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# Mediterranean diet, interoception and mental health: Is it time to look beyond the 'Gut-brain axis'?

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#### ABSTRACT

Objective: A Mediterranean style diet (i.e., high in fruit, vegetables, fish, pulses, and wholegrains) is said to benefit psychological health. Many low-level interoceptive processes, such as those involved in the 'gut-brain' axis, are suggested to play a mechanistic role in in this relationship. However, interoceptive sensations in other domains, and at higher hierarchical levels of abstraction, have hitherto been overlooked. One domain often studied in relation to psychological health is cardioception. Therefore, we examined whether the Mediterranean diet was associated with first-order perceptual and second-order metacognitive cardioception.

Methods: Participants completed the Heartbeat Detection Task, the Heartbeat Counting Task, and the EPIC-Norfolk Food Frequency Questionnaire from which diet was quantified.

Results: Adherence to a Mediterranean style diet was associated with higher cardioceptive accuracy (i.e., perceptual performance) across both tasks. In addition, those consuming a Mediterranean diet had a better ability to detect errors in first order perceptual performance, and a lower prediction error (the magnitude of the difference between accuracy and confidence).

*Discussion:* These findings indicated that deepening our understanding of how interoceptive processes beyond the 'gut-brain' axis are shaped by diet could deepen our understanding of the link between diet and mental health and wellbeing.

### 1. Introduction

The effect of diet on psychological health is increasingly recognised. Indeed, several recent reviews have detailed how 'healthy' diets, such as the Mediterranean diet, high in fruits, vegetables, legumes, nuts, whole grains, and fish, are associated with lower levels of depression [1], and better overall mental health and wellbeing [2–5]. However, whilst these data are promising, many questions remain unanswered, such as who will benefit and under which circumstances. Answering these questions will require a mechanistic understanding of the key psychological and biological processes underpinning the relationship.

As defined by a recent expert group, interoception is "the process by which the nervous system senses, interprets, and integrates signals originating from within the body, providing a moment-by-moment mapping of the body's internal landscape across conscious and unconscious levels" [6]. In this context, it is often suggested that the bidirectional interaction between the brain and the gut, coined the 'gut-brain axis', is key to understanding the link between nutrition and mental health [2,5]. However, the possibility that other interoceptive

sensations, such as afferent cardiac signals, might contribute has not been considered. This is surprising given an emerging literature associating cardioception with a range of physical and mental health concerns including depressed mood [7], stress [8], self-injurious behaviour [9], disordered eating and obesity [10,11], and developmental difficulties [12]. Furthermore, despite an increasing appreciation of their role in mental health [11], dietary influences on higher-level interoceptive processes, such as the ability to meta-cognitively track the accuracy of one's interoceptive perceptions, has hitherto been overlooked [13] (see Fig. 1 for an illustration of the hierarchical neural circuitry involved in interoception). Therefore, to facilitate a better understanding of the processes through which diet influences mental health, we examined the effect of habitual dietary style on cardioception across hierarchical levels.

Those studying diet have long recognised the importance of low level interoceptive signals in implicitly shaping experiential feeling states and cognition (Fig. 1: green). For example, an area of substantial interest has been the dietary modification of the 'gut-brain axis' i.e., postprandial neural (e.g., vagal afferents), humoral (e.g., blood glucose, hormones

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such as insulin, CCK, peptide YY, GLP-1) and / or inflammatory (e.g., IL-6) signals [14–18]. These studies have provided compelling experimental evidence that dietary perturbation of those interoceptive signals [e.g., by altering the macronutrient content of a meal] influences cognitive, motivational and / or affective states. However, a focus on 'gut-brain' signalling means that little is currently known about the effect of diet in other interoceptive domains.

Notably, in recent years the concept of 'interoception' has expanded considerably [6,19]. Therefore, it is important to recognise that interoception includes sensations related to a broad range of bodily functions, including those not traditionally studied by those interested in diet. Furthermore, according to the above definition, interoception operates *hierarchically* (Fig. 1: pink and blue). That is, sensing,

interpreting, and integrating information about the internal bodily state reflects both first order (i.e., detection accuracy) and second order (i.e., confidence and meta-cognitive insight in one's detection accuracy) interoceptive processes. Measuring these processes simultaneously in the same study is important to isolate specific interoceptive difficulties that might be associated with diet [20] (Table 1: interoceptive taxonomy used in the present study).

Importantly, an emerging literature has documented how cardioceptive accuracy shapes the affective response to stress [8], mood [7], memory [28], attention [29] and decision making [30]. Additionally, maladaptive second order interoceptive processes are emerging as an important correlate of mental and physical health problems [12,27, 31]. However, hitherto, only a handful of studies have considered the

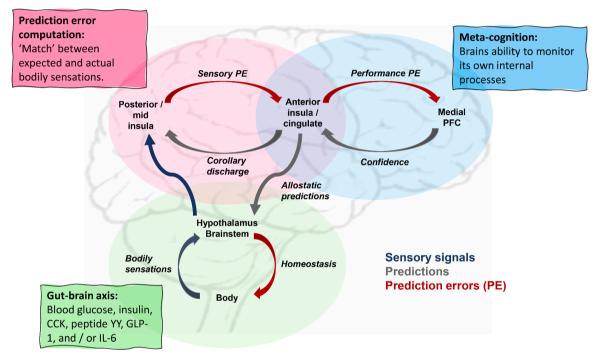


Fig. 1. . Hierarchical neural circuits thought to play a role in interoception.

