%), followed by online gambling (14%) and card games (14%). Education differed between the two groups ($\chi^2 = 12.866$, $p = .002$), with more of the healthy group attaining university education and more of the gambling disorder group reporting high school or college-level education. Relationship status and employment status did not differ significantly between groups, although the gambling disorder group reported a somewhat higher level of unemployment (15 compared to 5) (see Table 1).

[Insert Table 1 about here]

In terms of comorbid mental health on the DSM5 Cross Cutting Tool, the gambling disorder group was significantly more likely to endorse the Level 1 screening item in every domain except mania (see Table 2). The Level 2 domain severity scores in the participants who screened positive were significantly higher in the gambling disorder group for depression ($p = 0.008$), anxiety ($p = 0.016$), somatic symptoms ($p = .007$) and anger ($p = .034$). Several of these comparisons are compromised by low cell counts of participants screening positive. The group with gambling disorder scored higher on the DASS ($p < .001$). There was a greater number of smokers in the gambling disorder group than the control group ($\chi^2 = 14.8$, $p < 0.001$) but there was no significant difference in severity of nicotine dependence in the participants who endorsed smoking.

[Insert Table 2 about here]

3.2 Interoception Measures

The group with gambling disorder and the control group did not differ significantly on the Body Vigilance Scale ($t_{83} = 1.59$, $p = 0.115$, $\eta_p^2 = .030$, 95% CI [-6.42, 0.71]) or the Body Awareness Questionnaire (U = 797.5, $p = .489$) (see Table 3). On the heart beat counting task, the groups did not differ significantly on interoception accuracy ($t_{80} = 1.28$, $p = 0.204$, $\eta_p^2 = .020$, 95% CI [-0.22, 0.48]) or the interoception confidence rating ($t_{80} = 1.44$, $p = 0.155$, $\eta_p^2 = .025$, 95% CI [-2.99, 18.5]). There was no difference in the time estimation judgments ($t_{80} = -0.026$, $p = 0.980$, $\eta_p^2 = .000$, 95% CI [-0.11, 0.11]). Numerically, the group with gambling disorder recorded higher scores than the healthy group on body vigilance, body awareness, and interoception accuracy, and lower interoception confidence, but effect sizes were uniformly small. In the overall sample, we confirmed that the BAQ and BVS scores were significantly related ($r_{83} = 0.48$, $p < .001$) but neither scale was related to interoception accuracy or confidence (all r = -0.05 to +0.06). We recoded the interoception accuracy variable bi-directionally, to test whether there was a reliable tendency for participants to under- or over- estimate the number of heart beats within a time interval. Across both groups, the scores indicated a significant tendency to under-estimate the number of heart beats (i.e. scores reliably < 1) (M = 0.58, SD = 0.33, one-samples t-test $t_{81} = 11.3$, $p = .001$, CI [-0.49, -0.34]), but there was no significant group difference (gambling disorder M = 0.63, SD = 0.32; control M = 0.51, SD = 0.35, t_{80} = - 1.60, p = 0.113, η_p^2 = .031, 95% CI [-0.27, 0.03]).

[Insert Table 3 about here]

3.3 RSA

The group with gambling disorder showed significantly lower RSA, t_{82} = 2.34, p = .021, η_p^2 = .063, 95% CI [0.10, 1.23], with moderate effect size. There were no differences in the length of the time series (i.e. number of heart beats available for analysis) (gambling disorder M = 333.7, SD = 55.4, controls M = 320.9, SD = 39.4; t_{82} = 1.16, p = .247, η_p^2 = .016, 95% CI [-34.479, 9.002]) or the overall resting heart rate (gambling disorder M = 73.1, SD = 12.6, controls M = 70.1, SD = 8.65; t_{82} = 1.22, p = .227, η_p^2 = .018, 95% CI [-7.902, 1.905]). In prior research on heart rate variability, age, smoking, and depression are identified as important covariates that could potentially account for group differences (Harte & Meston, 2014; Holzman & Bridgett, 2017; Rottenberg, 2007). In this study, the gambling disorder and control groups differed significantly in smoking behaviour and depression (see Table 2), as is typical for gambling disorder (Kessler et al., 2008). In a sensitivity analysis, we entered smoking status (0 or 1), age, and DASS Total Score as step 2 predictors of RSA in a linear regression model, after entering Group at step 1 (see Table 4). With the addition of the 3 covariables, the effect of Group was no longer statistically significant (p = .434); age was a significant predictor (p = .006) and the predictor for smoking status was p = .071. In a second model restricted to participants who smoked, both age (p = .006) and Fagerstrom severity score (p = .019) significantly predicted lower RSA. When we repeated the between-groups test in only the non-smoking participants (gambling disorder n = 24, control n = 31), RSA did not differ significantly (gambling disorder M = 5.56, SD 1.29; controls M = 6.18, SD = 1.01;

$t_{53} = 1.996$, $p = 0.051$, $\eta_p^2 = .070$, CI [-0.00, 1.24]). As such, the differences observed for RSA in gambling disorder appear to be driven by smoking behaviour and age.

