Heart rate variability and interoceptive accuracy predict impaired decision-making in Gambling Disorder

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ABSTRACT

Background and aims: Gambling Disorder (GD) entails maladaptive patterns of decision-making. Neurophysiological research points out the effect of parasympathetic arousal, including phasic changes in heart rate variability (HRV), and interoceptive accuracy (IA, *i.e.,* the ability to track changes in bodily signals), on decision-making. Nevertheless, scarce evidence is available on their role in GD. This is the first study exploring the impact in GD of respiratory sinus arrhythmia (RSA), an index of HRV, and IA on decision-making, as measured by the Iowa Gambling Task (IGT). *Methods:* Twenty-two patients experiencing problems with slot-machines or video lottery terminals gambling and 22 gender- and age-matched healthy controls (HC) were recruited. A resting ECG was performed before and after the completion of the IGT. IA was assessed throughout the heartbeat detection task. We conducted a MANCOVA to detect the presence of significant differences between groups in RSA reactivity and IA. A linear regression model was adopted to test the effect of factors of interest on IGT scores. *Results:* Patients with GD displayed significantly decreased RSA reactivity ($P = 0.002$) and IA ($P = 0.024$) compared to HCs, even after controlling for affective symptoms, age, smoking status, and BMI. According to the linear regression model, cardiac vagal reactivity and IA significantly predict decision-making impairments on the IGT ($P = 0.008$; $P = 0.019$). *Discussion and conclusions:* Although the exact pathways linking HRV and IA to impaired decision-making in GD remain to be identified, a broader exploration relying upon an embodiment-informed framework may contribute to shed further light on the clinical phenomenology of the disorder.

KEYWORDS

interoception, somatic marker, autonomic nervous system

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INTRODUCTION

Gambling Disorder (GD) features a persistent and maladaptive urge to be involved in gambling activities, which may entail an abnormal preference towards high-risk pattern of decision-making (Brevers, Koritzky, Bechara, & Noël, 2014). Decision-making is broadly

defined as the faculty to favor certain choices by pondering their conceivable punitive or rewarding outcomes. Impairments in decision-making abilities are thought to play a pivotal role in the onset and maintenance of addictive disorders, including GD. Indeed, deficits in decision-making have been associated with several parameters of gambling severity, such as gambling frequency, amount of money lost, and gambling urge intensity (Moccia et al., 2017). Additionally, there is evidence supporting the prognostic value of laboratory measures of decision making for several clinical outcomes, including poorer treatment compliance or increased relapse rates (Rochat, Maurage, Heeren, & Billieux, 2019).

Neurophysiological research points out the role of autonomic arousal, including phasic changes in heart rate variability (HRV), in sustaining decision-making (Dulleck, Ristl, Schaffner, & Torgler, 2011). HRV represents the time variation between heartbeats considered as successive peaks of QRS complexes (*i.e.,* the combination of three of the graphical deflections seen on a typical ECG corresponding to the depolarization and the subsequent contraction of heart ventricles) and it is often considered as a proxy of the parasympathetic nervous system (PNS) activity (Laborde, Raab, & Kinrade, 2014). The PNS is a division of the autonomic nervous system, which controls through its efferents, such as the vagus nerve, several automatic processes, including digestion, respiration, as well as heart rate. Research suggests that the amplitude of respiratory sinus arrhythmia (RSA), a HRV metric referring to the spontaneous variation in heart rate that occurs during the breathing cycle, is a reliable index of PNS activity, reflecting the contribution of the vagus nerve to cardiac functioning (Laborde, Mosley, & Thayer, 2017). This is of relevance, as there is evidence that impaired PNS activity may account in GD clinical phenomenology, including decision-making. Goudriaan, Oosterlaan, de Beurs, and van den Brink (2006) reported blunted anticipatory parasympathetic responses, including skin conductance, to risky choices in GD. Similarly, there is evidence for abnormal PNS activity in situations associated with imaginal recall of winning versus losing scenarios in GD (Sharpe, 2004). Taken together, these findings point at a role of the PNS in impaired risk/reward assessment in GD.