Note. Visceromotor areas such as the anterior insula (AI) and anterior cingulate cortex (ACC) (with input from other agranular cortices, such as the hippocampus) estimate the balance between the anticipated bodily requirements (based on past experiences), and currently available autonomic, metabolic and immunological resources [1]. These balance estimates provide the basis for allostatic predictions to the hypothalamus, brainstem, and spinal cord nuclei – predictions that nuance homeostatic set points that mediate physiological homoeostasis through autonomic reflexes [2]. Simultaneously, AI/ACC inform hierarchically lower areas, such as posterior and mid-insula, about the interoceptive consequences that are expected to arise as consequences of those allostatic predictions (i.e., expected autonomic, metabolic, and immunological states of the body) [1]. In turn, the posterior and mid-insula compare these predictions against actual interosensory input (i.e., actual autonomic, metabolic, and immunological states of the body) and compute prediction errors that update the predictions by AI/ACC [2]. At higher hierarchical levels, metacognitive regions such as the medial prefrontal cortex (mPFC), monitor prediction errors and compute 'interoceptive surprise' [3]. When expected bodily states are successfully fulfilled through regulatory action, interoceptive surprise is low [1]. However, a persistent inability to predict the interosensory outcomes of actions leads to irreducible prediction error and chronic interoceptive surprise [2]. In turn this may lower interoceptive confidence and result in what has been coined 'low allostatic self-efficacy' (i.e., a lack of control over bodily states) [3]. It was suggested that in this way, persistent interoceptive surprise may constitute an important component in the pathogenesis of fatigue, depression and anxiety [4].

Traditionally, researchers interested in understanding the link between nutrition and mental health have focused predominantly on the 'gut-brain' axis (green), while higher level interoceptive processes (pink and blue) have tended to be ignored. However, interoceptive surprise may arise from dysfunctions of any components of this closed loop system – many of which may be modified by a Mediterranean style diet. For example,

- (1) Actual perturbations of bodily state that evade attempts of correction (e.g., accumulation of oxygen reactive species (ROS)) may be ameliorated by the antioxidant rich foods in the Mediterranean style diet [5].
- (2) A Mediterranean diet, rich in omega 3 fatty acids, was associated with having a higher vagal tone [6], therefore, interosensation (which relies on the integrity of vagal afferent pathways and viscerosensory areas; posterior and mid-insula) may benefit from this dietary style.
- (3) Brain derived neurotropic factor (BDNF) is important for synaptic plasticity mechanisms underlying learning [7]. Adherence to a Mediterranean diet was associated to an improvement in plasma BDNF concentrations in individuals with depression [8]. In the visceromotor brain regions (e.g., AI/ACC), BDNF was associated with a long-lasting increase in synaptic transmission [9]. Thus, a Mediterranean diet could afford a greater propensity to learn and update internal models about the sensory outcome of actions, thereby ameliorating aberrant interoceptive predictions.
- (4) A Mediterranean diet was associated with having a larger brain volume in areas of the brain associated with metacognition, specifically the cingulate and frontal cortices [10,11]. In addition, the consumption of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) during was associated with activity in the dorsal anterior cingulate during an inhibitory control task [12]. Thus, maintaining the structural and functional integrity of these brain regions could prevent maladaptive metacognitive computation (e.g., inflexible confidence levels) [13,31,53,57,64,68-71,83-85].

**Table 1** Interoceptive taxonomy.

Afferent signal	Variation in strength / concentration of one or more neurohumoral signals such as a change in blood glucose, hormone e.g., insulin, ghrelin, CCK, GLP-1, PYY or vagal transmission.
Interoceptive accuracy	One's ability to correctly monitor internal changes, measured using objective task performance [21]. For example Heartbeat Detection Task [22], or Heartbeat Counting Task [23] performance.
Postdictive interoceptive confidence	One's postdictive confidence in their ability to accurately monitor internal changes associated with a particular interoceptive task or channel – has been analysed separately [24]. It was suggested that raw confidence ratings might reflect one's subjective belief about the accuracy of their interoceptive percept within a particular domain [25].
Interoceptive metacognitive awareness (or insight)	One's meta-cognitive judgement regarding one's interoceptive accuracy, assessed as the correspondence between objective accuracy and postdictive subjective confidence ratings [21]. Here we examined two measures of metacognition: (i) calibration: how well confidence tracks accuracy on a trial-by-trial basis; and (ii) a prediction error index (PI) capturing the magnitude of the difference between confidence and accuracy.

*Note*: Evidence indicates that some interoceptive components (i.e., accuracy and awareness) are empirically dissociable [21,26,27].

effect of diet on cardioceptive accuracy, and so far these have been restricted to acute consumption of glucose [32], protein [33], or caffeinated energy drinks [34]. To our knowledge no study has considered the effects of habitual diet, and to date no studies have investigated the effects of diet on second order interoceptive processes. Nonetheless, unpacking how diet influences these interoceptive processes might be key to understanding the effects of diet on mental and cognitive health.

In this context, we sought to determine the association between diet and multiple aspects of cardioception. Cardioceptive accuracy, confidence, and insight were assessed using the Heartbeat Counting Task [23], and the 'gold-standard' Heartbeat Detection Task [22]. Currently, the Mediterranean dietary style has the largest body of evidence connecting it with better cognitive and affective health [35–40]. Therefore, we focused on the Mediterranean dietary pattern here. Specifically, we hypothesised that a diet high in fruit and vegetables, would be associated with better cardioception (Table 1).

