The link between depressed mood and heart rate variability: a mediating role for disinhibited eating and diet?

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Keywords: Heart rate variability; Heart rate complexity, Disinhibited eating; Diet; Mood.

Abstract

Consistently it has been reported that a depressed mood and low heart rate variability (HRV) are linked. However, studies have not considered that the association might be explained by dietary behaviour. The resting inter-beat interval data of 266 adults (Study 1: 156 (51M), Study 2: 112 (38M)) were recorded for six minutes and quantified using linear (HF power: 0.15–0.4 Hz) and nonlinear indices (Sample entropy). Participants also completed the Profile of Mood States and the Three Factor Eating questionnaires. The Alternative Healthy Eating Index was used to quantify diet quality. In study 1 mood was associated with HRV; an effect partially mediated by diet. Study 2 replicated the finding: disinhibited eating (the tendency to lose control over one's eating) and diet sequentially mediated the association between mood and HRV. Diet plays a role in the link between mood and HRV and studies should consider the influence of this factor.

1. Introduction

Depression and cardiovascular disease (CVD) are two of the most frequently occurring diseases in the developed world (Mathers and Loncar, 2006; Murray and Lopez, 1996) and are often comorbid (Celano and Huffman, 2011; Grippo and Johnson, 2009). Not surprisingly attention has been directed towards understanding the factors that connect the two disorders (Celano and Huffman, 2011; Grippo and Johnson, 2009; Hare et al., 2013; Kemp et al., 2010; Raison, Capuron and Miller, 2006) with low heart rate variability (HRV) suggested as a mediating pathway. Indeed there is evidence that HRV indices are reduced in disorders characterised by emotional dysregulation (Chalmers et al., 2014; Kemp et al., 2010) and are associated with an increased risk of CVD (Tsuji et al., 1996). However, whilst it is assumed that HRV (usually HF power: 0.15–0.4 Hz) directly reflects the capacity for self-regulated emotional responding (Appelhans and Luecken, 2006), an alternative view is that individuals who have difficulty regulating emotions are at risk of adopting emotion regulation strategies such as the consumption of 'comfort' foods, with a resulting decrease in the quality of the diet (Luppino et al., 2010). As the vast majority of studies examining the association between HRV indices and mood have not systematically controlled for the influence of diet, two studies assessed this unexplored indirect pathway. It is reported for the first time that the mood / HRV association might be explained, at least in part, by changes in dietary behaviour.

Worldwide an unhealthy diet is a leading cause of premature mortality (Forouzanfar et al., 2015) and is increasingly linked to the development of affective disorders (Dash, O'Neil and Jacka, 2016). For instance, consuming a 'western' style diet of refined carbohydrates, processed or fried foods, sugary products and alcohol was associated with a higher rate of depression and anxiety (Jacka et al., 2010). On the other hand a Mediterranean dietary pattern (high in fruits, vegetables and fish) may confer protection against the development of

depression (Sánchez-Villegas et al., 2009). However, such associations are likely to be bidirectional – whilst diet might influence mood and wellbeing, mood will also influence dietary behaviour. It is well recognised that negative affect influences the total amount of food consumed as well as food choice (Gibson, 2006). For example naturalistic studies that have examined mood related food behaviour during times of increased workload (such as the examination period) found increases in the intake of total energy and fat (McCann, Warnick and Knopp, 1990). In addition, experimental induction of negative mood increased intake of high calorie foods (i.e foods containing a high amount of sugar and fat) in individuals who were depressed (Privitera et al., 2016). In those suffering from affective disorders a lack of adherence to self-care regimens (e.g diet and exercise) exacerbates the associated adverse physiological effects; including reductions in HRV indices (Katon, 2003). Taken together a plausible hypothesis is that a depressed mood might induce poor dietary choice behaviour which in turn may have consequences for HRV.

Indeed there is sporadic evidence that diet might influence HRV. For example a Mediterranean dietary pattern was found to be associated with higher HRV including HF power (0.15–0.4 Hz) and the length of the R-R interval (Dai et al., 2010). In addition supplementation of omega 3 fatty acids for four weeks improved HRV (LF/HF ratio and R-R interval length) in patients with coronary disease (Villa et al., 2002). Previously we reported that a supplement high in the antioxidant carnosine influenced the HRV (HF/LF ratio) of young adults (Young, Benton and Carter, 2015). Given this emerging evidence it is surprising that little consideration has been given to the fact that dietary behaviour might mediate the association between depressed mood and HRV. Therefore two studies were designed to consider this possibility.

2. Study 1

2.1. Methods

2.1.1. Participants

One hundred and fifty six medication free young adults (51 male) between 18 and 34 years of age participated in this study (Table 1). Participants were excluded if they reported a cardiovascular or metabolic disorder, gastrointestinal problems, were pregnant, had a current diagnosis of a mood or eating disorder, and/or were taking medications or herbal supplements to manage body weight or control appetite. BMI ranged from 16.8 – 37.2 kg/m^2.

2.1.2. Procedure

Participants were instructed to refrain from drinking alcohol and taking part in any physical activity twenty four hours prior to the start of the study. All data were collected between the hours of 9am and 12noon – participants were asked to abstain from consuming any food and drink (including caffeinated beverages) before attending the laboratory. Upon entry into the laboratory, after providing written informed consent, the participants completed the European Prospective Investigation into Cancer and Nutrition Norfolk Food Frequency Questionnaire (FFQ) (Mulligan et al., 2014) and the Profile of Mood States (POMS) (Lorr, McNair and Fisher, 1982). Participants then had their height and weight measured before being fitted with a RS800 Polar heart rate monitor electrode transmitter belt (T61) using conductive gel (Polar Electro, Kempele, Finland). Finally participants rested quietly in a semi – supine position for six minutes while R-R interval data were recorded. The procedure was approved by Swansea University ethics committee (reference number: 08.25.2015.2) and carried out in accordance with the principles laid down by the declaration of Helsinki 2013. All participants completed the study.

