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Original article

Dietary inflammatory index and mental health: A cross-sectional analysis of the relationship with depressive symptoms, anxiety and well-being in adults

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SUMMARY

Background & aims: The relationship between diet, inflammation and mental health is of increasing interest. However, limited data regarding the role of dietary inflammatory potential in this context exist. Therefore the aim of this work was to examine associations between the inflammatory potential of habitual diet and mental health outcomes in a cross-sectional sample of 2047 adults (50.8% female).
Methods: Diet was assessed using a self-completed food frequency questionnaire from which dietary inflammatory index (DII®) scores were determined. Depressive symptoms, anxiety and well-being were assessed using the CES-D, HADS-A and WHO-5 screening tools.
Results: Logistic regression analyses revealed that higher energy-adjusted DII (E-DII®) scores, reflecting a more pro-inflammatory diet, were associated with increased risk of depressive symptoms (odds ratios (OR) 1.70, 95% confidence intervals (CI) 1.23–2.35, $p = 0.001$) and anxiety (OR 1.60, 95% CI 1.15–2.24, $p = 0.006$) and lower likelihood of well-being (OR 0.62, 95% CI 0.46–0.83, $p = 0.001$), comparing highest to lowest tertile of E-DII. In gender-stratified analyses associations were noted in women only. Women with the highest E-DII scores were at elevated risk of depressive symptoms (OR 2.29, 95% CI 1.49–3.51, $p < 0.001$) and anxiety (OR 2.00, 95% CI 1.30–3.06, $p = 0.002$), while likelihood of reporting good well-being was lower (OR 0.55, 95% CI 0.36–0.79, $p = 0.002$), relative to those with the lowest E-DII scores.
Conclusions: These findings, which suggest that a pro-inflammatory diet is associated with adverse mental health, may be of clinical and public health significance regarding the development of novel nutritional psychiatry approaches to promote good mental health.

1. Introduction

The prevalence of mental health disorders, which has been increasing over recent decades, represents a major public health concern. Current worldwide prevalence of depression is estimated to be 350 million [1]. According to the WHO more than one in four of European adults have experienced a psychological disorder [2]. Data from the Global Burden of Disease Study highlight the significant contribution of mental health and depressive disorders to the global burden of non-communicable disease, through years lived with disability [1]. Thus identification of new preventive measures or strategies to attenuate disease development is essential. Multifactorial processes, most likely involving biological, social, genetic and environmental factors, contribute to an individual's psychological health and well-being [3]. There is growing interest in the possible contribution of modifiable lifestyle behaviours, such as habitual dietary intake, to the development of common mental

Abbreviations: CES-D, centre for epidemiologic studies depression scale; CRP, C reactive protein; CVD, cardiovascular disease; DII, dietary inflammatory index; FFQ, food frequency questionnaire; HADS, hospital anxiety and depression scale; IL-6, interleukin 6; OR, odds ratio; TNF-α, tumour necrosis factor α; WHO-5, World Health Organization-5 well being index.

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health disorders. Moreover, rather than focussing on selected nutrients or foods the emerging field of nutritional psychiatry has turned its attention to investigating the relationship between dietary patterns and mental health.

Healthy dietary patterns such as the Norwegian and Mediterranean diets, which are characterized by a high intake of fruit, vegetables, wholegrains, fish and lean meats, have been associated with lower likelihood of developing depression [4,5]. Conversely, increased risk of depression has been reported among those with an unhealthy or Western-style diet, which is typified by high consumption of energy-dense, high-fat and high-sugar products, processed and red meats, refined grains and alcohol [6,7]. However meta-analysis and systematic reviews have not yet provided confirmation, partly due to a limited number of studies [4,5]. Dietary patterns and dietary quality also have been linked with well-being, anxiety and stress [8–11], indicating that the biological mechanisms underpinning diet-mental health associations extend beyond depressive symptoms. Inflammation has been proposed as a substrate for mechanisms linking diet to mental health. Increasing evidence suggests that depression is associated with increased concentrations of pro-inflammatory cytokines [12,13]. Despite a high degree of heterogeneity observed in earlier meta-analyses, a recent and the largest meta-analysis of cytokines and chemokines in major depressive disorder (MDD) provides confirmation that concentrations of tumour necrosis factor α (TNF-α) and interleukin 6 (IL-6), amongst other cytokines and chemokines, are significantly elevated in individuals with MDD [14].