## 2. Methods

## 2.1. Procedure

Participants from the local area were recruited through posters on university notice boards and online adverts on popular social media websites (e.g., Facebook). Upon arrival they first provided their written informed consent and had conventional Ag/AgCl electrodes and transducers applied and connected to a BIOPAC MP150 and ECG100C amplifier module (BIOPAC, USA). The interoception tests were then completed as detailed below. Next, the participants completed the questionnaires, and height, weight and blood pressure were then measured. All participants were tested in the morning between the hours of 9am and 12noon and were instructed to refrain from consuming any food or drink for twelve hours before attending the laboratory to limit acute dietary influences. Participants were also told to refrain from physical activity and alcohol consumption for at least twenty-four hours prior to commencing the study, and to maintain their usual bed / wake times. Adherence to these requirements was confirmed verbally when participants arrived at the laboratory. The procedure was approved by Swansea University department of Psychology ethics committee and was conducted in accordance with the principles laid down by the declaration of Helsinki 2013.

## 2.2. Participants

The effect of diet on cardioception has not previously been studied, therefore we based our sample size requirements on a medium effect size and five predictors. To have an 95% chance of rejecting the null (twotailed), with alpha at 0.01, we would need 123 participants. In the event 191 participants took part, however, due to time constraints, only 116 completed the heartbeat detection task. Three cases had to be removed due to a poor ECG signal and therefore unreliable triggering off the heartbeat. One case was removed due to missing data on the food frequency questionnaires, and one other case has a BMI of 41.00 kg/m<sup>2</sup> and was flagged as an outlier in all analysis (Cooks distance > 1). This left a sample of 186 participants for the heartbeat counting task, and 111 participants for the heartbeat discrimination task. Given the heterogeneity between males and females in both interoception and diet we restricted this preliminary investigation to females. All participants were between 18 and 30 years of age and studying at Swansea University. Psychology students received course credits in return for their participation, however, no financial remuneration was provided. Participants were excluded if they had a cardiovascular or metabolic disorder, gastrointestinal problems, were pregnant, had a current clinical diagnosis of a mood or eating disorder, and/or were taking medications or herbal supplements to manage body weight or control appetite. Smokers were also excluded from this study. BMI ranged from 16.3 to 37.0 kg/  $m^2$ .

#### 2.3. Interoception measurement

## 2.3.1. Heartbeat counting task (HCT)

The HCT was performed using a computerised version of the mental tracking method tracking [23] with intervals of 30, 35, 40, 45 and 50 s that were separated by 30 s resting periods. Prior to each trial, a timer counted backward from 3, and the word "start" appeared. Then the screen went blank, and participants silently counted their felt heartbeat until "stop" appeared on the screen. During each trial R-R intervals were recorded, and participants were clearly instructed to silently count their heartbeats without the use of an exteroceptive aid (such as taking one's pulse). At the end of each period, participants reported the number of felt heartbeats using the computer keyboard. The participants were not informed about the length of the counting phases, nor about the quality of their performance. At the end of each counting trial the participants immediately rated their confidence in their perceived accuracy of response. These confidence judgements were made using a computerised 100 mm visual analogue scale anchored with, 0 indicating "Not at all confident" and 100 "Completely confident".

## 2.3.2. Heartbeat detection task (HDT)

A limitation of the heartbeat counting task is that participants can use knowledge about their heart rate to guide responses. The HDT overcomes this limitation and is therefore thought to provide a better measure of cardioceptive precision (i.e., sensitivity to the heartbeat) [41]. Unlike the HCT, the HDT has been shown to have good internal, construct, and face validity [41]. The task was a visual modification of that suggested by Ring and Brener [41] and based on previous work in our laboratory [11]. R peaks were detected online by adjusting the gain on the ECG module so that the largest gain was applied without causing any clipping /distortion of the signal. This signal was then sent to DTU100 (Digital Trigger Unit), and the trigger output is input into the PC via the parallel port. This input informs the PC to immediately display the visual image on the screen for  $\sim\!\!100$  ms. The task used in the present study consisted of six R-wave to stimulus intervals [R + 0, R + 100 ms, R + 200 ms, R + 300 ms, R + 400 ms and R + 100 ms, 110 ms, 125 ms, 150 ms, 200 ms, 210 ms, 225 ms or 250 ms, shuffled randomly

until all possibilities were used (i.e., on this type of trial stimuli were asynchronous with the heartbeat)]. Participants viewed eight trials of each R-wave to stimulus interval. Each trial consisted of a circle being presented on the screen for 60ms, and each trial consisted of eight circle presentations triggered by the participant's heartbeat. The task required participants to judge whether heartbeat sensations are or are not simultaneous with the circle presentation. Participants indicated their response on the keyboard: 1= in synch, 2= not in synch. After each trial participants rated their confidence in their response on a single visual analogue scale (0 - not at all confident, 100 - completely confident). Overall, this task took approximately forty-five to sixty minutes to complete depending on resting heartrate and response speed.

## 2.4. Habitual diet

The European Prospective Investigation into Cancer and Nutrition Norfolk Food Frequency Questionnaire (EPIC-Norfolk FFQ) [42] was used to collect dietary data. During data collection 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 have consumed specific foods over the preceding year. This questionnaire has been previously validated by Bingham, et al. who compared it to a 16-day weighed food record [43] and nutrient biomarkers [44]. The FETA software was then used to further process the data. FETA uses UK based food composition databases to produce nutrient data as well as basic food groups [42]. Importantly, this produces food groups that are captured cleanly, for example, fruit juice fraction of a juice drink – which may be only 10% of the total product – counts toward total fruit, but the rest of the beverage counts toward added sugars. Similarly, the skim milk fraction of whole milk counts toward the dairy constituent, but the butterfat in whole milk counts toward calories from solid fat.