2.1.3. Measures

2.1.3.1. Heart rate variability (HRV)

Interbeat interval measurements were collected using a Polar RS800 HR monitor set to R-R interval mode (Polar Electro, Kempele, Finland) at a sampling rate of 1000 Hz. This instrument has been previously validated for the accurate measurement of R-R intervals and analysing HRV (Nunan et al., 2009).

2.1.3.2. Body mass index (BMI)

Body mass was measured using an electronic scale (Kern KMS-TM, Kenr and Sohn GmbH, Germany) that, to avoid problems associated with movement, took 50 assessments over a 5 second period and produced an average value. Height was measured using a portable stadiometer.

2.1.3.3. Habitual diet

Dietary data were collected using the European Prospective Investigation into Cancer and Nutrition Norfolk Food Frequency Questionnaire (EPIC-Norfolk FFQ) (Mulligan et al., 2014). A common unit or portion size for each food was specified and subjects were asked to indicate on a 9 point scale ranging from 'never' to '6+ per day', how often they tend to consume specific foods. This FFQ has been previously validated by comparison with a 16-day weighed food record (Bingham, et al., 1994) and nutrient biomarkers (Bingham et al., 2001). Data were further analysed using FETA software that uses UK based food composition databases to produce nutrient data as well as basic food groups (Mulligan et al., 2014). Importantly this gives rise to food groups that are captured cleanly. For example, for 'fruit juice' a fraction of the juice drink -- which may be only 10% of the total product --

counts toward total fruit, but the rest of the beverage counts towards added sugars. Likewise, the skim milk fraction of whole milk counts toward the dairy constituent, but the butterfat in whole milk counts toward calories from solid fat. From these food groups a modified version of the Alternate Healthy Eating Index (AHEI) score (McCullough et al., 2002) was created (Supplementary information Table S1) by taking the sum of 7 component scores [1: fruit; 2: vegetable; 3: ratio of white meat (seafood and poultry) to red meat; 4: ratio of polyunsaturated fatty acids (PUFA) to saturated fatty acids SFA); 5: total fibre; 6: nuts and seeds; and 7: multivitamin use]. The score ranged between 2.5 and 67.5 with higher values corresponding to a healthier diet – one that is high in fruit, vegetables, white meat and fish, PUFA, fibre and nuts and seeds and low in SFA and red meat. This approach was chosen to maintain consistency with other large UK based cohort studies that have examined the influence of dietary patterns on mental and physical health (Akbaraly et al., 2013). Alcohol was not included in our modified AHEI but was considered a covariant in the main analysis.

2.1.3.4. Physical activity

Participants were asked how often they took part in moderate and vigorous exercise such as walking, cycling, sports, gardening, housework and home maintenance and for how long. They were then classified according to whether they did or did not meet the World Health Organization recommended levels of physical activity. This metric has been used in previous studies examining the association between mood and HRV (Jandackova et al., 2016).

2.1.3.5. Depressed mood

Depressed mood was measured using the 12 item Elated – Depressed subscale of the Profile of Mood States Bi-Polar questionnaire (POMS) (Lorr et al., 1982). Participants were presented with a list of words or phrases and had to rate on a scale of 0–3 (0 ‘not at all’, 3 ‘a

lot like this') how much they had felt in the past week including today. A higher score indicated a better mood.

2.1.4. Statistical analysis

2.1.4.1. Heart rate variability analysis

All R-R interval data were analysed using Kubios HRV Analysis Software 2.0 (The Biomedical Signal and Medical Imaging Analysis Group, Department of Applied Physics, University of Kuopio, Finland). Data were visually inspected for artefacts caused by incidences such as ectopic beats or poor conductivity. A very low threshold was chosen for artefact correction (0.45 from local average) so not to distort natural variability. Less than 0.8% of beats were identified as artefacts.

Spectral analysis was conducted to transform the time series into the frequency domain. The R-R interval series was converted to equidistantly sampled series by cubic spline interpolation at a rate of 4Hz. Welsh's periodogram, window width 144sec, window overlap 50%, which divides the R-R series into overlapping windows, was used to decrease the leakage effect, and the spectrum estimate was obtained by averaging the Fast Fourier Transform (FFT) spectra of these windowed segments. Average spectral power was estimated within the high frequency (HF power) (0.15–0.4 Hz) band and absolute HF power is reported as recommended by the Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology (Guidelines, 1996). As it has previously been reported that nonlinear complexity indices capture additional information (Young and Benton, 2015), sample entropy (SampEn) was also calculated using Kubios software. Entropy refers to system randomness, regularity and predictability and allows systems to be quantified by the amount of information within the signal. SampEn has been defined as the

negative natural logarithm for conditional properties that a series of data points a certain distance apart, m, would repeat itself at m + 1 where self-matches are not included in calculating the probability. A lower value of SampEn also indicates more regularity in the time series. This nonlinear measure was chosen because it was shown to be highly correlated with other nonlinear indices (Young and Benton, 2015) yet capture additional information to that obtained with frequency analysis (Young and Benton, 2015; Young and Watkins, 2016). The computation of sample entropy depends on two parameters; the embedding dimension m and the tolerance r. In the present study these were set as m= 2 and r= 0.2 SDNN (See Young and Benton (2015) for formulae to calculate sample entropy as well as a graphical representation). Four cases were removed due to poor R-R recording. As these were likely to be random events caused by technical failure, rather than a systematic bias, they were removed from the main analysis.