Limited data regarding the association between the inflammatory potential of habitual diet and mental health conditions exist. Lucas et al. identified a dietary pattern related to circulating levels of C reactive protein (CRP), IL-6 and TNF-α receptor 2 and examined its relationship with risk of depression among participants in the Nurses' Health Study [15]. They reported a 30–40% increased risk of depression, depending on definition, comparing highest to lowest quintiles (i.e. most pro-inflammatory vs. most anti-inflammatory). In recent years the Dietary Inflammatory Index (DII®) was developed to characterize an individual's diet on a continuum from maximally anti- to pro-inflammatory [16]. Thus far, the DII has been associated with CRP [17,18], IL-6 [19,20], and TNF-α [19]. To date, only three studies have examined the association between the DII and depression; all report increased risk of incident depression among those with the most pro-inflammatory diet [21–23]. However, no data on the relationship between dietary inflammatory potential and other mental health measures such as anxiety and well-being exist. Therefore, the primary objective of the present study was to examine associations between dietary inflammatory potential and a range of mental health measures including depressive symptoms, anxiety and psychological well-being in a cross-sectional sample of men and women.

2. Subjects and methods

2.1. Study design and subject recruitment

The Cork and Kerry Diabetes and Heart Disease Study (Phase II) was a single-centre, cross-sectional study conducted between 2010 and 2011 [24]. A population representative random sample was recruited from a large primary care centre in Mitchelstown, County Cork, Ireland (Mitchelstown cohort). The Livinghealth Clinic includes 8 general practitioners and serves a catchment area of approximately 20,000 with a mix of urban and rural residents. Mitchelstown cohort participants were randomly selected from all registered attending patients in the 50–69-year age group. In total, 3807 potential participants were selected from the practice list. Following exclusion of duplicates, deaths and ineligibles, 3043 were invited to participate in the study and of these 2047 White individuals (49.2% male) completed the questionnaire and physical examination components of the baseline assessment (response rate 67%). Ethics committee approval conforming to the Declaration of Helsinki was obtained from the Clinical Research Ethics Committee of University College Cork. All participants provided written informed consent. Following exclusion of individuals without food frequency questionnaire (FFQ) data the remaining 1992 participants were used in the analyses.

2.2. Clinical and anthropometric data

All participants attended the clinic in the morning after an overnight fast (minimum 8 h). Fasting blood samples were taken on arrival. Participants completed a General Health Questionnaire (GHQ), the FFQ, and the International Physical Activity Questionnaire (IPAQ). Data on age, gender, medical history and medication use were gathered through a self-completed GHQ. Depressive symptoms, well-being and anxiety were assessed using a range of questionnaires including the 20-item Centre for Epidemiologic Studies Depression Scale (CES-D) [25], designed to evaluate the frequency and severity of depressive symptoms, the Hospital Anxiety and Depression Scale (HADS), using only the anxiety subscale [26] and the World Health Organisation (WHO) −5 Well Being Index [27]. Subjects with CES-D scores ≥16, HADS scores ≥13 and WHO-5 scores of >13 were identified as having depressive symptoms, anxiety and good well-being, respectively. History of depression and anxiety was assessed using the following questions: “Have you ever had depression?” “Have you ever had anxiety?” Subjects were then asked “If yes, when did it start? In the last year/1–5 years ago/>5 years ago.” Data regarding antidepressant medication use were collected. Subjects who indicated a diagnosis of depression or anxiety or current anti-depressant medication use were classified as having a mental health disorder. The presence of cardiovascular disease (CVD) was obtained from the GHQ by asking study participants if they had been diagnosed with any one of the following seven conditions: Heart Attack (including coronary thrombosis or myocardial infarction), Heart Failure, Angina, Aortic Aneurysm, Hardening of the Arteries, Stroke, or any other Heart Trouble. Subjects who indicated a diagnosis of any one of these conditions were classified as having CVD. Type 2 diabetes was defined according to the American Heart Association guidelines of fasting plasma glucose (FPG) ≥ 7 mmol/L or doctor diagnosed diabetes. Blood pressure was measured according to the European Society of Hypertension Guidelines using an Omron M7 Digital BP monitor on the right arm, after a 5-min rest in the seated position. The average of the second and third measurements was used for analyses. Hypertension was defined as average systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg or being on hypertensive medication. Anthropometric measurements were recorded with calibrated instruments according to a standardised protocol. Body weight was measured in kilograms without shoes; to the nearest 100 g using a Tanita WB100MA® weighing scales (Tanita Corporation, IL, USA). Height was measured in centimetres to one decimal place using a Seca Leicester® height gauge (Seca, Birmingham, UK). BMI was calculated as weight (kg)/height $(m)^2$. Individuals with a BMI ≥ 30 kg/m^2 were defined as obese.