[Insert Table 4 around here]

4. Discussion

The present study assessed two distinct psychophysiological constructs under resting conditions in participants with gambling disorder (mostly non-treatment seeking individuals recruited through the community) and a healthy comparison group with no-risk or low-risk gambling. Using two self-report questionnaires of bodily sensitivity, and a behavioural test of heart beat counting, we saw no evidence in support of the hypothesized group differences in interoception, and effect sizes were uniformly small. We also analyzed resting state heart rate variability as a psychophysiological marker of emotion regulation capacity (Appelhans & Luecken, 2006; Holzman & Bridgett, 2017). In line with our hypothesis, the group with gambling disorder displayed significantly lower RSA, consistent with reduced parasympathetic control. The effect size for this group difference was medium, but sensitivity analyses indicated that RSA was explained largely by age and increased levels of smoking behaviour (a known confound of heart rate variability) in the group with gambling disorder.

As one of the first experiments looking to characterize people with gambling disorder in British Columbia, Canada, the demographic composition of our sample is noteworthy in several respects: we highlight that males and females were evenly balanced in our sample, in contrast to the predominance of male participants in some other research on gambling disorder (e.g. Michalczuk, Bowden-Jones, Verdejo-Garcia, & Clark, 2011; Steward et al., 2017), and that land-based slot machine gambling was the modal preferred form of gambling in half of our sample, with the other 50% showing a mixture of preferred games that included card games, poker, sports betting and online gambling.

Our findings on the interoception measures provide some added context to theories that emphasize physiological arousal as a key form of reinforcement in gambling (Baudinet & Blaszczynski, 2013; Sharpe et al., 1995). Most prior research testing these arousal theories has examined the magnitude of bodily signals - for example, heart rate increases or skin conductance responses – during gambling in groups with differing levels of problematic gambling. These studies do not yield a convincing pattern (Diskin & Hodgins, 2003; Griffiths, 1993; Leary & Dickerson, 1985; Moodie & Finnigan, 2005). But in addition to the physiological signal itself, it is important to consider whether the individual is subsequently able to detect that signal (interoception), and then as a third stage, the individual's emotional appraisal of that arousal as pleasant or aversive (Farb et al., 2015; Schachter & Singer, 1962; Verdejo-Garcia et al., 2012). The present data began characterizing these processes under resting conditions, in which people with gambling disorder were predicted to show impaired interoception; the data provided no evidence for this hypothesis. In the case of substance addictions, indirect evidence exists for interoceptive dysfunction, primarily through brain lesion and neuroimaging data on the insular cortex as an interoceptive hub (Abdolahi et al., 2015; Berk et al., 2015; Stewart et al., 2014). We are not aware of research specifically assessing heart beat detection in groups with substance use disorders, to enable qualitative comparisons with the present results. In prior work by Dunn et al. (2010) in healthy participants, resting state interoception moderated the relationship between task-related arousal and decision-making performance on the Iowa Gambling Task. Future research on gambling disorder could extend this work by distinguishing trait measures from state-related measures of interoception taken during gambling episodes. Future research may also consider the final appraisal stage, which is complex to operationalize in the laboratory. Emotional appraisal has been considered in the context of sensation seeking using self-report measures (Franken, Zijlstra, & Muris, 2006), and an intuitive prediction is that people with disordered gambling may be more likely to interpret physiological arousal as exciting (driving behavioural approach) rather than aversive (driving withdrawal).

The observed lowering of RSA in the group with gambling disorder provisionally supported a hypothesis of impaired parasympathetic control. Low heart rate variability is widely treated as a marker of impaired emotional regulation (Holzman & Bridgett, 2017), and has been widely reported in clinical groups with substance use disorders (Crowell et al., 2017; Quintana et al., 2013). Our hypothesis for RSA was also informed by an earlier study, in which regular slot machine gamblers with varying levels of disordered gambling showed lower RSA than a student group of novice gamblers (Murch et al., 2017), although the groups were not demographically comparable in that study. A physiological marker of deficient emotion regulation could have utility in treatment contexts given the potential for unobtrusive and arms-length monitoring, and would concur with other studies employing cognitive and self-report measures of emotion regulation in gambling disorder (Navas et al., 2017; Williams et al., 2012).