2.1.4.2. Regression analysis

Initially, the distribution of each variable was checked and where necessary logarithmic transform was used to correct skewed data. Hierarchical multiple regression (SPSS version 21) was used to assess the association between mood and HRV after controlling for lifestyle factors. As the effects of sex, smoking, alcohol and BMI have been discounted in previous literature (Kemp et al., 2014), these were controlled in the first step of the model. To determine the effects of depressed mood over and above these factors, mood was then entered in the second step. Finally the influence of diet (AHEI) was considered in the third step. Separate analyses considered the effects on HRV (HF power, hereafter HF-HRV), heart rate complexity (Sample entropy, hereafter HR-entropy) and the mean RR interval. The data reported are standardised coefficients and 95% confidence intervals.

2.1.4.3. Mediation analysis

The indirect effect of depressed mood on HRV indices, through habitual diet, was considered by conducting a mediation analysis using structural equation modelling (SEM) (AMOS version 22.0) (Figure 1). Coefficients were estimated using the maximum likelihood method and bootstrapped sampling (5000 samples) was used to estimate the indirect mediation effect. BMI, alcohol consumption, physical activity, smoking and gender were considered as covariates of both diet and HF-HRV / HR-entropy / R-R interval (for brevity covariates not shown in Figure 1 but see Table 2 for the effect of each covariate on HF-HRV and Table 3 for the effect of each covariate on diet). Goodness of fit was evaluated using the following four indices: (a) a chi-square statistic with $p > 0.05$ (i.e., statistically non-significant); (b) a goodness-of-fit index (GFI) above 0.96; (b) a comparative fit index (CFI) above 0.96; a root-mean-square error of approximation (RMSEA) smaller than 0.06. Unadjusted and adjusted standardised total, direct and indirect effects and 95% confidence intervals are reported. Cooks distance was used to detect possible outliers (Cook, 1977) with a threshold for determining influential observations set as $4/N$ in line with previous recommendations (Bollen and Jackman, 1985) – unless otherwise stated the analysis proceeded without the exclusion of subjects.

2.2. Results

2.2.1. HF-HRV

The first model was significant ($R^2 = 0.11$, $F(4,155) = 5.29$, $p < 0.001$; Table 2): as expected those who consumed the more alcohol (β = -0.181, LL -0.010, UL -0.001) and smoked (β = -0.292, LL -0.238, UL -0.077) had lower HF-HRV. However, neither BMI (β = -0.049, LL -0.011, UL 0.006) nor gender (β = 0.049, LL -0.048, UL 0.92) contributed significantly to the

model. Although the effect was small, the addition of depressed mood significantly increased the amount of variance that could be explained (R^2 change = 0.03, F (1,150) = 6.61, $p < 0.011$): those with a more depressed mood had lower HF-HRV (β = 0.195, LL 0.001, UL 0.001). The third model was again significant ($R^2 = 0.20$, F (6,155) = 6.39, $p < 0.001$) and diet added significantly to the model (R^2 change = 0.03, F (1,149) = 7.37, $p < 0.007$, β = 0.209, LL 0.001, UL 0.004).

Using SEM it was found that a depressed mood significantly influenced diet quality, over and above the influence of other covariates (β = 0.169, LL 0.016, UL 0.793; Table 3). In addition, the indirect effect mood → diet → HRV was significant (β = 0.011, LL 0.001, UL 0.002; Figure 1) with the indirect pathway accounting for 17% of the total effect (P_M 0.17). The model showed a good fit with the data: $\chi^2(1) = 1.320$ p = .517; GFI = 0.997; CFI = 1.000; RMSEA = 0.000 (90% CI [0.000, 0.140]) and supports the hypothesis that differences in habitual diet play an important role in the link between depressed mood and diminished HF-HRV.

2.2.2. HR-entropy

The first model was significant ($R^2 = 0.09$, F (4,155) = 3.92, $p < 0.005$); those consuming the most alcohol (β = -0.228, LL -0.004, UL -0.001) and those with the largest BMI (β = -0.166, LL -0.007, UL -0.001) had the lowest HR-entropy. However, gender did not influence HR-entropy (β = 0.028, LL -0.022, UL 0.032). The second model was also significant ($R^2 = 0.11$, F (5,155) = 3.99, $p < 0.002$) and depressed mood made a significant addition (R^2 change = 0.02, F (1,150) = 3.97, $p < 0.048$, β = -0.157, LL -0.002, UL -0.002). The addition of diet also significantly increased the amount of variance in HR-entropy that could be explained (R^2 change = 0.07, F (1,149) = 14.13, $p < 0.001$, β = 0.294, LL 0.001, UL 0.002); those with a healthier diet has higher HR-entropy. The addition of diet to the model reduced

the size of the association between HR-entropy and depressed mood but the direct effect remained significant (β = -0.149, LL -0.002, UL -0.003).

The indirect effect mood → diet →HR-entropy was also significant (β = 0.001, LL 0.001, UL 0.003) and accounted for 31% of the total effect (P_M 0.31). The model fit was a good: $\chi^2(1)$ = 0.023, p = .879; GFI = 1.000; CFI = 1.000; RMSEA = 0.000 (90% CI [0.000, 0.107]). The significant indirect effect of mood on HRC through diet supports the hypothesis that differences in diet contribute toward, although does not entirely explain, the association between mood and HR-entropy.

