



Depressed mood, brooding rumination and affective interference: The moderating role of heart rate variability

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ABSTRACT

Facilitated processing of negative information might contribute to the etiopathogenesis and maintenance of depressive symptoms. Cardiac vagal tone, indexed by heart rate variability (HRV), is believed to represent a proxy of the functional integrity of the neural networks implicated in brooding rumination, affective interference and depression. The present study examined whether HRV may moderate the relation between brooding rumination, affective interference and depressive symptoms in a sample of healthy individuals ($n = 68$) with different degrees of depressed mood. Self-report measures of depression and brooding were collected, whereas the emotional Stroop task was employed to measure affective interference. Three-minute resting-state electrocardiogram was recorded to obtain time- and frequency-domain vagally mediated HRV parameters. Stepwise linear regression analyses revealed that HRV was a significant moderator of the positive association between depression and brooding rumination, but not of the association between depression and affective interference. An integrated model is supported, in which vagally mediated HRV appeared to potentiate the positive link between depressive symptoms and brooding rumination. Considering that HRV and brooding rumination were found to have an interacting role in determining the severity of depressive symptoms, they may represent potential clinical targets in the prevention and treatment of depressive symptoms.

1. Introduction

Depression is a globally prevalent mood disorder primarily associated with a persistent state of sadness and/or loss of interest, with an impact on thought and behavior, showing consequent impairments in emotional and cognitive information processing (Kessler, 2012; LeMoult and Gotlib, 2019). Depressive disorders severely affect both psychological and physiological functioning and were defined as a leading cause of disease burden worldwide in 2010, with an increase of 37.5% as compared to 1990 (Ferrari et al., 2013). Several clinical predictors of depression occurrence and recurrence have been recognized, including age of illness onset, long-lasting subclinical symptoms, dysfunctional cognitive processing and emotion regulation strategies (Burcusa and Iacono, 2007; ten Doesschate et al., 2010). Most importantly, individual

differences in responses to negative occurrences have been extensively linked to heightened risk for depression onset (Joormann and Vanderlind, 2014). Indeed, the reduced ability to regulate negative emotions, a core feature of depression, results in prolonged states of negative affect following unpleasant events (Nolen-Hoeksema et al., 2008). In this context, cognitive theories of depression suggest that the higher sensitivity and facilitated processing of negative information may contribute to the etiopathogenesis and maintenance of the disorder (Beck and Bredemeier, 2016; Clark and Beck, 2010; Gotlib and Joormann, 2010; LeMoult and Gotlib, 2019; Nolen-Hoeksema et al., 2008; Treynor et al., 2003). The tendency to hold a highly negative self-concept, characteristic of depressed mood, seems to facilitate the processing and perceptual integration of unpleasant information (Kaiser et al., 2018; Sui and Humphreys, 2015).

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A particularly detrimental response to negative affect is rumination, which has extensively been described as a key vulnerability factor in the development and maintenance of depressed mood (Hong and Cheung, 2015; Joormann and Vanderlind, 2014; Lyubomirsky and Tkach, 2004; Raes, 2012; Treynor et al., 2003). Ruminative thinking is defined as the tendency toward repetitive thinking about negative information (e.g., unpleasant emotional experiences) and their consequences and it typically leads to adverse outcomes, including longer and more severe episodes of major depression (Nolen-Hoeksema et al., 2008; Ottaviani et al., 2016; Woody et al., 2014). Rumination does not only have an impact on the psychological domain, but it also plays a crucial role in physiological wellbeing. Indeed, the sustained cognitive representation and anticipation of stressful events triggers a cascade of biological reactions that have an impact on a variety of functions from the brain to the autonomic nervous system (Brosschot and Thayer, 2004; Brosschot et al., 2006; Ottaviani et al., 2016). Particularly, brooding rumination involves the tendency to dwell on the adverse consequences of one's negative affect, which increases the risk of the first onset depressive episode in individuals with familial risk (Gibb et al., 2012). Interestingly, at the neural level, rumination-related brain dysfunctions are partially overlapping with those found in depression. For instance, studies described patterns of decreased resting-state functional connectivity between prefrontal areas and amygdala, suggesting weakened prefrontal inhibitory control over subcortical affective structures in rumination (Connolly et al., 2017; Makovac et al., 2016; Ray et al., 2005; Veer et al., 2010).