2.3. Dietary inflammatory index

Diet was assessed using a modified version of the self-completed EPIC FFQ [28]. This FFQ was then incorporated into the Irish National

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Surveys of Lifestyle Attitudes and Nutrition 1998, 2002, 2006 [29–31] and the Cork and Kerry Phase 1 study [32] and has been validated for use in the Irish population. Information on the frequency of consumption of food items during the past 12 months was collected. The daily intake of energy and nutrients was computed from FFQ data using a tailored computer program (FFQ Software Ver 1.0; developed by the National Nutrition Surveillance Centre, School of Public Health, Physiotherapy and Sports Science, University College Dublin, Belfield, Dublin 4, Ireland), which linked frequency selections with the food equivalents in McCance and Widdowson Food Tables [33]. In computing the E-DII score, dietary information for each study participant is first linked to a regionally representative database that provides a global estimate of mean intake for each of the 45 parameters (i.e. foods, nutrients, and other food components), along with its standard deviation considered in the DII definition [16]. These parameters then are used to derive the participant's exposure relative to the standard global mean as a *z*-score, derived by subtracting the mean of the energy-adjusted regionally representative database from the amount reported, and dividing this value by the parameter's standard deviation. These *z*-scores are converted to percentiles (expressed as a proportion; i.e., with values ranging from 0 to 1) and then centering by doubling and subtracting 1. Clinical interpretation remains clear with these additional steps and inappropriate weighting is avoided and higher (i.e., more positive) DII scores invariably represent more pro-inflammatory diets. The resulting value is then multiplied by the corresponding food parameter effect score (derived from a literature review on the basis of 1943 articles [16]). All of these food parameter-specific E-DII scores are then summed to create the overall DII score for every subject. Twenty six of the 45 possible food parameters were used for DII calculation based on the FFQ in this study (carbohydrate, protein, fat, alcohol, fibre, cholesterol, saturated fat, mono-unsaturated fat, poly-unsaturated fat, niacin, thiamin, riboflavin, vitamin-B12, vitamin-B6, iron, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin D, vitamin E, folic acid, onion, garlic and tea).

2.4. Lifestyle data

Physical activity levels were assessed using the short-form IPAQ, which provided information on frequency, duration and intensity of physical activity [34]. Using the instrument's scoring protocol, physical activity was categorized into three groups; low, moderate and high, based on a combination of; frequency of activity, duration of each activity bout and metabolic equivalent (MET) minutes per week in all activity types. Smoking status was defined as never (having never smoked at least 100 cigarettes in entire life), former (having smoked at least 100 cigarettes in entire life and do not smoke now), and current smokers (smoking at present). Alcohol consumption included questions based on weekly intake to define non-drinkers (a person who responded to the question "How often do you have a drink containing alcohol" as never), moderate (women and men consuming less than 14 units and 21 units, respectively, in a typical week) and heavy drinkers (women and men consuming greater than or equal to 14 units and 21 units, respectively, in a typical week).

2.5. Biological analyses

Plasma and serum were prepared from fasting blood samples from each subject. Fasting plasma glucose concentrations were determined using a glucose hexokinase assay by Cork University Hospital Biochemistry Laboratory using fresh blood samples. CRP, TNF-α and IL-6 were determined using a biochip array system (Evidence Investigator; Randox Laboratories, Antrim, UK).

2.6. Statistical analysis

Statistical analysis was conducted using PASW Statistics version 20® for Windows (SPSS Inc., Chicago, IL). Continuous variables were expressed as means ± SEM and categorical variables as percentages. Variables were assessed for normality of distribution and skewed variables were normalized as appropriate. Differences between groups were analysed by independent samples *t*-tests for continuous variables and by Chi-Square test for categorical variables. Logistic regression analysis was used to determine if dietary inflammatory potential based on E-DII scores, stratified by tertiles, was associated with depressive symptoms, anxiety and poor well-being. All logistic regression analyses were repeated following stratification by gender. Antidepressant use, history of depression, age, gender, BMI, physical activity, smoking status and alcohol consumption were considered confounding factors. For all analyses a p-value of <0.05 was considered significant.