2.2.3. Mean R-R interval

Although the first model was significant ($R^2 = 0.06$, F (4,155) = 2.60, $p < 0.038$), the only significant predictor was alcohol consumption (β = -0.141, LL -0.003, UL -0.001); those who consumed the largest amount of alcohol had the shortest R-R interval. Mood did not add significantly to the model (R^2 change = 0.03, F (1,150) = 0.06, p = 0.793, β = -0.022, LL -0.001, UL 0.001). However the third model, containing diet, was significant ($R^2 = 0.13$, F (6,155) = 3.704, $p < 0.002$). Those who consumed a healthier diet had a longer R-R interval (β = 0.276, LL 0.001, UL 0.002). The effect of gender was also significant (β = -0.178, LL -0.036, UL -0.002) with males having a shorter R-R interval than females.

Although there was no main effect of depressed mood on the length of the R-R interval, a low mood was related to consuming a poorer diet (β = 0.161, LL 0.016, UL 0.793) and a poor diet in-turn was related to having a shorter R-R interval (β = 0.276, LL 0.001, UL 0.002), as such the indirect effect of mood on R-R interval length through diet was significant (β = 0.003, LL 0.001, UL 0.008). Overall the model fitted the data well: $\chi^2(1)$ = 1.272, p = .529; GFI = 0.997; CFI = 1.000; RMSEA = 0.000 (90% CI [0.000, 0.139]). These findings suggest that in

the early stages of pathology depressed mood does not directly affect R-R interval length but does have an influence through changes in dietary behaviour.

3. Study 2

The second study sought to replicate and extend the findings of study 1. It was hypothesised that diet quality would mediate the association between depressed mood and HRV, as shown in study 1. However, also included was a measure of disinhibited eating; as a low mood is thought to disinhibit eating behaviour (Heatherton, Striepe, and Wittenberg, 1998) it was considered whether disinhibited eating and diet quality sequentially mediate the link between depressed mood and HRV.

3.1. Methods

3.1.1. Participants and procedure

One hundred and twelve young adults (37 male) (BMI 17.51 – 35.81 kg/m^2) between 18 and 30 years of age participated in this study (Table 1). The inclusion criteria, pre-study requirements, experimental procedure and methods were the same as in study one with the addition of the Three Factor Eating Questionnaire (TFEQ) (Stunkard and Messick, 1985). The procedure was approved by Swansea University ethics committee (Reference number: 08.25.2015.2) and carried out in accordance with the principles laid down by the Declaration of Helsinki.

2.1.2. Measures

3.1.2.1. Disinhibited eating

The tendency towards disinhibited eating was measured using the 16 item disinhibition subscale of the TFEQ (Stunkard and Messick, 1985). This scale measures loss of cognitive control of eating using true-false items (e.g “Sometimes when I start eating, I just can't seem to stop”, “when I feel anxious I find myself eating”).

3.1.2.1. Restrained eating

Restrained eating (conscious restriction of food intake in order to control body weight or to promote weight loss) is known to moderate the effects of disinhibited eating (Dykes et al., 2004), therefore restrained eating was included in the analysis as an additional covariate. The 21 item cognitive restraint subscale of the three factor questionnaire (Stunkard and Messick, 1985) was used. Sample questions include: ‘When I have eaten my quota of calories I am usually good about not eating any more’ ‘I deliberately take small helpings as a means of controlling my weight’.

3.1.3. Statistical analysis

R-R interval data were missing for two participants due to poor recording. It is likely that these were random events due to equipment failure and not the result of systematic bias so they were excluded leaving N= 110. The distribution of each variable was checked and where necessary logarithmic transforms was used to correct skewed data. Initially the total effect (the sum of the direct and indirect effects) of depressed mood on HRV, after controlling for BMI, alcohol consumption, physical activity, and gender, was calculated using hierarchical linear regression. As in study 1, covariates were controlled in the first step of the

model, depressed mood in the second step, disinhibited eating in a third and diet in the final step.

To explore the possibility that disinhibited eating and poor diet quality sequentially mediates the link between depressed mood and HF-HRV / HR-entropy / mean R-R interval, SEM was conducted using AMOS version 22.0. Path analysis was used to estimate the direct and indirect connections the between the variables in the model (Figure 2); the analysis methods replicated that in study 1 with disinhibited eating as an additional mediator. BMI, alcohol consumption, physical activity, restrained eating and gender were considered as possible covariates of disinhibited eating, diet and HRV (for brevity covariates not shown in Figures 2 and 3 but see Table 4, 5 and 6 for association between each covariate and HF-HRV, disinhibited eating and diet respectively). Goodness of fit was again evaluated using the following four indices: (a) a chi-square statistic with $p > 0.05$ (i.e., statistically non-significant); (b) a goodness-of-fit index (GFI) above 0.96; (b) a comparative fit index (CFI) above 0.96; a root-mean-square error of approximation (RMSEA) smaller than 0.06. Standardised coefficients and 95% confidence intervals are reported.

3.2. Results

3.2.1. HF-HRV

The findings from study one were replicated; a depressed mood was associated with lower HF-HRV ($R^2 = 0.21$, $F(6,109) = 4.55$, $p < 0.001$; $\beta = 0.194$, LL 0.006, UL 0.079; path *c*) after the consideration of BMI, alcohol consumption, physical activity and gender, that is the total (adjusted) effect of depressed mood on HRV was significant before the influences of disinhibited eating and diet were considered (Table 4 and Figure 3).