In the present data, the RSA difference between groups was partly explained by group differences in smoking behaviour: 52% of the gambling disorder group were smokers, compared to a minority (11%) of controls. When smoking status and age were entered alongside group in predicting RSA, the effect of group was rendered non-significant. Within the smokers, RSA was significantly predicted by severity of nicotine dependence on the Fagerstrom scale. Past research has established a substantial overlap between gambling disorder and tobacco use / nicotine dependence, both at an event level (i.e. smoking while gambling) and a syndromic level (i.e. comorbidity) (McGrath & Barrett, 2009). People with gambling disorder who smoke display greater gambling severity (Petry & Oncken, 2002) and other mental health problems (Potenza et al., 2004). Smoking is an established predictor of heart rate variability (Barutcu et al., 2005), seemingly as a consequence of nicotinic action (Harte & Meston, 2014). In the present study, we did not control carefully for smoking recency, but participants were allowed smoking breaks, so that it is unlikely that the RSA effects are related to nicotine withdrawal. Controlling for smoking status has been seen to alter results in other studies of gambling disorder (Balodis et al., 2018; Mooney, Odlaug, Kim, & Grant, 2011). Our data highlight the importance of assessing smoking behaviour in psychophysiological studies of gambling disorder, especially in future studies on heart rate variability. We note that in an analysis restricted to the non-smokers, there was a non-significant trend for RSA to be lower in the group with gambling disorder than the healthy control ($n = 24$ vs 31, $p = .051$); based on this medium effect size (Cohen's $d = 0.54$), future studies should aim to recruit at least 55 participants per group to achieve a power of 80% for establishing a reliable difference if one exists.

Several limitations should be noted. With regard to our sample, our group with gambling disorder was predominantly recruited from the community, and thus comprised a minority of gamblers seeking or receiving treatment. Although PGSI scores indicated reasonable severity in our sample, a clinical sample could evidence stronger effects; for example on heart rate variability. The most common preferred game in our sample was slot machine gambling, and we recognize hypotheses that slot machine gamblers may be primarily motivated by escape and not physiological arousal (Schull, 2012). Gambling harms likely arise through a combination of personal vulnerabilities and the specific effects of gambling products (Yücel, Carter, Harrigan, van Holst, & Livingstone, 2018). Our selection criteria included (and assessed) many of the common comorbidities with gambling disorder. As other mental problems are the rule more than the exception in gambling disorder, this approach benefits generalizability, but the increased heterogeneity may compromise power.

With regard to our assessments, our behavioral measure focused on cardiac interoception. Some caveats have been noted with the heart beat counting procedure, including the lack of association with another measure of heart beat detection that involves judging tones that are presented at varying delays relative to the R-wave (Ring & Brener, 2018). It is possible that other domains of interoception may be more relevant to gambling; for example a task by Kerr et al (2015) assessed heart, stomach, and bladder interoception in anorexia nervosa. Nevertheless, the Body Vigilance Scale and Body Awareness Questionnaire were included in our assessment to test a broader range of bodily sensations, with convergent results. Finally, it is notable that our findings pertain to resting conditions using measures that emphasize trait-like individual differences. Gambling-induced *changes* in both interoception or parasympathetic control in people with disordered gambling remains a fruitful target of further study.

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Conflict of Interest statement

LC is the Director of the Centre for Gambling Research at UBC, which is supported by the Province of British Columbia government and the British Columbia Lottery Corporation (BCLC). The BCLC is a Canadian Crown Corporation. The Province of British Columbia government and BCLC had no involvement in the research design, methodology, conduct, analysis or write-up of the study, and impose no constraints on publishing. LC has received a speaker honorarium from Svenska Spel (Sweden) and accepted travel/accommodation for speaking engagements from the National Center for Responsible Gaming (US) and National Association of Gambling Studies (Australia). He has not received any further direct or indirect payments from the gambling industry or groups substantially funded by gambling. He has received royalties from Cambridge Cognition Ltd. relating to the licensing of a neurocognitive test. EHLO has received a speaker honorarium from the Massachusetts Council on Compulsive Gambling (USA) and accepted travel/accommodation for speaking engagements from the National Council for Problem Gambling (USA) and the 4th International Multidisciplinary Symposium on Gambling Addiction (Swiss Centre du Jeu Excessif). She has not received any further direct or indirect payments from the gambling industry or groups substantially funded by gambling. DK, WSM, CBG and BDD have no disclosures.