Furthermore, inflexible and perseverative styles of thinking, such as brooding, highly influence attention processes, which, in turn, are central in the maintenance of dysfunctional regulation strategies and negative mood (Disner et al., 2011; Nolen-Hoeksema et al., 2008; Wells, 2011; Fergus et al., 2012). Specifically, brooding is associated with several detrimental consequences, such as the development of dysfunctions in the processing of affective content (Fergus et al., 2013; Wells, 2011). Indeed, some evidence suggests that individuals with the tendency to ruminate disproportionately attend to unpleasant content and show difficulties in inhibiting unpleasant information when it is irrelevant to the attentional task demands (Joormann, 2006; Siegle et al., 2002). In this context, individual differences in early perception of emotional material are considered crucial factors linked to the persistence of negative affect (Beck and Bredemeier, 2016; Clark and Beck, 2010; Disner et al., 2011; Gotlib and Joormann, 2010; LeMoult and Gotlib, 2019; Joormann, 2010). Indeed, there is consistent evidence showing that individuals with depressed mood show a preferential processing of mood-related unpleasant material in all domains of information processing (Clark and Beck, 2010; Gotlib et al., 2004; LeMoult and Gotlib, 2019). Besides, there is also evidence reporting the presence of reduced processing of pleasant information in depression, suggestive of attentional avoidance of pleasant and rewarding stimuli (e.g., Nandrino et al., 2004; Shane and Peterson, 2007; for a review see Winer and Salem, 2016). Moreover, such biases in attention influence executive functioning, making it more difficult to exert top-down cognitive control and to inhibit task-irrelevant responses in the presence of affective cues (Disner et al., 2011; Goeleven et al., 2006; Kaiser et al., 2015). For instance, performance impairments in individuals with depressed mood in tasks requiring cognitive control for affective cues have been attributed to the interfering effects of attentional biases (Joormann, 2004; Kaiser et al., 2015). This phenomenon, defined as affective interference, has been repeatedly reported in individuals with depressed mood for unpleasant content (Gotlib et al., 2004; Gotlib and Joormann, 2010; Peckham et al., 2010). In general, affective interference seems to be a result of an impairment in overriding prepotent responses and in inhibiting the processing of salient but irrelevant information to the ongoing task, leading to an overloading of cognitive control (Kaiser et al., 2015). At the neural level, affective interference for unpleasant stimuli was associated with decreased activity of prefrontal structures which, in turn, leads to an impaired attenuation of amygdala activity,

resulting in prolonged enhanced activation of amygdala to emotional stimuli (De Raedt and Koster, 2010; Disner et al., 2011; Siegle et al., 2002).

A task that has been largely employed to measure affective interference is the emotional version of the Stroop task (Stroop, 1935), whereby participants are asked to indicate the print color of emotional (pleasant and unpleasant) and neutral words while ignoring the meaning of the words themselves. The emotional Stroop task has been employed to study the cognitive processes with regards to the time taken to name colors of unpleasant and pleasant words compared to neutral items across clinical and non-clinical populations. Several recent behavioral and neuroimaging studies that employed the emotional Stroop task have provided converging evidence for higher affective interference for unpleasant mood-congruent stimuli in individuals with clinical depression (Fritzsche et al., 2010; Mitterschiffthaler et al., 2007), with subclinical depression (Gantiva et al., 2018; Kaiser et al., 2015), in healthy individuals subjected to sad mood induction (Gilboa-Schechtman et al., 2000; Isaac et al., 2012; Provenzano et al., 2019), and women with familiarity to depression (van Oostrom et al., 2013).

A peculiar measure that could reflect depression's etiopathogenetic processes, including rumination and affective interference, is heart rate variability (HRV). Resting HRV refers to the temporal variations between successive heartbeats while the individual is in a condition of rest, which ensures optimal adaptation to environmental demands (Koch et al., 2019). Considering that the heart is under tonic inhibitory control via the vagus nerve and predominantly dominated by fast vagal modulation, low resting HRV reflects reduced vagal control (Levy, 1990; Thayer and Lane, 2000). Reduced resting HRV has been consistently reported in individuals with depression, as compared to healthy controls, and these findings have underlined the potential role of autonomic nervous system dysregulation in its pathophysiological mechanisms (e.g., Dell'Acqua et al., 2020; Hamilton and Alloy, 2017; Hartmann et al., 2019; Messerotti Benvenuti et al., 2015; for reviews see Kemp et al., 2010 and Koch et al., 2019).

Moreover, besides the relation between reduced resting HRV and depressive symptoms, a series of studies have additionally linked changes in resting HRV to a wide variety of psychological processes, including brooding rumination and affective interference in healthy samples (Geisler et al., 2010; Hansen et al., 2004; Kok and Fredrickson, 2010; Park and Thayer, 2014). In particular, individuals with higher HRV typically show less ruminative thinking, whereas those with reduced HRV typically tend to engage in maladaptive emotion regulation strategies, such as brooding rumination (Brosschot et al., 2010; Thayer and Lane, 2000). For instance, recent meta-analytic evidence showed that individuals who tend to engage in brooding rumination are characterized by reduced HRV both during resting conditions and following stressful or sad mood induction (Ottaviani et al., 2016). Correspondingly, several longitudinal studies have highlighted the crucial role of HRV in the association between brooding rumination and depressive symptoms, where reduced HRV predicted a positive relation between the two psychological features (Carnevali et al., 2018; Stange et al., 2017). Particularly, Carnevali et al. (2018) reported that HRV at time 1 (~13 months after time 0) mediated the association between rumination at time 0 and depression at time 2 (~34 months after time 0). Likewise, another multi-wave study reported similar results with the employment of HRV recorded during a sad mood induction (Stange et al., 2017). These findings suggest that reduced vagal tone in individuals with high levels of rumination could be implicated in the development of depressive symptoms in a non-clinical population.