Neurophysiological research on autonomic reactivity in GD has paid little attention to the individual's capacity to consciously detect changes in internal states of autonomic arousal, focusing, instead, predominantly on the amplitude of autonomic bodily signals *per se* (Brevers & Noël, 2013; Clark, Studer, Bruss, Tranel, & Bechara, 2014; Kennedy et al., 2019). Exposure to gambling-cues may result in enhanced autonomic arousal, which may be experienced subjectively by individuals with GD as abnormal bodily sensations that may ultimately lead to gambling urges (Sharpe, Tarrier, Schotte, & Spence, 1995). Interoceptive accuracy (IA) broadly refers to the ability to detect and track subtle changes in internal bodily sensations, including muscles, skin, joints, and viscera afferent signals (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015). According to

several lines of evidence, interoceptive processes may contribute to the onset and maintenance of addictive disorders (Verdejo-Garcia, Clark, & Dunn, 2012). Besides, the representation of bodily homeostatic milieu in brain areas such as the insular cortex is hypothesized to influence cognitive-affective processing, including decision-making (Bechara & Damasio, 2005).

The Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994) has been regarded among the most widely adopted and ecologically valid measure of decision-making in individuals with GD. One of the reasons for its ecological validity is that optimal performance on this task is attained through dealing with uncertainty in a context of reward and punishment, as in "real-life" decisions. Some choices lead to immediate and more substantial benefits but also carry the risk of greater loss, while other choices result in smaller immediate gains but provide greater benefits in the long run. Hence, the key aspect of this task is that participants have to forgo short-term gains for long-term gains (Brevers, Bechara, Cleeremans, & Noël, 2013). Individuals with GD perform poorly on the IGT, frequently chasing the larger, immediately rewarding gains, which ultimately lead to long-term losses (Moccia et al., 2017). Choosing among different options according to their long- and short-term outcomes implies similar neurobiological processes in human and translational models of decision-making, and thus, a disadvantageous pattern of preference for "high-risk/high-reward" options may represent a behavioral substrate of vulnerability to addictive disorders (Winstanley & Clark, 2016). Intriguingly, and consistent with this conceptual framework, IA and HRV were found to moderate IGT performance in healthy subjects (Drucaroff et al., 2011; Dunn et al., 2010).

To our knowledge, this is the first study that, focusing on an accurately selected group of GD individuals addicted to slot machines or video lottery terminals (VLT), explored the joint impact of IA and phasic changes in RSA on decision-making impairments as measured by the IGT. We hypothesized that individuals with GD report blunted RSA reactivity and decreased IA as compared to gender- and age-matched healthy controls (HCs), and that RSA and IA may predict the performance on the IGT.

METHODS

Participants

Twenty-two treatment-seeking male patients, aged from 18 to 65 (mean age 47.5±12.5), with a diagnosis of GD according to DSM-5 criteria were consecutively recruited from GD specialized outpatient clinics of Fondazione Policlinico Universitario Agostino Gemelli IRCCS-Università Cattolica del Sacro Cuore, Rome, Italy. The Structured Clinical Interview for DSM-5 Clinician Version (SCID-5-CV; First, Williams, Karg, & Spitzer, 2017) was employed to establish GD diagnosis and psychiatric comorbidity. Patients were also screened for Personality Disorders using the Structured