Table 1. Group characteristics

	Gambling Disorder	Controls	Statistics
Gender (M:F:Other)	25:24:1	17:17:1	$\chi^2 = 0.074$, $p = 0.964$
Age	42.5 (12.8)	38.1 (13.2)	$t_{83} = 1.52$, $p = 0.132$
Relationships			
Dating/Common-law	24 (48%)	14 (40%)	
Single/Divorced	21 (42%)	16 (46%)	
Married	5 (10%)	5 (14%)	$\chi^2 = 0.68$, p = 0.711
Education†			
Degrees	17	26	
Some College/Trade	23	8	
High school or prior	8	1	$\chi^2 = 12.87$, p = 0.002
Employment†			
Employed	25	26	
Student	3	0	
Unemployed	15	5	
Retired	5	2	$\chi^2 = 6.76$, p = 0.080
Preferred Gambling Form			
Slots	25	-	
Poker	4	-	
Card Games	7	-	
Sports	4	-	
Online Forms	7	-	
Lotto/scratch-cards	2	-	
Keno	1	-	

† For education and employment, some participants chose not to disclose this information (education 48 vs 35; employment 48 vs 33)

Table 2. Clinical descriptives in the two groups. For the DSM-5 Cross Cutting Tool, the 'positive' row displays the mean (SD) severity score from the Level 2 items, in the subset of participants who screened positive on the Level 1 items.

		Gambling Disorder	Controls	Statistics
Depression				
	Screen n	33	10	$\chi^2 = 11.5$, $p = .001$
	Positive	23.2 (6.70)	16.4 (5.64)	$U = 72.5$, $p = .008$
Anxiety				
	Screen n	33	14	$\chi^2 = 5.63$, $p = .018$
	Positive	20.3 (5.44)	16.4 (4.01)	$U = 128.0$, $p = .016$
Substance Use				
	Screen n	22	3	$\chi^2 = 12.4$, $p < .001$
	Positive	4.32 (2.44)	2.67 (2.89)	$U = 19.0$, $p = .236$
Mania				
	Screen n	30	15	$\chi^2 = 2.43$, $p = 0.119$
	Positive	6.03 (3.32)	6.67 (2.97)	$U = 197.0$, $p = .498$
Repetitive Thought				
	Screen n	21	2	$\chi^2 = 13.7$, $p < .001$
	Positive	8.52 (3.33)	9.00 (4.24)	$U = 17.5$, $p = .700$
Sleep Disturbance				
	Screen n	30	9	$\chi^2 = 9.75$, $p = .002$
	Positive	29.9 (4.63)	26.9 (3.65)	$U = 82.5$, $p = .079$
Somatic Symptoms				
	Screen n	30	6	$\chi^2 = 15.5$, $p < .001$
	Positive	10.1 (4.59)	5.00 (2.68)	$U = 27.0$, $p = .007$
Anger				
	Screen n	30	6	$\chi^2 = 15.5$, $p < .001$
	Positive	15.1 (2.89)	12.7 (1.51)	$U = 40.5$, $p = .034$
Smokers n		26	4	$\chi^2 = 14.8$, $p < .001$
FTND in Smokers		4.69 (2.65)	4.00 (2.45)	$U = 44.0$, $p = .622$
DASS		22.9 (12.3)	8.77 (6.28)	$U = 257.5$, $p < .001$

DASS = Depression Anxiety and Stress Scale-21 item version; FTND = Fagerstrom Test for Nicotine Dependence

Table 3. Group characteristics on the heart beat detection test and the two body awareness questionnaires, mean (SD)

	Gambling Disorder	Controls
BVS	17.1 (8.34)	14.3 (7.83)
BAQ	76.1 (16.2)	72.9 (18.5)
Interoception Accuracy	0.59 (0.27)	0.51 (0.34)
Heart Beat Confidence	38.6 (24.4)	46.4 (23.7)
Time Estimation Accuracy	0.67 (0.26)	0.67 (0.20)
RSA	5.35 (1.36)	6.02 (1.16)

Table 4. Results of sensitivity analyses testing impact of age, smoking, and mood symptoms on RSA.

	Unstandardized beta (B)	CIs	Standardized beta, β	p value
Model 1: Smoking Status (all participants)				
Step 1: Group	-0.665	-1.23, -0.101	-0.251	.021
Step 2: Group	-0.279	-0.983, 0.426	-0.105	.434
Step 2: Age	-0.029	-0.050, -0.009	-0.292	.006
Step 2: Smoking (no/yes)	-0.561	-1.172, 0.049	-0.204	.071
Step 2: DASS Total	-0.002	-0.029, 0.024	-0.021	.864
Model 2: Smoking severity (smokers only)				
Group	-0.790	-2.379, 0.800	-0.193	.315
Age	-0.065	-0.110, -0.021	-0.505	.006
FTND	-0.211	-0.383, -0.038	-0.388	.019
DASS Total	0.051	0.006, 0.095	0.453	.027

DASS = Depression Anxiety and Stress Scale-21; FTND = Fagerstrom Test for Nicotine Dependence