Disinhibition added significantly to the model (R^2 change = 0.09, F (1,102) = 13.25, p < 0.001; Table 4) and those highest in disinhibited eating had significantly lower HF-HRV (β = -0.317, LL -0.102, UL -0.030). Notably, when disinhibited eating was entered into the model, the mood → HF-HRV association was diminished (β = 0.134, LL -0.007, UL 0.063; Table 4). Poor diet also contributed significantly to the model (R2 change = 0.02, F (1,101) = 3.89, p < 0.050); a poor diet was associated with having a lower HF-HRV (Table 4; Figure 2 path b_2) (β = 0.196, LL 0.001, UL 0.082) even after all other variables had been considered. The indirect path connecting disinhibited eating with HF-HRV through poor diet (Figure 2 path $d_{21}b_2$) (β = -0.077, LL -0.172, UL -0.010) also reached significance. This latter finding suggests that a propensity towards disinhibited eating results in a poorer diet that in turn reduces HF-HRV.

As expected a depressed mood was also associated with greater disinhibited eating (Table 5; Figure 2 path a_1) (β = -0.237, LL -0.406, UL -0.032) but did not directly result in a poorer diet quality (Table 6; Figure 2 path a_2) (β = 0.145, LL -0.021, UL 0.309): that is when disinhibited eating was included in the model the mood → habitual diet association was diminished. Disinhibited eating predicted poor diet quality (Table 6; Figure 2 path d_{21}) (β = -0.326, LL -0.492, UL -0.156) and as such the indirect path connecting depressed mood with diet through disinhibited eating (Figure 2 path a_1d_{21}) was significant (β = 0.071, LL 0.011, UL 0.161); those who reported a more depressed mood were more likely to be disinhibited eaters and in turn this led to the consumption of a poorer diet (Figure 3).

The path between depressed mood and HF-HRV via diet (Figure 2 path a_2b_2) was not significant (β = 0.028, LL -0.001, UL 0.095), although the indirect effect depressed mood → disinhibited eating → HF-HRV (Figure 2 path a_1b_1) achieved significance (β = 0.097, LL 0.032, UL 0.193); a depressed mood was associated with higher disinhibited eating which in

turn was associated with a lower HF-HRV. The serial mediation, depressed mood → disinhibited eating → poor diet → HF-HRV (Figure 2 path a_1 d_{21} b_2) was also significant (β = 0.013, LL 0.001, UL 0.095); those who reported a depressed mood had higher disinhibited eating which lead to a poor diet – in turn a poor diet was associated with reduced HF-HRV (Figure 3). Together the indirect pathways accounted for 47% of the total effect (P_M 0.47).

Interestingly, when the effects of the mediators were considered the direct effect (Figure 2 path c′) of depressed mood on HF-HRV was no longer significant (β = 0.105, LL -0.063, UL 0.273), suggesting complete mediation. The hypothesised model showed an excellent fit with the data: $\chi^2(1) = 1.042$ p = .307; GFI = 0.996; CFI = 0.999; RMSEA = 0.002 (90% CI [0.000, 0.225]) (Figure 3).

3.2.1.1 Alternative models

Although our a priori hypothesised model fitted the data well there are number of alternative models that are theoretically possible. In particular it is possible that HRV mediates the association between dietary behaviour and depressed mood. In order to discount these possibilities we ran the analysis testing a range of alternative hypothesis. The results are available as supplementary information. Overall our a priori model was the best for to the data.

3.2.2. HR-entropy

When the effects on HR-entropy were considered the results were similar to those for HF-HRV: disinhibited eating (β = -0.211, LL -0.389 UL -0.034) and diet (β = 0.306, LL 0.112, UL 0.500) independently predicted HR-entropy. Those high in disinhibited eating had the lowest HR-entropy as did those with the poorest diet quality. Although the total effect of depressed mood was not significant (β = 0.062, LL -0.112, UL 0.237), the serial indirect path

depressed mood → disinhibited eating →diet → HR-entropy reached significance (β = 0.021, LL 0.004, UL 0.064). A more depressed mood was associated with greater disinhibited eating, which in turn was associated with a poorer diet and reduced HR-entropy. Disinhibited eating also mediated the effect of depressed mood on HR-entropy independently of diet (β = 0.046, LL 0.064, UL 0.126), although diet did not mediate the effect of depressed mood on HR-entropy independently of disinhibited eating (β = 0.044, LL -0.001, UL 0.127). This model fitted the data well: $\chi^2(1) = 0.472$, p = .492 GFI = 0.998; CFI = 1.000; RMSEA = 0.000 (90% CI [0.000, 0.222]).

3.2.3. Mean R-R interval

When considering the effects on the average R-R interval the total effect of depressed mood on R-R interval length was significant (β = 0.191, LL 0.001, UL 0.321) after accounting for BMI, alcohol consumption, physical activity and gender: those with a poorer mood had a shorter R-R interval. However, the direct effect, after accounting for disinhibited eating and diet, was not significant (β = 0.021, LL -0.002, UL 0.063). As reported above, a depressed mood was associated with more disinhibited eating (β = -0.237, LL -0.406, UL -0.032), which in turn predicted the consumption of a poorer diet (β = -0.326, LL -0.492, UL -0.156). However, disinhibited eating was not related to RR interval length when diet was entered into the model (β = -0.117, LL -0.287, UL 0.051). As such diet mediated the link between disinhibited eating and RR interval length (β = -0.121, LL -0.239, UL -0.049). The indirect effect depressed mood → disinhibited eating → RR interval was not significant (β = 0.022, LL -0.006, UL 0.038) and neither was the indirect path depressed mood → diet → RR interval (β = 0.039, LL -0.004, UL 0.121). However the serial mediation depressed mood → disinhibited eating → poor diet → RR interval reached significance (β = 0.020, LL 0.001, UL 0.063); those who reported a depressed mood had higher disinhibited eating which lead to a

poor diet – in turn a poor diet was associated with a shorter RR interval. The model fitted the data well: $\chi^2(1) = 0.304$, p = .581 GFI = 0.999; CFI = 1.000; RMSEA = 0.000 (90% CI [0.000, 0.207]).