Clinical Interview for DSM-5 Personality Disorders (SCID-5-PD; First, Williams, Benjamin, & Spitzer, 2016). Diagnostic interviews were conducted at study entrance by raters with extensive training and high interrater reliability ($k > 0.8$). The following inclusion and exclusion criteria were strictly adopted to ensure a reliable study sample: all participants met DSM-5 criteria for GD, without any current comorbid psychiatric disorder or substance abuse. Moreover, participants had to demonstrate adequate command over written and spoken Italian language and report cognitive function within the normal range according to Raven's progressive matrices test (Raven, 2000). Twenty-two gender- and age-matched HCs were recruited through local online advertising. All HCs were screened for lifetime personal history of DSM-IV-TR Axis I and II disorders using the SCID-I/NP (First, Spitzer, Gibbon, & Williams, 2002) and SCID-II (First, Gibbon, Spitzer, Williams, & Benjamin, 1997). Participants with DSM-IV-TR Axis I or II disorders were excluded from the HC group. All other eligibility criteria were the same as those for the GD group. Additional exclusion criteria for both groups included unstable medical illnesses (head trauma, neurological and cardio-respiratory diseases, and diabetes), as well as current intake of medications altering the cardio-respiratory activity (Quintana, Alvares, & Heathers, 2016). Furthermore, since there is evidence that cardiac vagal tone is affected by regular exercise (Nakamura, Yamamoto, & Muraoka, 1993), only individuals not regularly involved in athletic, or endurance sports were recruited. The final sample comprised 44 individuals, 22 with GD and 22 gender- and age-matched HCs, a number that was comparable with previous neurophysiological research assessing HRV and IA in selected clinical groups (Ambrosecchia et al., 2017; Henry, Minassian, Paulus, Geyer, & Perry, 2010; Lavoie et al., 2004; Quintana, Guastella, McGregor, Hickie, & Kemp, 2013).

Procedure

Age, body mass index (BMI), smoking status, demographics, and family history of psychiatric disorders, were recorded for each participant at the time of admission. After arrival at the laboratory, participants completed the Depression Anxiety and Stress Scale-21 (DASS-21; Lovibond & Lovibond, 1995) and the Gambling Severity Assessment Scale (G-SAS; Kim, Grant, Potenza, Blanco, & Hollander, 2009) to assess subthreshold affective symptoms and GD severity over the previous week, respectively. Study took place on two consecutive experimental sessions a day apart, with IA assessment and psychometric testing on the first day and the IGT on the second. Participants were required to abstain from caffeine, tobacco, and alcohol, for 2 h before the experimental sessions. ECG was recorded for the entire duration of IA assessment on Day 1. Moreover, to detect differences in RSA reactivity, a 3-min resting ECG was performed before (Baseline) and after the completion (Recovery) of the IGT on Day 2. Participants were fitted with three 10 mm Ag/AgCl pre-gelled electrodes (ADInstruments, UK) placed on the wrists in an Einthoven's triangle configuration

ECG recording. ECG data were converted and amplified with an eight-channel amplifier (PowerLabT26; ADInstruments UK) and displayed, stored, and analyzed with LabChart 7.3.1 software package (ADInstruments Inc, 2011). All tasks were carried out while participants were seated in a quiet and illuminated room. They were instructed to relax and remain as still as possible during recording to minimize motion artifacts.

Measures

Heartbeat detection task. IA was assessed throughout the heartbeat detection task (Schandry, 1981). On the heartbeat detection task, participants were required to silently count their own heartbeats over four different time intervals (25, 35, 45, and 100 s) presented in random order. Time intervals were signaled by an initial audio-visual start cue, followed by a stop cue to indicate the onset and offset of the timed window. After each timing period, the participant was asked to tell the experimenter the number of heartbeats detected. During the task, no feedback on the length of the counting phases or the quality of their performance was given, and participants were not permitted to use any tools or strategies (e.g., feeling pulse on the wrist) that could assist heartbeat counting. IA was calculated from the absolute difference between the estimated and actual number of recorded heartbeats according to the following equation: $1/4\sum(1-(|\text{recorded beats}- \text{counted beats}|)\text{recorded beats})$. By using this formula, IA score may vary between 0 and 1 such that perfect heartbeat tracking is represented by a score of 1 and poor interoception by scores closer to zero.