To quantify the Mediterranean diet we used the method established by [45]. Predetermined nutritional guidelines were used to establish cut-off values and a value of 0, 1, or 2 was assigned for each of the nine components of the Mediterranean diet: 1) vegetables, 2) fruits, 3) legumes, 4) fish and seafood, 5) wholegrains, 6) meat, 7) dairy, 8) alcohol, 9) unsaturated oils (Supplementary Table 1). Components that are unhealthy if consumed frequently (e.g., red meat and high fat dairy) were assigned a value of 0 for high intake, 1 for moderate intake, and 2 for low intake. Conversely, healthy components (i.e., vegetables, fruits, legumes, fish and seafood, wholegrains) were assigned a value of 0 for low intake, 1 for moderate intake, and 2 for high intake. Alcohol consumption was assigned a value of 0 for high intake, 1 for low intake and 2 for moderate intake. Unsaturated oil consumption was assigned a value of 0 for nonconsumption, 1 for low to moderate intake, and 2 for high intake. The total Mediterranean diet score was calculated by summing the scores for each component, with higher scores reflecting greater adherence to the Mediterranean diet.

## 2.5. Covariates

## 2.5.1. Body mass index (BMI)

BMI was associated with both interoception [10], and consuming a poor quality diet [46], therefore we statistically controlled for this potential confound. Body mass was measured using an electronic scale (Kern KMS-TM, Kenr and Sohn GmbH, Germany). This scale takes 50 assessments over a 5 s period and produced an average value. Height was measured using a portable stadiometer. BMI was calculated using the formula: weight (lb) / [height (in)] $^2$  x 703.

## 2.5.2. Mood

Acute psychological state may influence the way interoceptive signals are processed [8]. Participants were asked to report how they felt "at this moment" using visual analogue scales with pairs of adjectives at the ends of 100 mm lines; Composed/Anxious; Hostile/Agreeable;

Elated/ Depressed; Unsure/Confident; Energetic/Tired; Confused/Clearheaded [47]. Scales were summed to produce a composite mood score which was controlled in the main analyses by entering this factor as a covariate.

## 2.5.3. Blood pressure

Cardiac signal strength may impact on different measures of inter-oception [20]. Therefore, systolic blood pressure (SBP), a physiological variable that correlates with baroreceptor activity and served as a marker of afferent signal strength [20], was measured twice while the participant was seated. An electronic BP monitor was used (Omron HEM-7430; Omron Corp) on the right upper arm, with a 1 min delay between measurements. On occasion the difference between the 2 SBP measurements exceeded 10 mm Hg. When this happened a third measurement was taken, and the mean of the last two measurements was used.

## 2.5.4. 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. Total activity was then qualified using Cooper activity points [48]. This metric quantifies activity in terms of its cardiovascular benefit which was previously associated with interoceptive processing [49,50].

## 2.6. Data preparation

#### 2.6.1. Heartbeat counting accuracy

The following transformation:  $1 - \sum$  (abs(Actual - Reported))/ (Actual+Reported) was used to calculate heartbeat tracking scores. These scores were then averaged to form a mean heartbeat tracking score. The interoception score varied between 0 and 1 with a higher score indicating better accuracy.

## 2.6.2. Heartbeat counting confidence and insight

Average confidence across all post-trial scales was used an index of postdictive interoceptive confidence. Here we examined two measures of metacognition: (i) calibration: how well confidence tracks accuracy on a trial-by-trial basis which was calculated as the within-participant Pearson correlation, r, between confidence and accuracy [21]; and (ii) a prediction error index (PE), capturing the magnitude of the difference between confidence and accuracy, which was operationalised as the absolute difference between objective interoceptive accuracy and average postdictive interoceptive confidence [21]. See Fig. 2 for a schematic illustration of prediction error and calibration.

## 2.6.3. Heartbeat detection accuracy

 $\chi^2$  was used to determine the distribution of each participants' responses (synchronous or asynchronous) across trials (R-wave to stimulus intervals). When this  $\chi^2$  test was significant participants qualified as heartbeat detectors. That is, participants were deemed capable of detecting their heartbeat when they preferentially responded 'synchronous' to one particular R-wave to stimulus interval over the others [41]. Importantly, this measure allows for the possibility that individuals may vary in where on the cardiogram they sense the heartbeat e.g., 200 ms versus 400 ms. Based on this classification thirty-seven individuals were considered accurate heartbeat detectors. Fig. 3 displays illustrative detector and non-detector histograms.

## 2.6.4. Heartbeat detection confidence and insight

Average confidence scores for each stimulus-onset-asynchrony (SOA) (i.e., random, 0, 100, 200, 300, 400 ms) were calculated depending on whether the participant responded 'yes' or 'no' to the simultaneous judgement. This gave rise to twelve average confidence ratings per participant. Note that for some participants it was not possible to calculate average confidence for a type of trial e.g., if a

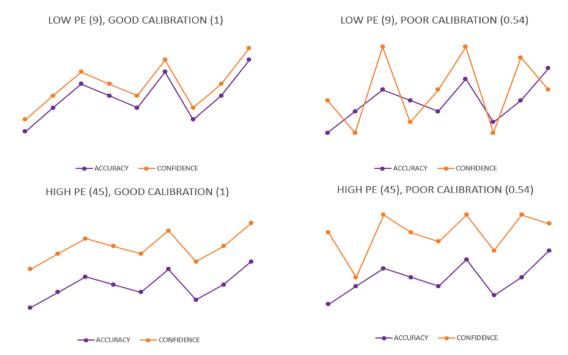


Fig. 2. Illustration of the difference between prediction error and metacognitive calibration.

Note. PE – prediction error, accuracy – accuracy of heartbeat counting, confidence – confidence in heartbeat counting. Each data point represents hypothetical accuracy / confidence on a particular trial. Numbers in brackets represents a hypothetical score.