3. Results

3.1. Clinical and demographic characteristics according to E-dietary inflammatory index tertiles

Mean (SD) and range of the E-DII in the Mitchelstown cohort ($n = 1992$) were −1.28 (1.51) and −5.10 to 3.68. Clinical and demographic characteristics according to tertiles of E-DII are presented in Table 1. Greater depressive symptoms and reduced well-being were observed among individuals in the highest tertile of dietary inflammatory index, and thus the most pro-inflammatory diet. Although there was a trend towards higher anxiety scores with a more pro-inflammatory diet this did not attain statistical significance. Individuals in the top tertile of E-DII were more likely to be male, current smokers and to be more sedentary. No differences in age, disease prevalence, total dietary intake or alcohol consumption were observed between groups.

3.2. E-DII and mental health status

Logistic regression analyses (Table 2) revealed that higher E-DII scores, reflecting a more pro-inflammatory diet, were associated with increased risk of having depressive symptoms (OR 1.70, 95% CI 1.23–2.35, $p = 0.001$) and anxiety (OR 1.60, 95% CI 1.15–2.24, $p = 0.006$) and lower likelihood of well-being (OR 0.62, 95% CI 0.46–0.83, $p = 0.001$), comparing highest to lowest tertile of E-DII, adjusted for age and gender. Additional adjustment for BMI and lifestyle factors little attenuated these findings, comparing top vs. bottom tertiles. However, when history of depression and use of anti-depressants were included as potential confounders, only the association between E-DII and depressive symptoms persisted.

3.3. The relationship between E-DII and mental health outcomes according to gender

Stratified logistic regression analysis (Table 3) revealed gender differences in the associations between dietary inflammatory potential and mental health outcomes. Increased risk of depressive symptoms (OR 2.29 95% CI 1.49–3.51, $p < 0.001$) and anxiety (OR 1.99, 95% CI 1.30–3.06, $p = 0.002$) and reduced likelihood of reporting well-being (OR 0.55, 95% CI 0.36–0.79, $p = 0.002$) were observed among the female study participants, comparing highest to lowest tertile of E-DII. The association with depressive symptoms, but not anxiety or well-being, remained in the fully adjusted model (OR 2.23, 95% CI 1.15–4.36, $p = 0.018$, comparing highest to lowest tertile of E-DII). No associations were noted among the male participants.

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Table 1
Mitchelstown cohort characteristics according to tertiles of E-dietary inflammatory index.

	Tertile 1 ($n = 664$)	Tertile 2 ($n = 664$)	Tertile 3 ($n = 664$)	*P*
Age (yrs)	60.07 ± 0.21	59.75 ± 0.22	59.36 ± 0.21	0.064
Gender (% male)	34.8	49.7	62.5	0.000
CESD score	8.41 ± 0.28	9.54 ± 0.32	9.96 ± 0.33	0.001
HADS-A score	4.04 ± 0.18	4.23 ± 0.14	4.48 ± 0.15	0.08
WHO-5 score	17.38 ± 0.21	16.70 ± 0.22	16.48 ± 0.22	0.007
Mental health disorder (%)	15.6	18.2	18.8	0.27
Cardiovascular disease (%)	9.63	11.29	10.39	0.61
Type 2 diabetes (%)	8.37	8.93	8.89	0.79
Obesity (%)	29.95	33.75	33.43	0.17
Hypertension (%)	33.50	29.10	26.85	0.14
Daily energy intake (kcal)	2014 ± 31	2053 ± 32	2014 ± 32	0.61
Smoking status				
Never	54.02	52.23	47.91	0.001
Former	35.14	33.49	33.02	
Current	10.83	14.28	19.07	
Alcohol consumption				
Non-drinker	22.51	19.52	18.91	0.08
Moderate	66.83	63.60	65.15	
Heavy	10.65	16.88	15.94	
Physical activity levels				
Low	43.26	45.81	55.62	<0.0001
Moderate	34.48	31.59	23.16	
High	22.25	22.60	21.20	

Continuous variables are expressed as means ± SEM; categorical variables are expressed as percentages. ANOVA is used for continuous variables and Chi-Square test is used for categorical variables. yrs: years; %: percentage; kcal: kilocalories.