IGT. All participants were administered a computerized version of the IGT. Subjects were provided with $2000 to start with. The computer screen displayed four rectangular decks. Participants chose a card by clicking on the appropriate deck on each trial of the IGT. Following each draw, a specified amount of virtual play money is awarded ($100 in decks A and B and $50 in decks C and D). However, the turning of some cards also carries an unpredictable penalty (which is large in decks A and B and small in decks C and D). The four decks differ in their long-term outcomes with decks A and B consistently delivering high immediate gains, but leading to greater loss over time, and decks C and D resulting in smaller immediate gains but providing greater gains in the long run. A NET score quantifying the amount of advantageous decision making was calculated as the number of draws from advantageous decks minus that from disadvantageous decks: NET score = (selected cards deck C + selected cards deck D) − (selected cards deck A + selected cards deck B). Accordingly, a score below zero indicates that participants adopted a disadvantageous strategy in the long run (more card selections in decks A and B) whereas a score above zero implied a more advantageous deck preference (more card selections in decks C and D). Following other studies, the NET score was further divided into 5 blocks, each of 20 consecutive card choices. All participants received standard instructions for the IGT. Briefly, they were advised
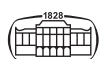
that the task consisted in winning as much as possible and avoiding losses by drawing cards, one at a time, from the four decks. They were informed that each card drawn indicate how much they had won and whether there was also a penalty. They were also instructed that some decks are more advantageous than others and that they are free to switch from one deck to another at any time and as frequently as they liked.

ECG recording. The ECG was sampled at 1 kHz and online filtered with the Mains Filter. The peak of the R-wave of the ECG was detected from each sequential heartbeat and the R-R interval was timed to the nearest msec. R-R intervals were inspected and edited for artifacts. Editing consisted of a software artefacts detection [artefacts threshold 300 msec; LabChart's ECG Analysis module (ADInstruments Inc, 2011)] followed by a visual inspection of the ECG recorded signal. Artefacts were then edited by integer division or summation. The amplitude of RSA was calculated with CMetX, a time-domain method that allows derivation of components of HRV within specified frequency bands as spectral techniques (Berntson et al., 1997). The amplitude of RSA was estimated as the variance of heart rate across the band of frequencies that are associated with spontaneous respiration. RSA estimates were calculated using the following procedures: a) linear interpolation at 10 Hz sampling rate; b) application of a 241-point FIR filter with a 0.12–0.40 Hz bandpass; c) extraction of the band passed variance; d) transformation of the variance in its natural logarithm (Allen, Chambers, & Towers, 2007; Ferri, Ardizzi, Ambrosecchia, & Gallese, 2013). According to guidelines, this procedure was applied to distinct epochs of 30 s (Berntson et al., 1997). RSA-values corresponding to Baseline and Recovery were computed accordingly as the average of the six 30 s epochs. RSA reactivity was operationalized as the change in RSA absolute values [expressed in $\ln(msec)^2$] between baseline and recovery.

Statistical analysis

We first compared individuals with GD and HC on demographic, clinical characteristics, and IGT performance on the basis of contingency table/χ^2 for categorical measures and Student's *T*-Test for continuous variables. To detect the presence of significant differences between GD individuals and HCs in phasic changes in cardiac vagal activity and interoception we performed a multivariate analysis of covariance (MANCOVA) using RSA reactivity and IA as dependent variables, group (GD vs. HCs) as independent factor, and DASS-21 total score, age, smoking status, and BMI as covariates. This was necessary in the light of the evidence pointing at an effect of affective symptoms, age, smoking, and BMI on cardiac vagal activity and interoceptive measures (Ambrosecchia et al., 2017; Hina & Aspell, 2019; Laborde et al., 2017; Murphy, Geary, Millgate, Catmur, & Bird, 2018; Pollatos, Traut-Mattausch, & Schandry, 2009). When the initial model was significant, we conducted a series of one-way analyses of covariance (ANCOVA) to test

differences between groups on dependent variables. We used a statistical model corrected for multiple comparisons according to the Bonferroni procedure ($P < 0.05$/number of comparisons) to minimise the likelihood of type I statistical errors. We reported effect sizes using partial eta-squared (η^2_p; small effect = 0.01, medium effect = 0.06, large effect = 0.14). To further confirm the presence of significant differences between GD individuals and HCs in resting state RSA, we also conducted supplemental analyses considering repeated measures of cardiac vagal activity from baseline to recovery (please, see **Table S4 in supplementary material**).

In the second part of the analysis, a linear regression model was adopted to predict the severity of decision-making impairments based on factors that significantly differed between the two groups in univariate/bivariate analysis. Unstandardized betas for effect size were provided. The level of significance was of 5%. Possible multicollinearity between the variables of interest was tested through the variance inflation factor (VIF) indicators. All statistical analysis were performed using SPSS v. 25 (IBM Corp., USA).