Further, individual differences in resting cardiac vagal modulation were associated with higher affective interference for unpleasant cues (Kryptos et al., 2011; Park and Thayer, 2014). Specifically, several empirical studies have reported that individuals with reduced resting HRV showed impairments in inhibiting unpleasant stimuli relative to individuals with higher resting HRV (Kryptos et al., 2011; Park et al., 2012; Park et al., 2013). Likewise, individuals with resting higher HRV

were quicker in inhibiting their responses in an emotional stop-signal task compared to individuals with lower resting HRV only in unpleasant trials (Kryptos et al., 2011). Altogether, these findings suggest that reduced HRV may reflect affective interference, which is highly associated with depressive symptoms.

An explanation for the association between HRV, brooding rumination and affective interference could lay in the evidence that HRV is strictly integrated in a network that involves brain structures known to be implicated in the two processes. Particularly, according to the neurovisceral integration model (Thayer and Lane, 2000, 2009; Thayer et al., 2012), HRV is the result of the output from a prefrontal-subcortical network, also defined as the central autonomic network (CAN; Benarroch, 1993; Mulcahy et al., 2019; Valenza et al., 2019), which is involved, among others, in the central control of autonomic functioning (Mulcahy et al., 2019; Thayer et al., 2009; Thayer et al., 2012). It is interesting to note that the CAN includes numerous cortical and subcortical structures that are also involved in depression, brooding rumination and affective interference, that is, the anterior cingulate, the insula, and the ventromedial prefrontal cortices as well as the central nucleus of the amygdala and the hypothalamus (Park et al., 2014; Thayer et al., 2009; Mulcahy et al., 2019). Individuals with lower HRV showed reduced prefrontal-amygdala functional connectivity during rest (Mather and Thayer, 2018; Sakaki et al., 2016; Thayer et al., 2012). Besides, these prefrontal-amygdala patterns are those associated with depressive symptoms, brooding rumination and affective interference (Connolly et al., 2017; De Raedt and Koster, 2010; Disner et al., 2011; Makovac et al., 2016; Ray et al., 2005; Siegle et al., 2002; Veer et al., 2010).

Given that HRV is considered to be a measure implicated in depression and, at the same time, in two processes that are considered central for its onset and maintenance, the main goal of the present study was to investigate the potential moderating role of HRV in the association between depressive symptoms and brooding rumination and affective interference for unpleasant stimuli. A comprehensive approach was adopted in order to concurrently examine the role of reciprocal interactions of HRV, brooding and affective interference for unpleasant cues in predicting depressive symptoms. The current study adopted the conceptualization of depression as a continuum of severity instead of a categorical condition (e.g., Hankin et al., 2005; Lesnewich et al., 2019; Liu, 2016). To this end, depression and brooding rumination were assessed through self-report measures, whereas affective interference was assessed with the emotional variant of the Stroop task. Altogether, it was hypothesized that HRV would represent a moderator underlying the relation between depressive symptoms and brooding rumination and affective interference for unpleasant stimuli.

2. Methods

2.1. Participants

The present study was conducted within an extensive research project and some participants' data was already presented in a previous publication (Dell'Acqua et al., 2020). A total of 68 right-handed university students voluntarily took part in the present study (20 males, 48 females, mean (M) age = 20.4, standard deviation (SD) = 2.0). An a-priori power analysis was conducted using G*Power 3 software (G*Power 3 software, Faul et al., 2009). Although a recent meta-analysis (Ottaviani et al., 2016) has examined the association between HRV and brooding showing a small-to-medium effect size ($f = 0.15$), no previous work has estimated the interactions tested in the present study. Considering that ordinal interactions typically have low power, a small effect size was expected ($f = 0.10$) (e.g., McClelland and Judd, 1993). The power analysis revealed that 64 participants were needed to obtain a small effect size ($f = 0.10$) and a statistical power of 0.8 (given $\alpha = 0.05$, number of measurements = 3). The enrolled sample was medically healthy and free from psychotropic medication, as assessed with an ad-

hoc anamnestic interview. Overall, participants smoked on average 1.4 (SD = 2.7) cigarettes per day and consumed on average 1.4 (SD = 1.7) units of alcohol per week. Exclusion criteria included the current and past history of cardiovascular, psychiatric, and neurological diseases. All participants had a normal or corrected-to-normal vision and were naive to the purpose of the experiment. Participants were compensated 13 € for their participation. The present study was conducted with the adequate understanding and written consent of the participants in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee, University of Padua (prot. no. 3612).