4. Discussion

The primary objective of the present studies was to consider the hitherto unexplored possibility that mood might be associated with reduced HRV by virtue of differences in dietary behaviour. Key findings were that: (1) in young otherwise healthy participants the association between mood and HF-HRV (HF power: 0.15–0.4 Hz) is small (Cohen's *d* = 0.39 in both studies); (2) consuming a unhealthy diet was associated with having a reduced HF-HRV (HF power: 0.15–0.4 Hz) – an effect characterised by a larger effect size (Cohen's *d* = 0.52 in study 1 and 0.61 in study 2). In addition, those consuming the poorest diet consistently had lower HR-entropy (Sample entropy) and a shorter R-R interval: (3) across both studies dietary behaviour mediated the link between mood and HRV (including HF power, Sample entropy and R-R interval length); (4) the validity of the a priori pathway was supported by two independent samples and fitted the data better than the alternative models (Supplementary information).

These findings are potentially important for a number of reasons. Firstly, prospective studies have implicated poor affect regulation in the aetiology of a host of cardiovascular related conditions (Gan et al., 2014; Hare et al., 2013; Schnatz et al., 2011). Indeed disturbances in autonomic cardiac control might be one pathway through which poor affect regulation influences cardiovascular health (Grippo and Johnson, 2009). However, although it is often assumed that there is a direct pathway connecting the prefrontal cortex of the brain to the heart (Makovac, Thayer and Ottaviani, 2016), previous studies have not controlled for the influence of diet. For example Brunoni et al. (2013) studied the effect of transcranial direct

current stimulation (tDCS), or antidepressant medication, on mood and HRV (defined as HF (0.15–0.4 Hz) and the root mean squared successive differences in the interbeat interval (RMSSD)) in newly diagnosed patients with depressive disorder. At baseline, those with depressive disorder had lower HRV than controls, however, individual differences in dietary behaviour were not considered. Interestingly, whilst both tDCS and medication improved mood, parallel changes in HRV indices were not observed. Such effects might have occurred if a third factor, for example diet, was influencing HRV rather than there being a direct effect of mood per se. That is, the treatment might have improved mood without effecting HRV as it did not target the cause of the reduced HRV. This is an important consideration if treatment directed towards depression is also expected to ameliorate the increased incidence of CVD in this population.

It is important to consider whether reduced HF- HRV may be an indicator of diminished self - regulatory capacity, rather than negative affect, per se (Reynard et al., 2011). For instance, low resting HRV has been associated with reduced persistence on an anagram task (RMSSD) (Segerstrom and Nes, 2007), the adoption of maladaptive emotion regulation strategies (HF (0.15–0.4 Hz) (Volokhov and Demaree, 2010), poorer impulse control (RMSSD) (Williams et al., 2015), difficulties in engaging in goal-oriented behaviour (RMSSD) (Williams et al., 2015), problems in identifying emotions (RMSSD) (Williams et al., 2015) (N.B. although these studies used different HRV indices they have been repeatedly shown to correlate highly (Williams et al., 2015)). Given that these are all risk factors for unhealthy dietary behaviour (Nowakowski, McFarlane and Cassin, 2013; Papies and Hamstra, 2010; Waxman, 2009) it is surprising that no study has considered the possibility that disinhibited dietary behaviour might explain these associations. The present studies support the suggestion that there is an indirect pathway connecting mood and disinhibition to HRV via dietary behaviour.

Nonetheless it is important to recognize that candidate mechanisms are not mutually exclusive, and more than one potential mechanism may link depression with adverse outcomes. In this context, in study 1, we observed only partial mediation of the mood – HF-HRV association by diet. Similarly, in study 2 the direct association between disinhibition and HF-HRV remained significant even after controlling for diet quality. As such it is plausible that the two factors combine to result in chronically reduced HRV. Interestingly, recent studies have found that disinhibited eaters are characterised by reduced functional connectivity between the amygdala, striatum and dorsomedial prefrontal (dmPFC) cortex (Dietrich et al., 2016): the activity of similar regions has been found to covary with HF-HRV (Chang et al., 2013; Jennings et al., 2015). Indeed we recently reported that disinhibited eaters were characterised by lower HF-HRV and HR-entropy (Young and Watkins, 2016). Therefore it is plausible that by virtue of reduced prefrontal cortex activity, disinhibited eaters are predisposed towards attenuated HRV – a phenomenon that is then exacerbated by the consumption of a poor diet. Further research should consider whether other facets of self-control are related to HRV, either directly or indirectly via an increased propensity towards risky health behaviours. For example, reduced HF-HRV has been found to predict cravings in alcohol dependent outpatients (Quintana et al., 2013), whilst at the same time chronic alcohol ingestion adversely influences HF-HRV (Karpyak et al., 2014; Quintana et al., 2013). Although not the primary objective of the present studies, we found a negative association between HF-HRV and alcohol consumption. It is plausible that a range of externalising affect regulatory strategies, including alcohol consumption, poor diet and smoking, mediate the link between mood and HRV – this should be further explored.