Ethics

The study was approved by the local Ethics Committee and was undertaken in accordance with the Principles of Human Rights, as adopted by the World Medical Association at the 18th WMA General Assembly, Helsinki, Finland, June 1964 and subsequently amended at the 64th WMA General Assembly, Fortaleza, Brazil, October 2013. All participants gave their written informed consent to participate in the study after complete explanation of the procedures. Enrolled subjects did not receive any form of payment.

RESULTS

Demographics, clinical features, and IGT performance

As expected from the matching procedure, individuals with GD and HCs did not differ for age. The two groups were similar also for civil status, occupation, living condition, and BMI (Table 1). Individuals with GD and HCs significantly differed for smoking status, family history of psychiatric disorders, and educational level (Table 1). Moreover, Individuals with GD scored significantly higher on the DASS-21 and the G-SAS compared to HCs (Table 1). Unsurprisingly, subjects with GD also performed worse on the IGT with NET total scores significantly lower than HCs (GD: -5.7 ± 22.5, HCs: 22.7 ± 39.2, overall sample = 8.8 ± 34.6, t = 2.89, df = 42, P = 0.006; see also **Table S5** in supplementary material).

RSA and IA

The MANCOVA, indicated a significant global effect (Wilks' Lambda = 0.60, F = 11.49, df = 2, P < 0.001) of variables of interest on the two diagnostic groups. Multivariate normality was respected as indicated by values

Table 1. Clinical and demographic characteristics of the sample

Characteristics	GD (N = 22)	HC (N = 22)	Overall	df	χ2 or t	P
Age (M±SD)	47.5 ± 2.6	40.3 ± 2.8	44.0 ± 13.2	1	−1.8	0.071
Body Mass Index (M±SD)	25.1 ± 0.8	24.8 ± 3.9	24.9 ± 3.9	1	−2.1	0.834
Education level (n%)				1	9.8	**0.002**
Graduate	3 (13.6)	13 (59.1)	16 (36.4)			
Undergraduate	19 (86.4)	9 (40.9)	28 (63.6)			
Living alone (n%)	3 (13.6)	7 (31.8)	10 (22.7)	1	2.1	0.150
Occupation (n%)				1	2.0	0.154.
Employed	18 (81.8)	21 (95.5)	39 (88.6)			
Unemployed	4 (18.2)	1 (4.5)	5 (11.4)			
Smoking (n%)	20 (90.9)	11 (50.0)	31 (70.5)	1	8.8	**0.003**
Marital status (n%)				1	0.0	1.00
Married	6 (27.3)	6 (27.3)	32 (72.7)			
Unmarried	16 (72.7)	16 (72.7)	12 (27.3)			
Family history of psychiatric disorders (n%)	13 (59.1)	1 (4.5)	14 (31.8)	1	15.1	**<0.001**
G-SAS (M±SD)	21.9 ± 11.1	1.8 ± 3.0	11.9 ± 13.0	1	−8.1	**<0.001**
DASS-21 (M±SD)	30.1 ± 17.5	18.3 ± 12.9	24.2 ± 16.4	1	-2.5	**0.016**

Significant results in **bold** characters.
Abbreviations: M = mean; SD = standard deviation; df, degrees of freedom; χ^2, chi-squared test; P, statistical significance; t = Student's t; SD standard deviation; G-SAS = Gambling Symptom Assessment Scale; DASS-21 = Depression, Anxiety and Stress Scale; GD = Gambling Disorder; HC = healthy controls.