2.2. Procedure

The study was split in two experimental sessions within the same week. Prior to the experimental sessions, participants were required to avoid alcohol consumption the day before and to avoid caffeine and nicotine the same day of the appointment. During the first session, after reading and signing the informed consent, participants were first administered a demographic interview. Then, participants were seated in a dimly lit, sound-attenuated room. After the sensors were attached, the electrocardiogram (ECG) was recorded at rest over a three-minute period for each participant. Short-term recording (<5 min) has been documented to be a reliable method to measure HRV (Baek et al., 2015; Shaffer et al., 2016). During the second session, participants completed a computerized emotional version of the Stroop task and self-report psychological questionnaires. The instructions were explained orally to each participant. The entire procedure lasted approximately 1 h and 30 min.

2.3. Self-report questionnaires

Depressive symptoms were assessed using the Beck Depression Inventory-II (BDI-II; Beck et al., 1996; Italian version by Ghisi et al., 2006). The BDI-II is a reliable and valid self-report questionnaire that was used to assess the severity of current depressive symptoms in the past two weeks. Specifically, the BDI-II is composed of 21 items, each based on a four-point Likert scale and scores range from 0 to 63, with the higher scores indicating greater depressive symptoms. According to the Italian validation of the BDI-II, a score equal or below 11 represents absence of depression, a score between 12 and 21 represents mild-to-moderate depression and a score above or equal to 22 corresponds to the 99th percentile and represents severe depression (Ghisi et al., 2006). Rumination was assessed using the Ruminative Response Scale (RRS; Treynor et al., 2003; Italian version by Palmieri et al., 2007). The RRS is a 22-item self-report measure of rumination. Particularly, ten items have been identified to assess two components of rumination: brooding and reflective pondering. The measure consists of five brooding items (e.g., "think about a recent situation, wishing it had gone better") and five reflection items (e.g., "analyze recent events to try to understand why you are depressed"), which are scored on a Likert scale ranging from 1 (never) to 4 (always). It has excellent internal consistency and validity (Treynor et al., 2003). In the present work, brooding was selectively analyzed because it is thought to be a more maladaptive form of rumination than is reflection, a response style that is more oriented toward reappraisal (Woody et al., 2014).

2.4. Emotional Stroop task and behavioral data reduction

Italian words belonging to three categories (pleasant, neutral and unpleasant) were selected from the Affective Norms for English Words (ANEW, Italian version by Montefinese et al., 2014) based on valence and arousal scores. Specifically, the words were selected on the basis of their standardized ratings of affective arousal and valence. The mean (SD) normative valence ratings were 8.07 (0.31), 5.50 (0.26) and 1.94 (0.41) for pleasant, neutral and unpleasant words, respectively. The mean (SD) normative arousal ratings were 6.82 (0.51), 4.36 (0.28) and

6.79 (0.58) for pleasant, neutral and unpleasant pictures, respectively. Pleasant and unpleasant stimuli were matched for arousal ($p = .96$). Particularly, unpleasant words were selected as the 40 words mostly related to depression. Also, a posteriori computation of three measures of similarity with the concept of “depression” (affective distance, semantic distance and strength of lexical association) revealed that 22 words out of 40 (55%) had both affective and semantic distance within the first quintile as compared to all other ANEW words, and 7 of these words were also associated with the word “depression”. All the 120 words were included in the supplementary material (Appendix 1, Table A). Words were presented one at a time via Psychopy software (Peirce et al., 2019) in four colors (red, yellow, blue, or green) on a light grey background in the center of the screen. Participants were asked to indicate, through the use of the keyboard, the word color as quickly as they could, while ignoring its meaning and valence. Each word consisted of a trial and a total of 120 words were included in the present experiment. Intertrial interval consisted of 500 ms. Each word was presented twice in two different colors, yielding to a total of 240 trials. Two versions were employed in order to counterbalance the presentation of the words. A practice block with 30 trials was provided. Trials were pseudorandomized in order to avoid keyboard response position or emotional category repetitions and thus minimize the priming effects. The task was self-paced and response times (RTs) were measured as the time it took for each participant to indicate the color through the use of four keys of the keyboard (left, right, up, down arrows). RTs were calculated in milliseconds (ms). Error trials and trials with RTs shorter than 300 ms were discarded from the analysis ($<0.1\%$ of trials were discarded) (Blanchette and Richards, 2013). Since the distributions of the RTs were skewed and/or kurtotic, we log-transformed RTs for each trial to improve normality. Affective interference was determined by the Stroop interference index (RTs emotional words – RTs neutral words), whereby positive values indicate increased interference for the emotional stimuli and negative values indicate reduced interference for the emotional stimuli with respect to the neutral ones. The Stroop interference index was calculated for each individual as follows:

$$\text{Positive Stroop interference index} = \text{Mean log (RTs pleasant words)} - \text{Mean log (RTs neutral words)}$$

$$\text{Negative Stroop interference index} = \text{Mean log (RTs unpleasant words)} - \text{Mean log (RTs neutral words)}$$

2.5. ECG recording and HRV estimation

Physiological data acquisition was accomplished using a computer running eego™ software and using an eego amplifier (ANT Neuro, Enschede, Netherlands). The ECG was recorded from three Ag/AgCl electrodes that were positioned on the participant's chest in a modified lead II configuration. The ECG was recorded continuously for 3 min while participants were seated comfortably during undisturbed resting conditions and asked to fix their gaze to a cross presented at the center of the screen. Impedance was kept below 5 kΩ and each ECG signal was amplified, band-pass filtered (0.3–100 Hz) and sampled at 1000 Hz.