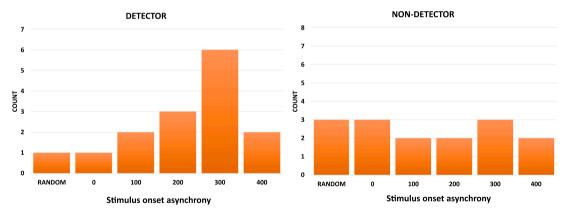


Fig. 3. Illustrative detector and non-detector histograms.

participant answered yes to all trials, then there were no confidence ratings for a 'no' response. If this occurred (n = 2) these participants were not included. Note that preliminary analysis revealed that those classified as detectors were significantly less likely to report feeling their heartbeat early in the cardiac cycle (0ms and 100ms), and more likely to report feeling later in the cardiac cycle (200 – 400 ms) (Supplementary information). As such analysing confidence dependant on SOA allowed us to determine whether diet was associated with overall confidence levels, and whether this varied according to the accuracy of the response which gives an indication of the ability to detect errors in first-order perceptual performance.

## 2.7. Statistical analysis

Sample characteristics were described using means, standard deviations, and frequencies as reported in Table 2. To test the hypothesis that a Mediterranean diet was associated with interoception, hierarchical multiple linear regression was used for all continuous outcome measures (heartbeat counting accuracy, heartbeat counting confidence,

**Table 2**Means (SD) for variables included in the present study.

	Mean	Std. Deviation
MED	6.13	1.87
Kcal / d	1706.59	519.54
BMI (kg/m <sup>2</sup> )	22.96	3.56
Physical activity	827.80	305.63
SBP (mmHg)	123.41	7.48
State mood (VAS)	51.72	23.92
HBC IAc	0.66	0.21
HBC confidence	48.28	22.74
HBC IAw	-0.06	0.72
HBC PE	1.01	0.75
HBD IAc	33% detectors	-
HBD confidence	57.52	15.27

Note. MED – Mediterranean diet score, BMI – Body mass index, SBP – Systolic blood pressure, VAS – Visual analogue scale, HBC – Heartbeat counting, HBD – Heartbeat detection, IAc – Interoceptive accuracy, IAw – Interoceptive awareness.

prediction error, and insight). Similarly, hierarchical binary logistic regression was used to examine the association between diet and heartbeat detection accuracy. In all analysis, covariates were entered as a in Step 1, and dietary components were entered simultaneously in Step 2. It was previously suggested that one source of metacognitive inefficiency is noise in the sensory input to confidence computation [51], therefore analysis concerning metacognitive measures also involved a third hierarchical step where the potential confounding influence interoceptive accuracy was considered. To determine the effects of diet on heartbeat detection confidence a 6 (SOA: Random, 0 ms, 100 ms, 200 ms, 300 ms, 400 ms) X 2 (RES: responded 'yes', responded 'no') repeated measures ANCOVA was used. This latter analysis allowed us to determine whether the effects of diet on heartbeat detection confidence depended on SOA and the participants' response. Covariates and diet were entered as continuous covariates. In all analyses 5000 bootstrapped samples were drawn with replacement from the dataset and 95% confidence intervals are reported. To control for the proportion of type 1 errors we employed Benjamini and Hochberg's false discovery rate (FDR) was employed. The FDR was controlled at  $\delta = 0.05$ . Where significant interactions did not reach this threshold, this is indicated in the text. Cooks distance, with a threshold of 0.1, was used to detect possible outliers (60). All analyses were carried out using SPSS version

#### 3. Results

Means (SD) for the covariates (mood, physical activity, blood pressure, BMI) and the Mediterranean diet score are shown in Table 2. Participants had a mean total Mediterranean diet score of  $6.13\pm1.87.$  33% of those who took part in the heartbeat detection task (n = 112) were classified as heartbeat detectors.

## 3.1. Heartbeat counting accuracy

Five outliers with a Cook's distance >0.1 were identified. However, their removal did not influence the result, therefore they were retained. The model accounted for 14% of the variance in heartbeat counting accuracy (adjusted  $\rm R^2=0.14$ ,  $\it F(6,185)=5.21$ ,  $\it p<0.001$ ). Interestingly, those who consumed a MED diet were more accurate ( $\it \beta=0.192,p$ )

= 0.007, 95% CI [0.06, 0.03]). In addition, those who took part in more aerobic activity had higher heartbeat counting accuracy ( $\beta$  = 0.31, p < 0.001, 95% CI [0.00, 0.01]). No other effects were significant: SBP ( $\beta$  = -0.04, p = 0.951, 95% CI [-0.04, 0.04]); Mood ( $\beta$  = 0.02, p = 0.688, 95% CI [-0.01, 0.01]); BMI ( $\beta$  = 0-.01, p = 0.867, 95% CI [-0.09, 0.08]); Kcal ( $\beta$  = 0.02, p = 0.727, 95% CI [-0.00, 0.01]).

## 3.2. Heartbeat detection accuracy

Overall, the model explained 13% (Nagelkerke  $R^2$ ) of the variance in heartbeat detection accuracy. Those who consumed a MED style diet were more likely to be classified as detectors (Exp(B) = 0.27, p =0.026, 95% CI [0.01, 0.57]) (Fig. 4). No other effects of diet were significant: BMI (Exp(B) = 0.03, p = 0.612, 95% CI [-0.11, 0.17]); Activity (Exp(B) = 0.00, p = 0.759, 95% CI [-0.02, 0.01]): SBP (Exp(B) = -0.01, p = 0.718, 95% CI [-0.08, 0.05]); Mood (Exp(B) = 0.01, p = 0.192, 95% CI [-0.06, 0.03]); Kcal (Exp(B) = 0.01, p = 0.147, 95% CI [0.00, 0.02]).