Table 2. Analysis of covariance for RSA reactivity and IA by DASS-21, BMI, age, and smoking status as covariates

		Type III sum of squares	df1	df2	Mean square	F	P	η^2p
RSA reactivity	Group	2.43	1	38	2.43	11.2	**0.002**	0.228
	DASS-21	0.24	1	38	0.24	1.1	0.292	0.029
	BMI	0.30	1	38	0.30	1.3	0.245	0.035
	Age	0.05	1	38	0.05	0.2	0.620	0.007
	Smoking	0.24	1	38	0.24	1.1	0.294	0.029
IA	Group	0.47	1	38	0.47	5.5	**0.024**	0.126
	DASS-21	0.04	1	38	0.04	0.5	0.474	0.014
	BMI	0.01	1	38	0.00	0.0	0.860	0.001
	Age	0.08	1	38	0.08	0.9	0.340	0.024
	Smoking	0.00	1	38	0.00	0.0	0.900	0.000

Significant results in **bold** characters.
Abbreviations: df1 = Degrees of freedom between groups; df2 = Degrees of freedom within groups; F = value of variance of the group means; η^2p = partial eta squared measure of effect size; RSA = Respiratory Sinus Arrhythmia; IA = Interoceptive Accuracy; BMI = body mass index; DASS-21 = Depression Anxiety and Stress Scale.

obtained with Box's Test for Equivalence of Covariance Matrices (χ^2 = 3.67, df = 3; P = 0.30). A series of univariate ANCOVAs we performed afterward indicated that patients with GD displayed a significant reduction in RSA reactivity [F = 11.2, df = 1; P = 0.002, η^2_p = 0.228; GD: -0.15 ± 0.36 ln(msec)^2; HCs: 0.39 ± 0.54 ln(msec)^2], as well as significantly decreased IA (F = 5.5, df = 1; P = 0.024, η^2_p = 0.126; GD: 0.37 ± 0.3; HCs: 0.61 ± 0.3) compared to HCs, even after controlling for DASS total score, age, smoking status, and BMI. Of note, none of these covariates resulted significant (Table 2). According to the linear regression model, cardiac vagal reactivity and IA also significantly predict decision-making impairments on the IGT. Indeed, both RSA and IA were positively associated with overall NET scores (Table 3). There was no significant multicollinearity in the model, as indicated by the fact that the VIF of all variables of interest was < 3 (O'brien, 2007).

DISCUSSION

In line with our hypothesis, patients with GD displayed increased vagal withdrawal as well as reduced IA as compared to HCs. Furthermore, we observed that in our sample both RSA reactivity and IA were significant predictors of decision-making abilities as indexed by the IGT. To the very best of our knowledge, no previous studies have investigated this relationship in GD. A prior study conducted by Kennedy et al. (2019) in non-treatment seeking individuals with problem gambling did not detect significant

Table 3. Linear regression: effect of predictors on NET total score

| Predictors | Estimate | SE | 95% Confidence Interval | | t | P | β |
			Lower	Upper			
Education level	18.76	9.94	−0.019	0.547	1.887	0.067	0.263
Family history of psychiatric disorders	6.84	11.63	−0.228	0.414	0.588	0.560	0.093
Smoking status	−13.97	10.38	−0.467	0.094	−1.346	0.0187	−0.186
RSA reactivity	25.67	9.20	0.108	0.684	2.789	**0.008**	0.396
IA	38.07	15.47	0.059	0.617	2.461	**0.019**	0.338
DASS-21	0.34	0.310	-0.134	0.459	1.107	0.275	0.162
G-SAS	0.16	0.497	-0.315	3.138	0.441	0.739	0.062

Significant results in **bold** characters.
Abbreviations: P, statistical significance; SE = standard error; t = t statistic; β = standardized regression coefficient; RSA = Respiratory Sinus Arrhythmia; IA = Interoceptive Accuracy G-SAS = Gambling Symptom Assessment Scale; DASS-21 = Depression, Anxiety and Stress Scale.

differences in baseline RSA and several measures of interoception, including IA. However, sample composition of Kennedy and colleagues' study was different from this study in several respects, including an equal distribution between male and female GD subjects, as well as the heterogeneity of gambling activities in which participants engaged. Indeed, there is evidence that GD clinical phenomenology may vary by form of problematic gambling (Petry, 2003) and that GD severity increased with VLT involvement (Delfabbro, King, Browne, & Dowling, 2020) as well as with male gender (González-Ortega, Echeburúa, Corral, Polo-López, & Alberich, 2013), so that it is difficult to draw direct comparison.