In order to assess time- and frequency-domain vagally mediated HRV parameters, the ECG signal was analyzed offline using the Biopac Acqknowledge 5.0 software (Biopac Systems Inc., USA). All ECG data were visually inspected, and artefacts were removed. A digital trigger detecting R-waves was applied to the ECG signal to obtain RR intervals, corresponding to the inverse of heart rate. One participant was excluded due to

extended artefacts in the ECG signal. Among all time- and frequency-domain parameters of HRV, it was decided to calculate only the most frequently used HRV measures in the literature (e.g., Koch et al., 2019; Patron et al., 2012; Thayer et al., 2012) and the most appropriate measures for short-term recordings (Task Force, 1996). These indices were calculated using Kubios HRV Analysis Software 3.3.1 (Matlab, Kuopio, Finland). In the time-domain, standard deviation of NN intervals (SDNN), which reflects the cyclic components responsible for the variability of heart rate expressed in ms, was computed (Task Force, 1996). In the frequency-domain, High Frequency (HF) power (0.15 to 0.40 Hz), an index of cardiac vagal tone, was obtained in ms^2 through autoregressive (AR) spectral analysis. AR method is a popular tool for spectral analysis of HRV and the length of data required for analysis is shorter than fast Fourier transform (Kamath et al., 1987; Task Force, 1996). Both time- and frequency-domain indices were logarithmically transformed before the statistical analyses to normalize their distribution.

2.6. Statistical analysis

Considering that variables such as gender, age, sleep, smoking and drinking habits have been shown to affect resting HRV, they were preliminary analyzed (Laborde et al., 2017). To test whether these variables had an influence on resting HRV, Pearson's correlation was calculated for the relation between HRV parameters and age, sleep (average hours/per night), smoking (cigarettes/per day) and alcohol consumption (units/per week). Additionally, considering that the male gender was fairly underrepresented, independent t -tests were carried out to test whether gender influenced the dependent variable of the linear regression models (BDI-II). Moreover, Cronbach's alpha value of the self-report questionnaires (BDI-II and RRS) was calculated to determine the scales' internal consistency; similarly, the reliability of the RTs to pleasant, neutral and unpleasant words was evaluated by computing split-half correlations corrected with the Spearman-Brown formula (2000 random splits). In regard to the emotional Stroop task, an analysis of variance (ANOVA) with Category (pleasant, neutral and unpleasant)

as within-subject factor was conducted on log-transformed RTs. Significant main effects and/or interactions ($p < .05$) were followed by Tukey HSD post-hoc tests in order to correct for multiple comparisons.

Further, to assess whether the link among depressive symptoms, brooding rumination and affective interference was moderated by HRV, two stepwise linear regression models with forward selection using the Akaike information criterion (AIC) for variables selection (Akaike, 1974) were conducted, one for each HRV measure (lnSDNN, lnHF), using *lm* function (*stats* package; R Core Team, 2017). The stepwise approach involves the creation of a regression model from a set of candidate predictor variables by adding and removing predictors until an optimal model to explain the dependent variable is reached. Essentially, stepwise linear regression is a method of regressing multiple variables that are automatically added while those that are not significant are being simultaneously removed, thus providing the best predictors to explain the dependent variable. This method starts with an initial model and then takes sequential steps by adding or removing the included predictors. At each step, the model is tested with the computation of a p -value of an F-statistic (Draper and Smith, 1998). In this

analysis, BDI-II was included as dependent variable, while the potential predictors were HRV measures (i.e., lnSDNN or lnHF), the “brooding” subscale of the RRS, the Stroop negative index, two-way (i.e., HRV measure \times Brooding; HRV \times Negative index) and three-way interactions (HRV measure \times Brooding \times Negative index). Stepwise forward linear regression model incorporates a forward selection procedure to test which predictors have the greatest influence on the dependent variable, thus detecting the best regression model. The best regression model was chosen using the *stepAIC* function (MAAS package; Venables and Ripley, 2002), which relies on the AIC criterion (Bolker et al., 2009). All continuous variables were centered and scaled: the mean of each variable was subtracted by each individual value and the resulting value was then divided by the standard deviation of its distribution. The collinearity was tested by calculating the Variance Inflation Factors (VIF) with the *vif* function of the *car* package (Fox et al., 2019). A *p* value of .05 was the cut-off for significance. The Benjamini–Hochberg procedure was applied to control the false discovery rate (Hochberg and Benjamini, 1990).