#### 3.3. Heartbeat counting confidence

Two outliers with a Cook's distance > 0.1 were identified but retained as they did not influence the results. 10% of the variance in heartbeat counting confidence was explained by the model (adjusted  $R^2=0.10$ , F(6,185)=3.49, p=0.003). Both MED ( $\beta=0.21$ , p=0.003, 95% CI [0.91, 4.35]) and activity levels ( $\beta=0.19$ , p=0.008, 95% CI [0.04, 0.05]) were positively associated with interoceptive confidence. However, no other effects were significant: BMI ( $\beta=0.07$ , p=0.308, 95% CI [-0.42, 1.35]); SBP ( $\beta=0.01$ , p=0.848, 95% CI [-0.38, 0.47]); Mood ( $\beta=-0.01$ , p=0.810, 95% CI -0.15, 0.11]); Kcal ( $\beta=0.06$ , p=0.348, 95% CI [0.91, 4.35]).

## 3.4. Heartbeat counting insight

The model accounted for < 1% of the variance in heartbeat counting insight (adjusted R $^2$  = 0.01, F(6, 185) = 0.46, p = 0.832). There were no significant effects: BMI ( $\beta$  = 0.03, p = 0.971, 95% CI [-0.02, 0.03]); SBP ( $\beta$  = 0.01, p = 0.822, 95% CI [-0.01, 0.01]); Mood ( $\beta$  = -0.04, p = 0.513, 95% CI [-0.00, 0.03]); Kcal ( $\beta$  = -0.06, p = 0.383, 95% CI [0.00, 0.01]). Neither MED ( $\beta$  = -0.07, p = 0.342, 95% CI [-0.08, 0.03]) nor

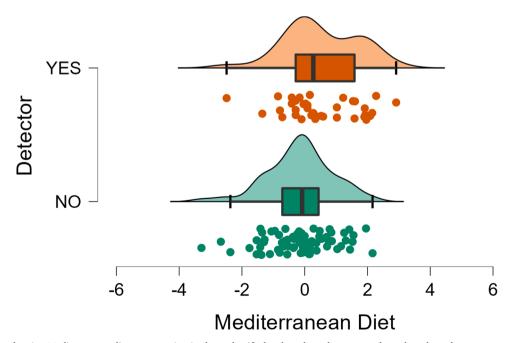


Fig. 4. Raincloud plot showing Mediterranean diet consumption in those classified as heartbeat detectors and non-heartbeat detectors. *Note:* date are adjusted means and 95% CI.

activity levels ( $\beta=0.03$ , p=0.628, 95% CI [-0.00, 0.01]) influenced heartbeat counting insight. The addition of IAc to the model in an additional step did not alter these results ( $\beta=-0.02$ , p=0.978, 95% CI [-0.51, 0.52]).

## 3.5. Heartbeat counting prediction error

One outlier with a Cook's distance > 0.1 was identified, however removing this case did not influence the results, therefore they were retained. The model was able to explain 9% of the variance in heartbeat counting prediction error (adjusted  $R^2=0.09$ , F(6,185)=3.28, p=0.004). Interestingly, the consumption of a MED diet was associated with having lower interoceptive prediction error ( $\beta=-0.25$ , p<0.001, 95% CI [-0.16,-0.05]). There was no effect of BMI ( $\beta=-0.03$ , p=0.559, 95% CI [-0.03,0.02]); SBP ( $\beta=-0.21$ , p=0.119, 95% CI [-0.02,0.01]); Mood ( $\beta=0.06$ , p=0.320, 95% CI [-0.02,0.01]); Kcal ( $\beta=0.09$ , p=0.302, 95% CI [-0.00,0.01]) or activity levels ( $\beta=0.01$ , p=0.976, 95% CI [-0.00,0.00]). The addition of IAc to the model in an additional step did not alter these results ( $\beta=0.01$ , p=0.472, 95% CI [-0.47,0.54]).

#### 3.6. Heartbeat detection confidence

Greenhouse-Geisser correction is reported as the sphericity assumption was not met (p < 0.001). The Response X SOA interaction was significant (F(4.130,2220.185) = 10.97, p < 0.001,  $\eta^2 p = 0.090$ ) indicating that overall participants were able to discriminate their correct and incorrect responses. However, this effect was superseded by a significant SOA X Response X MED interaction (F(4.240 841.439) =4.45, p < 0.001,  $\eta^2 p = 0.041$ ); high MED consumers were less confident when they responded 'no' to 200 ms (p < 0.001), 300 ms (p < 0.001), and 400 ms (p < 0.001) trials, compared to when they answered 'yes' (Fig. 5). There was also a main effect of Kcal (F(1, 105) = 6.15, p =0.015,  $\eta^2 p = 0.055$ ); interestingly those who consumed more Kcal were more confident overall. In addition, those with higher SBP had lower confidence in their HBD performance ( $F(1, 105) = 5.46, p = 0.021, \eta^2 p$ = 0.049), and those who reported a better state mood had more confidence in their HBD performance (F(1, 105) = 5.45, p = 0.021,  $\eta^2 p =$ 0.049). These latter effects did not depend on SOA or the nature of the participants response. The effects of activity levels (F(1, 105) = 0.05, p= 0.824,  $\eta^2 p$  = 0.000), and BMI (F(1, 105) = 1.38, p = 0.243,  $\eta^2 p$  = 0.013) were not significant.