The decrease in RSA values we observed among individuals experiencing problems with slot-machines or video lottery terminals gambling may endorse a hypothesis of unbalanced parasympathetic control in GD. The neurovisceral integration model posits that the relation between HRV and cognitive and emotional regulation functions is attributable to the ability of vagally-mediated HRV to index activity in a flexible network of neural structures that is dynamically organized in response to environmental challenges (Thayer and Lane, 2009). The main assumption of this model is that the higher the vagal tone, the better executive cognitive performance, as well as better emotional functioning (Laborde et al., 2017). Indeed, there is evidence that phasic increases in HRV on tasks that require affective or executive processes facilitate effective emotional and cognitive regulation (Thayer & Lane, 2009). Besides, decreased resting HRV has been widely reported in subjects with substance use disorders (Crowell, Price, Puzia, Yaptangco, & Cheng, 2017; Quintana, McGregor, Guastella, Malhi, & Kemp, 2013). Alternatively, the finding of increased vagal withdrawal we observed in GD group during the IGT could be also attributable to the fact that individuals experiencing problem gambling may pay more attention to monetary cues, as decreases in RSA have been observed in tasks requiring sustained attention (Duschek, Muckenthaler, Werner, & del Paso, 2009; Porges & Raskin, 1969).

Our findings of decreased IA in individuals with GD also provide additional support for theories that emphasize the role of aberrant interoceptive processing in addictive disorders (Paulus & Stewart, 2014). Given that gambling reinforcing effects result in marked changes in bodily arousal (Sharpe et al., 1995), it is plausible that interoceptive processes may be implicated in GD clinical phenomenology. Moreover, trait individual differences in cardiac perception have been linked to a number of cognitive and affective phenomena, including time perception, anxiety and depressive symptoms, emotional reactivity and memory, alexithymia, as well as intuitive decision-making (Verdejo-Garcia et al., 2012). Of note, several of these dimensions are affected in subjects with GD (Bibby & Ross, 2017; Di Nicola, Pepe et al., 2020; Limbrick-Oldfield et al., 2020; Pettorruso et al., 2019; Rogier & Velotti, 2018), consistent with a key role of interoceptive processes in addictive disorders.

The findings of disadvantageous decision-making on the IGT, in combination with the predictive role of RSA reactivity and IA on NET total score are consistent with studies indicating deficient peripheral somatic processing signals in GD individuals (Lole & Gonsalvez, 2017; Lole, Gonsalvez, Barry, & Blaszczynski, 2014; Ulrich, Ambach, & Hewig, 2016). The somatic marker hypothesis provides a system-level framework describing how decision-making processes are shaped by emotional signals arising from peripheral changes in bodily arousal (Damasio, 1994). This bodily biofeedback may represent an influential embodied somatosensory pattern in the selection of adaptive behavior, giving rise to implicit or explicit knowledge for making advantageous decisions, and thus promoting self-regulation (Gallese & Sinigaglia, 2010; Verdejo-García & Bechara, 2009).

Before summarizing study conclusions, we must acknowledge some potential limitations. First, the relatively small sample size does not allow to extent the generalizability of our result to the whole population of individuals with GD. Second, to ensure the conceptual and methodological validity of the study, a sample of male subjects with GD addicted to slot-machines or VLT and without psychiatric comorbidity was selected. Accordingly, this issue might have led to a selection bias. However, selecting a well-

characterized clinical group of subjects with GD can be also considered as a study strength. Finally, IA evaluation relied upon behavioral assessment and lacked association with self-report measurement of interoception.

CONCLUSIONS

Despite the above-mentioned limitations, this is the first study to detect the presence of significant abnormalities in RSA reactivity and IA among a homogeneous sample of individuals with GD. The finding reported here may have practical implications, as HRV-based rehabilitation programs may represent a promising venue in the treatment of addictive disorders, including GD (Di Nicola, Pepe et al., 2020; Eddie, Vaschillo, Vaschillo, & Lehrer, 2015). Moreover, based on our findings, a broader exploration relying upon an embodiment-informed framework (Miller, Kiverstein, & Rietveld, 2020) may contribute to shed further light on the clinical phenomenology of the disorder.