3. Results

3.1. Descriptive statistics and control variables

The average BDI-II score of the sample was 11.8 (SD = 8.9) and scores ranged from 0 to 41. The present sample was composed of 42 participants with a BDI-II score equal or below 11 (absence of depression, 62% of the sample), 18 participants with a BDI-II score between 12 and 21 (mild-to-moderate depression, 25% of the sample) and 8 participants with a BDI-II score above 22 (severe depression, 12% of the sample). Further, the average RRS-brooding score of the sample was 10.6 (SD = 2.7) and scores ranged from 6 to 19. Regarding HRV measures (SDNN and HF) and emotional Stroop RTs, descriptive statistics are displayed in Table 1. Age, sleep, smoking and drinking habits did not significantly correlate with any of the HRV measures (all *ps* > .05). Independent *t*-tests showed that gender did not influence HRV measures (all *ps* > .05). Also, gender did not significantly influence BDI-II scores (*t* (66) = 1.46, *p* = .15), thus it was not included as a control variable in the multivariate models. Internal consistency resulted high for both the 21 items of the BDI-II (Cronbach's alpha = 0.90) and the 22 items of the RRS (Cronbach's alpha = 0.89); RTs reliabilities were also high (median value across the 2000 random splits > 0.9 in all cases).

3.2. Emotional Stroop task

The within-subject ANOVA did not yield any significant differences between the RTs in the three different emotional categories (*F*(2,134) = 1.19, *p* = .31, η_p^2 = 0.02).

3.3. The moderating role of HRV in the association between depressive symptoms, brooding rumination and affective interference

The optimal models detected by both stepwise regressions, namely

Table 1
Descriptive statistics of the study variables.

	Mean	Standard deviation	Range (min-max)
Stroop RTs pleasant ms (ln)	657.5 (2.8)	88.3 (0.1)	488.8–972.6
Stroop RTs neutral ms (ln)	653.6 (2.8)	92.0 (0.1)	485.2–991.4
Stroop RTs unpleasant ms (ln)	659.1 (2.8)	91.2 (0.1)	478.9–980.2
SDNN ms (ln)	54.9 (4.0)	30.8 (0.5)	22.0–228.0
HF ms ² (ln)	1860.3 (6.9)	2345.2 (1.1)	71.7–12,109.4

Note. RTs = response times; SDNN = standard deviation of all NN intervals in ms; HF = high frequency power; ms = milliseconds; ln = natural logarithm; Min = minimum value of the distribution; Max = maximum value of the distribution.

Table 2

Stepwise linear regression models for variables predicting depressive symptoms (BDI-II scores).

Predictor	B (SE)	<i>p</i>	p-FDR	R ²
Model 1				0.52
lnSDNN	−0.29 (0.09)	.002		
RRS Brooding	0.56 (0.09)	<.001		
lnSDNN \times RRS Brooding	−0.24 (0.09)	.013	0.026	
Model 2				0.52
lnHF	−0.29 (0.09)	.002		
RRS Brooding	0.61 (0.09)	<.001		
lnHF \times RRS Brooding	−0.23 (0.11)	.046	0.046	

Note. B = unstandardized coefficient; SE = standard error; p-FDR = Benjamini–Hochberg Adjusted *p*-value; lnSDNN = natural logarithm transformation of the standard deviation of all NN intervals in ms; lnHF = natural logarithm transformation of the high frequency power; BDI-II = Beck Depression Inventory-II; RRS Brooding = Brooding subscale of the Ruminative Response Scale.

the one with the lowest AIC value, included brooding, HRV (lnSDNN, lnHF) and their interaction as predictors of the BDI-II, are shown in Table 2. Regarding lnSDNN, the model revealed that lnSDNN was a significant moderator of the relation between depressive symptoms and brooding rumination (Model 1, Table 2). It is clear from the unstandardized regression slopes that brooding rumination positively predicted depression levels in individuals in both high and low lnSDNN conditions. However, the association between RRS brooding and BDI-II scores was stronger for those with reduced lnSDNN than for those with higher lnSDNN. In particular, the positive association between high levels of brooding rumination and depressive symptoms was most pronounced in individuals with low HRV, as shown in Fig. 1. Likewise, similar results were obtained in the model of lnHF, with a significant interaction between brooding rumination and lnHF (Model 2, Table 2). The independent effect of brooding rumination and HRV (lnSDNN and lnHF) on BDI-II was significant in each of the two models (Table 2). After applying the Benjamini–Hochberg procedure, the two models remained significant (Table 2).

4. Discussion

A core feature that may contribute to the etiopathogenesis and maintenance of depression is represented by higher sensitivity and facilitated processing of negative information (Beck and Bredemeier, 2016; Clark and Beck, 2010; Gotlib and Joormann, 2010; LeMoult and Gotlib, 2019; Nolen-Hoeksema et al., 2008; Treynor et al., 2003). The tendency to hold a highly negative self-concept, characteristic of depressed mood, seems to facilitate the processing and perceptual integration of negative information, leading to increased affective interference (Kaiser et al., 2018; Sui and Humphreys, 2015). Importantly, HRV is considered to be a measure implicated in depression and, at the same time, in two processes that are thought to be central for its onset and maintenance, that is, brooding rumination and affective interference. The present study represents a first attempt to concurrently examine the role of reciprocal interactions of HRV, brooding and affective interference for unpleasant cues in predicting depressive symptoms. The study was based on the assumption that cardiac vagal tone, indexed by HRV, reflects the functional integrity of neural networks implicated not only in depression, but also in brooding rumination and affective interference (Connolly et al., 2017; De Raedt and Koster, 2010; Disner et al., 2011; Makovac et al., 2016; Ray et al., 2005; Siegle et al., 2002; Thayer and Lane, 2009; Veer et al., 2010).