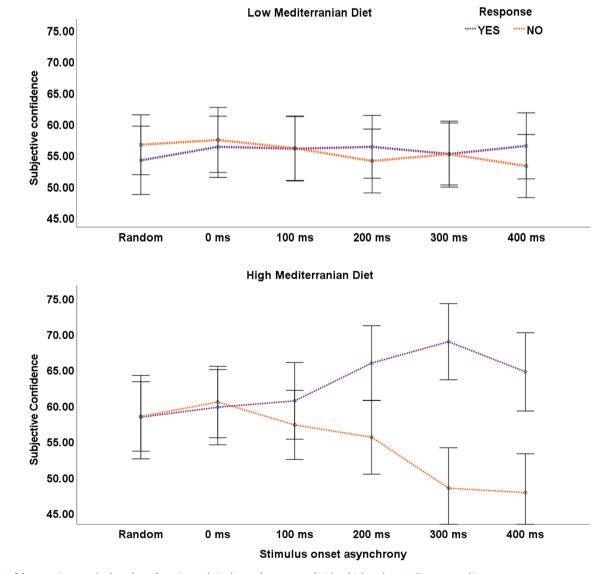


Fig. 5. Confidence ratings on the heartbeat detection task in those who consumed either high or low Mediterranean diet. *Note*: data are adjusted means (95% CI). For illustrative purposes, the Mediterranean diet variable was dichotomised using a median spilt.

## 4. Discussion

Evidence supports a role for adjunct nutritional interventions for improving mental health. Interoceptive signals are thought to play a mechanistic role, however, those sensations most strongly linked to psychological health have been overlooked by those studying diet. Therefore, for the first time, the present study determined whether a Mediterranean style diet (MED), high in foods thought to benefit brain health including fruits, vegetables, legumes, fish, and wholegrains [38], was associated with first order (perceptual), and second order (metacognitive) cardioception (Table 1 and Fig. 1). As hypothesised, those who adhered most strongly to MED dietary style had better heartbeat detection (Fig. 4) and counting accuracy. Interestingly, a MED diet was also associated with having a better ability to detect errors in first order perceptual performance (Fig. 5), and a lower prediction error (the magnitude of the difference between accuracy and confidence). These findings suggested a link between the consumption of foods that are high in antioxidants and anti-inflammatory properties and the brains capacity to metacognitively track the accuracy of interoceptive representations. Importantly, these effects were observed after controlling for total Kcal intake, SBP, BMI, activity levels and state mood. Populations low in cardioceptive and metacognitive accuracy, may benefit from a diet rich in fruit, vegetables, fish, wholegrains, and pulses.

Our results provided evidence of a link between the Mediterranean diet and cardioceptive accuracy. Specifically, adherence to a MED dietary pattern was associated with having more accurate heartbeat counting and detection performance (Fig. 4). This finding is consistent with an expansive literature connecting this dietary style with psychological health (e.g., major depression, anxiety) [38]. Thus, it is plausible that the ability to form accurate mental representations of afferent sensations underlying emotion might be a key mechanism connecting diet and mental health. Indeed, reduced access to cardiac afferent sensations has been linked to a range of emotion processing difficulties including alexithymia (a sub-clinical trait characterised by difficulty identifying and describing feelings and somatic sensations) [19], which has been shown to co-occur with a number of disorders, leading to the suggestion that atypical interoception may be the 'p-factor' accounting for symptom commonalities between psychiatric disorders [52]. Crucially, little is currently known about the aetiology of alexithymia or interoceptive deficits. The present data indicated that healthy dietary patterns could help ameliorate these difficulties by facilitating interoceptive accuracy. However, future experimental research will be needed to confirm this suggestion.

Interestingly, evidence indicates that the benefits of a MED diet on psychological health may partially come through the modulation of pathways involved in inflammation, oxidative stress, the HPA axis, and / or lipid metabolism [2,37,53]. For example, a recent study indicated that those who consumed a MED style diet had a lower allostatic load score [54]; a multi-system index comprised of biomarkers across four interconnected biological systems (metabolic, immune, cardiovascular, and neuroendocrine) which predicts physical and psychological health outcomes [55]. Therefore, it is plausible that through these mechanisms an antioxidant rich Mediterranean diet may help prevent the occurrence of unpredictable and uncontrollable bodily states (Fig. 1).

Indeed, many theoretical models connecting interoception and mental health propose that inflammatory states might lead to persistently imprecise ('noisy') interoceptive afferents, thereby reducing their influence on perception [56]. Similarly, it is plausible that adherence to a MED based diet may benefit cardioceptive accuracy by increasing cardiac afferent fidelity, thereby facilitating the development of accurate interoceptive representations (Fig. 1). For example, previous research found positive associations between plant-based diets rich in omega 3 fatty acids and cardiac vagal tone (assessed using high-frequency heart rate variability) [57,58,50]. In addition, accurate heartbeat detection was previously associated with both a higher heart rate variability [59], and a lower heart rate [11]. In the gastric domain,

vagal afferent responses to distension were reduced after a diet high in saturated fat [60]; a nutrient that tends to be low in the Mediterranean diet. In the future, studies designed to elucidate the specific neural and / or humeral processes connecting diet and cardioception might prove profitable. Regardless of the precise mechanisms, the present data indicated that diets high in fruit, vegetables, fish, pulses, wholegrains, and low in red and processed meats, may be efficacious as an adjunct intervention aimed at improving interoceptive abilities in populations characterised by poor cardioceptive accuracy e.g., those with depression who tend to perform poorly on cardioceptive accuracy tasks [61].

Interestingly, our data also suggested that habitual diet was associated with higher-level interoceptive processes. Specifically, those adhering to a MED diet were more confident in their heartbeat counting performance and had a lower heartbeat counting prediction error. The closer match between overall confidence levels and accuracy indicated that a MED diet may facilitate the development of more accurate metacognitive evaluations of cardioceptive accuracy. Indeed, on the heartbeat detection task, MED consumers were less confident when they responded 'no' to 200 ms and 300 ms trials i.e., during 'misses' (Fig. 5). This finding suggested that a MED diet could improve interoceptive error recognition thereby facilitating more accurate self-evaluative judgements [62].