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APPENDIX

Supplemental methods

Supplementary statistical analyses

In the main analyses we compared GD individuals and HCs in RSA reactivity, which was operationalized as the change in RSA absolute values between the two conditions of baseline and recovery. To further confirm the presence of significant differences between GD individuals and HCs in RSA, we conducted a one-way analysis of covariance (ANCOVA) with repeated measures to compare group means from baseline to recovery. Specifically, we set the diagnostic group (GD vs. HC) as between factor, the condition (Baseline vs. Recovery) as within factor, and DASS-21 total score, age, smoking status, and BMI as covariates, to generate F value and its associated significance level for within-subjects effects. Associated effect sizes (partial eta squared) were also reported. The level of significance was set at 5%.

Supplemental results

An ANCOVA with repeated measures determined that mean RSA significantly differed between baseline [GD: 4.35 ± 1.62 ln(msec)^2; HCs: 5.29 ± 1.16 ln(msec)^2] and recovery [GD: 4.20 ± 1.68 ln(msec)^2; HCs: 5.69 ± 1.12 ln(msec)^2] in the two diagnostic groups ($P = 0.002$), even after controlling for DASS total score, age, smoking status, and BMI. Of note, none of these covariates resulted significant (Table S4 and Figure S1).

Table S4. Repeated Measure ANCOVA (within subjects effects)

	Type III sum of squares	df1	df2	Mean square	F	p	$\eta^2 p$
Condition	0.11	1	38	0.11	1.0	0.314	0.027
Condition * Age	0.02	1	38	0.02	0.2	0.619	0.007
Condition * DASS-21	0.12	1	38	0.12	1.1	0.291	0.029
Condition * Group	1.21	1	38	1.21	11.1	**0.002**	0.228
Condition * Smoking	0.12	1	38	0.12	1.1	0.294	0.029
Condition * BMI	0.15	1	38	0.15	1.3	0.245	0.035

Significant results in **bold** characters.
Abbreviations: df1=Degrees of freedom between groups; df2=Degrees of freedom within groups; p=statistical significance; F = value of variance of the group means; $\eta^2 p$ = partial eta squared measure of effect size; BMI = body mass index; DASS-21=Depression Anxiety and Stress Scale.

Table S5. IGT NET scores of GD and HC groups

IGT NET (M ± SD)	GD (N = 22)	HC (N = 22)	Overall
NET 1	−2.5 ± 5.6	−1.9 ± 7.2	−2.2 ± 6.4
NET 2	−1.1 ± 5.1	5.7 ± 9.1	2.4 ± 8.1
NET 3	−1.1 ± 6.9	7.0 ± 10.1	3.1 ± 9.5
NET 4	−0.4 ± 7.9	6.9 ± 11.2	3.4 ± 10.4
NET 5	−0.4 ± 8.0	5.4 ± 12.9	2.6 ± 11.1

Abbreviations: M = mean; SD = standard deviation; IGT = Iowa Gambling Task; GD = Gambling Disorder; HC = healthy controls.
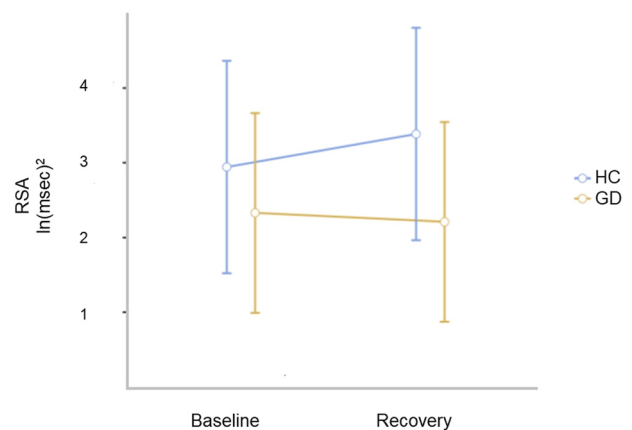

Fig. S1. Estimated marginal means and standard errors of RSA adjusted for age, DASS-21 total scores, smoking status, and BMI during baseline and recovery in HC and GD groups