Table 2
Logistic regression analysis of the association between E-DII and mental health outcomes.[a]

	Depressive symptoms		Anxiety		Well-being	
		p		*p*		*p*
Model 1						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.55 (1.13–2.14)	0.007	1.34 (0.96–1.86)	0.09	0.71 (0.53–0.95)	0.02
Tertile 3	1.70 (1.23–2.35)	0.001	1.60 (1.15–2.24)	0.006	0.62 (0.46–0.83)	0.001
Model 2						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.79 (1.19–2.71)	0.006	1.49 (0.99–2.26)	0.06	0.76 (0.53–1.10)	0.14
Tertile 3	1.60 (1.04–2.47)	0.03	1.55 (1.01–2.39)	0.05	0.70 (0.48–1.02)	0.006
Model 3						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.69 (1.06–2.69)	0.026	1.33 (0.83–2.11)	0.23	0.88 (0.59–1.31)	0.54
Tertile 3	1.36 (0.83–2.24)	0.220	1.38 (0.95–2.24)	0.20	0.85 (0.56–1.28)	0.43

Data are presented as OR (95% CI). DII values were stratified by tertiles. Reference group refers to that within the same comparative group. Model 1: Adjusted for age and gender. Model 2: Additionally adjusted for BMI, physical activity, smoking and alcohol consumption. Model 3: Additionally adjusted for antidepressant use and history of depression.
[a] $n = 664$ in each E-DII tertile.

3.4. Role of circulating inflammatory markers

Additional adjustments for circulating concentrations of CRP, TNF-α and IL6 (which were available for 1988 of the 1992 study participants) did not alter the main findings reported in Table 2. For example, inclusion of the inflammatory markers in model 1 generated similar ORs for increased likelihood of having depressive symptoms (OR 1.62, 95% CI 1.16–2.24, $p = 0.004$) and anxiety (OR 1.62, 95% CI 1.15–2.27, $p = 0.006$) and lower likelihood of well-being (OR 0.64, 95% CI 0.47–0.86, $p = 0.003$), comparing highest to lowest tertile of E-DII.

4. Discussion

To our knowledge, the current study is the first to investigate associations between the dietary inflammatory index and a range of mental health measures, including depressive symptoms, anxiety and psychological well-being, in an adult population. We provide evidence for an association between a pro-inflammatory diet and increased risk of adverse mental health outcomes. Participants with the highest E-DII score (representing the greatest pro-inflammatory dietary potential) displayed a 70% higher odds of depressive symptoms, a 60% higher odds of anxiety and a 38% lower likelihood of reporting good well-being relative to those with the lowest E-DII (and thus consuming diets with the greatest anti-inflammatory potential). These findings persisted after adjustment for BMI and lifestyle factors including physical activity, alcohol and smoking behaviours, but were no longer significant when history of depression and anti-depressant medication use were taken into account. Furthermore, these findings were gender specific; risk of depressive symptoms and anxiety were more than two-fold greater among women with the highest E-DII score and likelihood of reporting adequate well-being was 45% lower than their counterparts with the lowest E-DII score. No significant association was observed among men.

Mental health disorders are more prevalent among women than men [35]. Gender differences with respect to depression and anxiety have been reported, including age of onset and duration of symptoms, social adjustment and long-term outcomes [36]. The current work demonstrates associations between dietary

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Table 3
Gender stratified analysis of the association between E-DII and mental health outcomes.[a]

	Depressive symptoms		Anxiety		Well-being	
		p		*p*		*p*
Females (n = 1016)						
Model 1						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.78 (1.18–2.67)	0.006	1.46 (0.97–2.21)	0.07	0.65 (0.45–0.94)	0.02
Tertile 3	2.29 (1.49–3.51)	<0.001	1.99 (1.30–3.06)	0.002	0.55 (0.36–0.79)	0.002
Model 2						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	2.18 (1.25–3.80)	0.006	1.59 (0.92–2.73)	0.09	0.69 (0.43–1.10)	0.13
Tertile 3	2.37 (1.29–4.34)	0.005	2.00 (1.12–3.60)	0.02	0.60 (0.35–1.02)	0.06
Model 3						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.80 (0.98–3.31)	0.06	1.33 (0.73–2.42)	0.35	0.83 (0.49–1.41)	0.48
Tertile 3	2.23 (1.15–4.36)	0.02	1.87 (0.99–3.55)	0.055	0.67 (0.37–1.20)	0.17
Males (n = 976)						
Model 1						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.18 (0.71–1.95)	0.53	1. 08 (0.62–1.87)	0.78	0.84 (0.52–1.33)	0.84
Tertile 3	1.23 (0.70–1.83)	0.62	1.16 (0.69–1.95)	0.59	0.77 (0.49–1.20)	0.24
Model 2						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.34 (0.72–2.50)	0.36	1.17 (0.61–2.23)	0.64	0.91 (0.52–1.61)	0.76
Tertile 3	1.04 (0.56–1.93)	0.90	1.07 (0.57–2.01)	0.84	0.88 (0.51–1.52)	0.64
Model 3						
Tertile 1	1 [reference]		1 [reference]		1 [reference]	
Tertile 2	1.43 (0.68–3.01)	0.34	1.01 (0.48–2.15)	0.98	0.95 (0.51–1.79)	0.88
Tertile 3	0.78 (0.36–1.64)	0.50	0.89 (0.42–1.89)	0.77	1.09 (0.60–2.00)	0.79