Future research should also consider the role of individual dietary components. For example, a Mediterranean dietary pattern (Dai et al., 2010), omega 3 fatty acid (Villa et al., 2002), vitamin and mineral supplementation (Dai et al., 2010) and caffeine consumption

(Zimmermann-Viehoff et al., 2016) have all been associated with increased HRV (N.B. in these studies significant effects were reported across a broad range of HRV indices including R-R interval length and HF power: 0.15–0.4 Hz). Thus although there are infrequent reports of diet influencing HRV, efforts to date have not been systematic. The present study suggests that adopting a healthy dietary pattern in line with current government recommendations might lead to greater HF-HRV, HR-entropy and R-R interval length; however, more research is needed to elucidate dietary components that might be particularly helpful. In addition, it is currently unknown how dietary factors combine with psychological factors to influence psychosomatic health. Of note, in the present study participants were asked to abstain for the consumption of caffeine prior to attending the laboratory. As caffeine increases HF-HRV (Zimmermann-Viehoff et al., 2016) the possibility that caffeine abstinence resulted in reduced parasympathetic tone in habitual caffeine consumers (Zimmermann-Viehoff et al., 2016) cannot be discounted.

Interestingly, although it has been reported that females are characterised by higher vagally mediated HRV than males (Koenig and Thayer, 2016), no effects of gender were observed in the present study after controlling for other lifestyle factors (Tables 2 and 4). However, when the samples were combined an effect of gender emerged; females had higher HR-entropy and HF-HRV than males, although there were no differences in RR-interval length (Supplementary information Table S2) the effects were characterised by a small effect size: Cohen's d = 0.23 and 0.30 respectively. Importantly, males reported consuming a less healthy diet and consuming more alcohol than females (Table S2). This might explain why we failed to detect gender differences in our main analysis; it should be considered whether lifestyle factors also explain gender related differences in HRV.

The present study has a number of strengths including the use of SEM which allowed the model that best fits the data to be established while discounting alternate possibilities (Supplementary information). The findings were also replicated in two independent studies suggesting that the phenomenon is robust. Further, by studying a young healthy population we were able to decipher the mechanism connecting mood and HRV at an early stage in the pathological process. Nonetheless, the limitations of the present studies should also be considered. Firstly, it is to be established whether these findings might be generalised to those with clinical disorders. Secondly, the cross-sectional design does not allow cause and effect to be established, however, an emerging animal literature supports the role of diet in modulating cardiac vagal tone. For example, a high fat diet increased heart rate, impaired cardiac vagal modulation, and blunted the central autonomic cardiac control during sleep (Silvani et al., 2014). Finally, although the majority of studies of HRV have not measured respiration it is potentially a confounding variable, particularly with frequency domain measures. Indeed there remains ambiguity around the interpretation of HRV measures in general (Grossman and Kollai, 1993; Kollai and Mizsei, 1990; Malik, 1996), and the nonlinear indices in particular (Bolea et al., 2014; Perkiomaki et al., 2002; Tan, 2013). However, as we observed a similar pattern of findings across time, frequency domain and nonlinear measurements, the present findings suggest that diet influences the modulation of cardiac sympathetic and vagal activities, although more research is needed to elucidate the physiological underpinnings of HRV.

In summary, two studies found clear evidence that diet quality mediates the link between mood and HRV; findings that have a number implications. Firstly, it is possible that dietary modification may have the potential to slow the onset of CVD in vulnerable cross sections of the population. Secondly, these data suggest that poor self-regulation and diet might act synergistically to induce negative health consequences: if this is the case future research

might shed new light on the metabolic pathways linking mood, diet and HRV. Finally, whilst a vast literature supports the association between mood and HRV none have controlled for the effects of diet. If, as the present findings suggest, diet is a necessary component connecting HRV and mental health it is essential that future research examines its influence.

Contributions

HY and DB conceived and designed the methods and study. HW and AC ran the experiment and were responsible for data collection and entry. HY analysed and interpreted the data, and wrote the manuscript with input from all authors. All authors declare no conflict of interest.

Competing financial interests

The authors declare no competing financial interests.

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Table 1. Participant characteristics for study 1 and study 2.

	Study 1	Study 2
Characteristic	Mean (SD or range)	Mean (SD or range)
Age (years)	21.86 (18-34)	21.93(18-30)
Body mass index (kg/m^2)	23.44 (16.82–37.28)	23.16 (17.51–35.81)
Gender		
Females	105	74
Males	51	38
Current smoker	27	0
Yes	129	112
No		
Alcohol (units per week)	5.05 (0-38)	9.20(2-21)
R-R interval (milliseconds)	785.58(136.29)	754.84(110.19)
HF power	820.47(718.24)	722.26(696.88)
HR entropy	1.42 (0.26)	1.32 (0.25)
Mean RR interval	793.75(107.97)	749.57(100.29)
Depressed mood (POMS)	4.80(7.04)	6.88 (5.47)
Diet (AHEI)	33.22(17.63)	35.96(20.67)
Disinhibited eating (TFEQ)	NA	12.17(3.39)

R-R – Interbeat interval, HF – High frequency, HR – Heart rate, POMS – Profile of Mood States, AHEI – Alternative Healthy Eating Index, TFEQ – Three Factor Eating Questionnaire.

Table 2. Results of the hierarchical regression analysis that examined the effect of habitua variability (HF power: 0.15–0.4 Hz) after controlling for gender, smoking status, alcohol c and BMI.