First of all, it was demonstrated that both SDNN and HF were significant moderators of the association between depressive symptoms and brooding rumination. Specifically, from the graphical representation of the model, the association between brooding rumination and depressed mood was most pronounced for individuals with reduced HRV than for those with higher HRV. A potential explanation for this

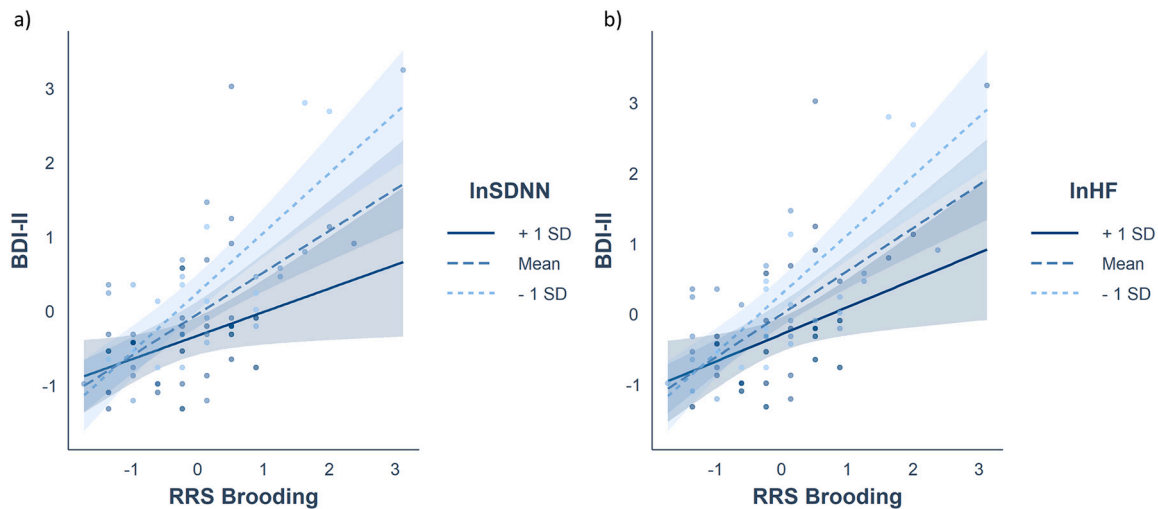


Fig. 1. Panel a) Interaction effect of RRS Brooding and lnSDNN on BDI-II. Note. Ninety-five % confidence bands for mean, +1 SD, -1 SD lnSDNN are presented in different colors. Panel b) Interaction effect of RRS Brooding and lnHF on BDI-II. Note. Ninety-five % confidence bands for mean, +1 SD, -1 SD lnHF are presented in different colors. BDI-II = Beck Depression Inventory-II, lnSDNN = logarithmic value of standard deviation of all NN intervals, lnHF = logarithmic value of high-frequency power.

association can be found in their common underlying neurophysiological mechanisms. Indeed, brooding rumination, depressive symptoms and reduced HRV are associated with reduced inhibitory control of prefrontal structures on the amygdala, which is implicated in defensive behavior. Whenever a threatening or a stressful event is experienced, the prefrontal cortex gets hypoactivated, leading to reduced inhibition of subcortical structures, parasympathetic withdrawal, and predominance of sympathoexcitatory circuits in order to produce an adaptive response to the event (Thayer and Lane, 2009). Hence, alterations in these inhibitory processes may lead to defensiveness and less flexible affective and cognitive responsiveness to environmental demands (Beauchaine and Thayer, 2015). Also, this account is consistent with the neuro-visceral integration model, which suggests that HRV provides an index of the successful functioning of the CAN, which is implicated in the integration of information from different systems, among which emotion regulatory processes (Mather and Thayer, 2018; Thayer and Lane, 2000; Thayer et al., 2009). Overall, the present study corroborates previous research indicating that brooding rumination is positively associated with depressed mood and heart rate variability (Brosschot et al., 2010; Carnevali et al., 2018; Nolen-Hoeksema et al., 2008; Ottaviani et al., 2016; Stange et al., 2017; Williams et al., 2017).