Numerous brain regions have been implicated in error awareness, including the insula and the medial pre-frontal cortex (mPFC) [63] (Fig. 1). It is suggested that in the insula afferent visceral signals (i.e., interoceptive prediction errors (IPE)) update predictions about the state of the body, while the mPFC monitors ascending prediction errors and determines their confidence relative to descending prior beliefs (Fig. 1). Interestingly, previous research has found that brain derived neurotropic factor (BDNF) in visceromotor brain regions, including the anterior insula and the ACC, increased synaptic transmission and plasticity [64]. In this way, BDNF is crucial to learning, and may play a key role in error detection and belief updating [65,66]. One factor known to influence BDNF concentrations is diet. In particular, there is evidence that the consumption of phenolic acids, and other phenolic compounds, which are high in the MED diet, increased BDNF levels [67]. In addition, adherence to a MED diet was associated with an improvement in plasma BDNF concentrations in individuals with depression [68]. Although more research examining diet induced alterations in BDNF expression in specific brain regions is needed, it is plausible that through these mechanisms a MED style diet could facilitate the learning and updating of internal interoceptive representations, increase confidence and reduce prediction error. Interestingly, a MED diet was also associated with having a larger brain volume in areas of the brain associated with metacognition, specifically the cingulate and frontal cortices [69,70]. In addition, the consumption of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), nutrients that tend to be higher in a MED style diet, were associated with activity in the dorsal anterior cingulate during an inhibitory control task [71]. Whilst speculative, a MED diet could facilitate metacognitive accuracy by maintaining the structural and functional integrity of these brain regions that subserve metacognitive computation. Further research is needed to confirm these suggestions.

Given the expansive literature connecting impaired metacognition and poor mental health [72], the present findings emphasise the importance of considering the effects of diet on cardiac interoception across the full range of hierarchical levels of abstraction. Indeed, deficiencies in metacognitive processes are emerging as a transdiagnostic marker of mental health conditions, for example, problems with theory of mind [73], mentalization [74], cognitive confidence [75], self-evaluation [76], self-regulation [27], and metacognitive accuracy [77] have been observed across several psychopathologies. In regards to interoception, 'mismatches' between subjective and objective interoceptive abilities were found in those with autism (a disorder characterised by an inability to process emotions of self or other) [12], elevated anxiety [24], and disordered eating [27]. Notably, recent models of metacognition have detailed how local metacognitive processes (i.e.,

those measured using task based parameters such as sensitivity, efficiency, and bias) may inform more global metacognitive estimates of self-efficacy, and possibly more global personal-level constructs such as self-esteem [72]. These models suggest a biologically plausible mechanistic process whereby aberrant neural metacognitive computations may contribute to poor mental health [31]. However, little is currently known about potential factors involved in the development of maladaptive metacognitive computations. Intriguingly, although experimental research is required, the present data suggested that dietary factors are worth considering. Research examining the neural computations involved in metacognitive benefits of a MED based diet might prove profitable. It is plausible that mental health difficulties experienced by those with low meta-cognitive accuracy e.g., anxiety [24] may be ameliorated by adherence to a MED dietary style.

This study is not without limitations. Whilst we controlled for BMI, SBP, state mood, and physical activity levels, the correlational design means that reverse causality cannot be excluded. For instance, we previously reported that a disordered eating style was associated with different cardioceptive components [27]. It is plausible that aberrant interoceptive processes might pre-dispose towards eating an unhealthy diet. However, we suggest that future longitudinal research that considers the possibility of a feedforward cycle whereby a poor diet blunts interoceptive processes which in turn perpetuates disordered eating and the consumption of a poor diet might be most useful. Due to gender differences in both interoception and dietary style, our sample was limited to females under the age of 30 and as such the present findings require replication in males and older adults. In addition, the sample might have been slightly underpowered to detect associations using the HBD task, therefore findings should be replicated in larger samples. Due to individual variation in the temporal perception of the heartbeat we were unable to calculate the more robust ROC AUC measure of metacognition. Whilst previous research using the heartbeat detection paradigm has computed this measures using the 200 ms epoch [21], the present observation that detectors often felt their heartbeat at either 200 ms, 300 ms, or 400 ms post R-peak meant we were not justified in calculating this index in the present sample. The limitations of FFQ data and dietary pattern quantification are well documented and RCTs confirming the present findings are needed [78]. In addition, there is a need to consider that the beneficial effects of a MED diet could be the result of what is not consumed e.g., saturated fats, refined sugars etc. These foods have been associated with interoceptive deficits in appetitive domains [79,80]. Therefore, future research which considers the interoceptive consequences of foods which reduce the predictability of postprandial states will be important. Finally, current validated cardioception paradigms rely solely on retrospective judgements. However, it is increasing recognised that interoception is a prospective regulatory process [81-83]. For example, there may be variation in the certainty with which one can predict future interoceptive afferents based on available actions [81]. Therefore, further research examining the impact on diet on prospective inference and confidence will be essential.

Together the present results suggested that a Mediterranean style may benefit cardioception; an interoceptive domain which is not usually considered by those studying diet. A MED diet was associated with better first order (perceptual) and second order (meta-cognitive) cardioception. Given the emerging links between cardioception and psychological health the present findings imply that greater attention to dietary interventions in mental health treatment settings may have the potential to improve patient outcomes. We hope that the present findings pave the way towards a greater appreciation of the influence of diet on interoceptive processes beyond the 'gut-brain' axis.

## Contributions

H.Y. and G.F. conceived and designed the methods and study. H.Y. ran the experiment. H.Y. and G.F. Analysed and interpreted the data, and wrote the manuscript with input from D.B.

#### **Declaration of Competing Interest**

All authors declare no conflict of interest.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.physbeh.2022.113964.

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