	Model 1			Model 2		
Variable	**B**	**SE B**	**β**	**B**	**SE B**	**β**
Gender	0.022	0.036	0.049	0.017	0.035	0.036
Smoking	-0.157	0.041	-0.292**	-0.143	0.041	-0.265**
BMI (kg/m2)	-0.003	0.004	-0.049	-0.002	0.004	-0.040
Alcohol	-0.005	0.002	-0.181*	-0.005	0.002	-0.155*
Physical Activity	0.093	0.035	0.146*	0.081	0.032	0.129
Depressed mood				0.006	0.002	0.195*
Diet						
R^2			0.112			0.163
F for change in R^2			5.298**			6.616**

N= 152 after removing four cases due to poor R-R recording. BMI – Body mass index. A depre having a lower HRV after controlling for alcohol consumption, smoking, gender, BMI and ph diminished after diet was entered into the model but the association between mood and HRV rem .01.

Table 3. Results of the regression analysis that examined the effect of mood on habitual diet whilst controlling for gender, smoking status, alcohol consumption, physical activity, and BMI.

Variable	**B**	**SE B**	**β**
Mood	0.404	0.197	0.169*
Gender	4.038	2.932	0.110
Smoking	-11.099	3.400	-0.254**
BMI(kg/m2)	-0.056	0.351	-0.012
Alcohol	0.216	0.195	0.089
Physical activity	4.236	2.396	0.125
R^2			0.118
F			4.045**

N= 152 after removing four cases due to poor R-R recording. BMI – Body mass index. A depressed mood was associated with consuming a poorer diet after controlling for alcohol consumption, smoking, gender, BMI and physical activity. *p < .05. **p < .01.

Table 4. Results of the hierarchical regression analysis that examined the effect of disinhibited on heart rate variability (HF power: 0.15–0.4 Hz) after controlling for gender, restrained eating, a activity, and BMI.

	Model 1			Model 2			Model 3	
Variable	**B**	**SE B**	**β**	**B**	**SE B**	**β**	**B**	**SE B**
Gender	0.037	0.041	0.085	0.035	0.040	0.078	0.037	0.038
Restraint	0.060	0.020	0.289**	0.062	0.019	0.295**	0.065	0.018
BMI (kg/m2)	-0.003	0.005	-0.052	-0.002	0.005	-0.037	0.001	0.005
Alcohol	-0.014	0.005	-0.270**	-0.015	0.005	-0.284**	-0.013	0.004
Physical Activity	0.018	0.039	0.044	0.021	0.038	0.049	0.012	0.036
Depressed mood				0.042	0.018	0.194*	0.028	0.018
Disinhibited							-0.066	0.018
Diet								
R^2			0.168			0.210		
F for change in R^2			4.212**			5.360*		

N= 110 after removing two cases due to poor R-R recording. BMI – Body mass index. A depressed m
a lower HRV after controlling for alcohol consumption, restrained eating, gender, BMI and physical act
after disinhibited eating and diet were entered into the model.

Table 5. Results of the regression analysis that examined the effect of mood on disinhibited eating whilst controlling for gender, restrained eating, alcohol consumption physical activity, and BMI.

Variable	**B**	**SE B**	**β**
Mood	-0.805	0.313	-0.237**
Gender	-0.326	0.692	-0.045
Restraint	0.033	0.059	0.055
BMI(kg/m2)	0.157	0.092	0.158
Alcohol	0.010	0.079	0.012
Physical activity	-0.020	0.646	-0.003
R^2			0.135
F			2.678**

N= 110 after removing two cases due to poor R-R recording. BMI – Body mass index. A depressed mood was associated with higher disinhibited eating after controlling for alcohol consumption, gender, BMI and physical activity.

Table 6. Results of the regression analysis that examined the effect of mood and disinhibited eating on diet whilst controlling for gender, restrained eating, alcohol consumption, physical activity, and BMI.

Variable	**B**	**SE B**	**β**
Disinhibition	-6.705	1.752	-0.326**
Mood	2.974	1.724	0.145
Gender	7.142	3.720	0.184*
Restraint	7.076	1.777	0.342**
BMI(kg/m2)	0.199	0.498	0.033
Alcohol	-0.538	.0426	-0.105
Physical activity	-8.631	3.478	-0.206*
R^2			0.326
F			7.041**

N= 110 after removing two cases due to poor R-R recording. BMI – Body mass index. Both depressed mood and disinhibited eating were associated with the consumption of a poorer diet after controlling for alcohol consumption, gender, BMI, restraint and physical activity.

FIGURE LEGENDS

Figure 1. Path coefficients for the mediation model which tested the effect of depressed mood on heart rate variability (HF power: 0.15–0.4 Hz) through its effects on diet.

N= 152 after removing four cases due to poor R-R recording. Depressed mood was associated with consuming a poor diet and reduced HF-HRV. The model provides evidence that the effect of depressed mood on HF-HRV is mediated by a poor diet. The model was a good fit to the data ($\chi^2(1) = 1.320$ $p = .517$). * Significant regression coefficient (adjusted for BMI, alcohol consumption, physical activity, smoking and gender).

Figure 2. The theoretical model depicting a serial mediation pathway connecting mood and heart rate variability through changes in eating behaviour.

The model allowed for the comparison of the direct and indirect paths. BMI, alcohol consumption, physical activity, restrained eating, and gender were also entered into the model as possible covariates of disinhibited eating, diet and HRV.

Figure 3. Path coefficients for the hypothesised model. N= 110.

Depressed mood was associated with reduced HF-HRV (HF power: 0.15–0.4 Hz) before the mediators were included in the model but not afterwards. The model provides evidence that the effect of depressed mood on HRV is mediated by disinhibited eating and a poor diet. The model was a good fit to the data ($\chi^2(1) = 1.042$ $p = .307$). * Significant regression coefficient (adjusted for BMI, alcohol consumption, physical activity, restrained eating and gender).