In contrast, stepwise regression did not identify as significant any model including the negative Stroop interference index, thus HRV did not emerge as a potential moderator of the association between depressive symptoms and affective interference. Considering that meta-analytic evidence documented that the emotional Stroop task was able to detect affective interference only in individuals with clinical depression, it could be suggested that the present sample of individuals with non-clinically relevant depressed mood was not sufficient to detect such effects (Epp et al., 2012). Indeed, the association between affective interference and depressive symptoms is still an object of debate and effect sizes have been inconsistent across studies that employed distinct computerized tasks. An explanation for these mixed findings could arise from the fact that sub-processes of attention (orienting, selecting, engaging and disengaging from stimuli) could be differentially associated with distinct degrees or subtypes of depressive symptoms (Kaiser et al., 2018; Petersen and Posner, 2012). Additionally, it is important to point out that the use of the emotional Stroop task to detect impaired processing of affective stimuli has been controversial (Peckham et al., 2010). As a matter of fact, the analysis on RTs at the emotional Stroop task did not reveal the expected effect of the emotional category, which may imply that the task was not sensitive enough to elicit affective

interference in the sample. For this reason, considering that an increased eye-gaze maintenance on unpleasant cues may reflect impaired disengagement and inhibition of these stimuli, the employment of eye-tracking paradigms in future studies is warranted (Armstrong and Olafson, 2012; Sanchez et al., 2013; Sears et al., 2010).

Although the current research involved a non-clinical population, these results could have several clinical applications, involving both top-down and bottom-up interventions. Considering that brooding rumination may have a key role in determining the severity of depressive symptoms, it could serve as a useful target in the clinical setting (Hong and Cheung, 2015; Joormann and Vanderlind, 2014; Lyubomirsky and Tkach, 2004; Raes, 2012; Treynor et al., 2003). A useful top-down strategy could be decentering, an adaptive metacognitive strategy involved in the processing of awareness of one's own subjective experience, by observing one's thoughts and feelings as temporary and objective events in mind (Lo et al., 2014; Stange et al., 2017). This ability to distance oneself from maladaptive thoughts may reduce the emotional impact of ruminative and perseverative mechanisms (e.g., Kang et al., 2013). Interestingly, decentering was found to be protective against the effects of reduced HRV on prospective symptoms of depression and to diminish the risk of depression onset conferred by the interaction between reduced HRV and brooding rumination (Stange et al., 2017). Among bottom-up strategies, which mainly involve psychophysiological regulation, HRV-biofeedback could be a potential efficacious intervention to reduce the exacerbation of depressive symptoms. HRV-biofeedback, a non-invasive technique that allows psychophysiological self-regulation, works by providing a direct feedback of HRV (through a screen or headphones), which helps individuals to actively modify that targeted physiological process (Lehrer, 2007). HRV-biofeedback has been found to be effective in restoring cardiac autonomic balance by increasing cardiac vagal tone, that, in turn, improves wellbeing (Lehrer, 2007; Lehrer et al., 2020). Interestingly, it was demonstrated that HRV-biofeedback training can relieve depressive symptoms and brooding rumination (e.g., Caldwell and Steffen, 2018; Patron et al., 2013).

The current study presents several strengths. First, several confounding variables such as gender, age, smoking habits, alcohol consumption and sleep were analyzed in order to control for their potential effect on HRV measures (Laborde et al., 2017). Additionally, the sample was free from psychotropic medications, which often represent a confounding variable when studying patients with depression. Also, the different psychological factors associated with HRV have rarely been

considered together and studies have mostly focused on sectorial fields. Here, a comprehensive approach was adopted where cardiac vagal tone was considered in relation with depressive symptoms, along with brooding rumination and affective interference. Moreover, the use of continuous measures allowed to avoid the drawbacks of information and statistical power loss associated with dichotomization (Altman and Royston, 2006).

However, in interpreting our results, some limitations, that may offer useful suggestions for future research, need to be acknowledged. First, the prevalence of female gender and the young age of the participants might not allow generalization of the findings. Second, despite most studies analyzed resting-state HRV, task-related measures should be examined in the future in order to explore the organism's response to, for example, the presentation of emotional cues in a task and during ruminative thinking. Lastly, the discrepancy of measurement approach between brooding and depressive symptoms (self-report) with affective interference (response times) might have influenced the findings of the study.

5. Conclusion

Taken together, the current study represents a first attempt to integrate HRV with depressive symptoms, brooding rumination and affective interference. An integrated model is supported, where reduced cardiac vagal tone and brooding rumination have a combined effect in predicting the degree of depressive symptoms. Hence, improvements of vagal modulation and metacognitive strategies aimed at reducing brooding ruminative thinking may represent potential clinical targets in the prevention and treatment of depressive symptoms.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijpsycho.2021.03.011>.

Data availability

All data and R code will be made available to researchers upon reasonable request.

CRediT authorship contribution statement

All authors developed the study concept and contributed to the study design; C.D.A., E.D.B. and S.M.B. conducted the study; C.D.A. and E.D.B. performed the data analysis and interpretation under the supervision of S.M.B., E.A., A.V. and D.P.; C.D.A. and E.D.B. drafted the paper, and S.M.B., E.A., A.V. and D.P. provided critical revisions. All authors approved the final version of the paper for submission.

Declaration of competing interest

The authors declare no conflicts of interest with respect to the authorship or the publication of this article.

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Biomarkers of Intergenerational Risk for Depression).

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