Data are presented as OR (95% CI). DII scores were stratified by tertiles. Reference group refers to that within the same comparative group. Model 1: Adjusted for age. Model 2: Additionally adjusted for BMI, physical activity, smoking and alcohol consumption. Model 3: Additionally adjusted for antidepressant use and history of depression.

[a] $n = 664$ in each E-DII tertile.

inflammatory potential and depressive symptoms, anxiety and psychological well-being, which were only evident among the female participants. While some of the earlier studies also reported associations between risk of depression among women these were female-only cohorts and dietary inflammatory potential was determined by two different methods (dietary inflammatory pattern and DII) [15,23]. Examination of the Nurses' Health Study revealed a 30–40% increased risk of depression, depending on definition, comparing highest to lowest quintiles of dietary inflammatory pattern (i.e. most pro-inflammatory vs. most anti-inflammatory) [15]. Twelve-year follow-up of middle-aged women in the Australian Longitudinal Study on Women's health ($n = 6438$) identified a 20% lower risk of depression among those whose diets were in the highest DII quartile compared to those in the lowest DII quartile [23]. To date, only two other studies have examined the relationship between DII scores and risk of depression among both genders [21,22]. In a Spanish cohort study of university graduates ($n = 15{,}093$), similar increased risk of depression was reported among the male and female participants (ORs 1.53 and 1.46, respectively). Consistent with our findings are recent data from the Whitehall II Study, which also revealed a gender-specific association between DII and recurrence of depressive symptoms [21]. In that longitudinal analysis of middle-aged men and women (mean age at follow-up was 60 years) the women with the highest DII score (i.e., most pro-inflammatory diet) were almost 3 times more likely to develop recurrent depressive symptoms, even after adjusting for a wide range of confounders. No association was observed in the male study participants. It may be that the younger age profile of the Spanish cohort (mean age across DII quintiles 36–40 years) compared to both the Mitchelstown and Whitehall II cohorts (mean age approximately 60 years) may, at least in part, account for the disparity in the reporting of gender-specific relationships. Further research to disentangle the gender–diet–depression relationship is warranted. In addition to the mental health outcomes reported in this study, higher DII scores have been associated with cognitive decline in a mixed gender French cohort, which included gender as a covariate in multivariable regression analyses [37]. Also, in Iranian women we found that increased levels of stress were associated with higher DII scores [38].

A pertinent observation in the current work was that adjustment for concentrations of circulating inflammatory markers did not alter the main findings, suggesting that relationship between E-DII and mental health is not modulated by inflammatory status (at least as represented by these markers). Consistent with this is the finding from the Whitehall II Study that the association between recurrence of depressive symptoms and DII was not altered when circulating CRP and IL6 concentrations were included as confounders in their regression models [21]. While the mechanisms underlying our observed associations between dietary inflammatory potential and depressive symptoms, anxiety and well-being are not fully elucidated, our data suggest, for the first time, that they are common across other mental health outcomes, and not just limited to depression. Of related interest are the recent reports of reductions in circulating IL-6 concentrations with anti-depressant medication and among treatment responders but not non-responders [39,40], suggesting that elevated pro-inflammatory status characterized by higher IL-6 concentrations, for example, might contribute to treatment resistance. Thus strategies to improve inflammatory status among individuals with depression or other mental health disorders may be worthwhile on many levels. Recent findings from a randomized controlled trial of dietary improvement among adults with major depression provide timely and important reassurance regarding the contribution of nutritional strategies, specifically personalized dietary therapy, to the management of individuals with depression [41].

Among the strengths of our study are the large number of participants aged 50–69 years old with evaluable data; equal representation by gender (49.2% male); assessment of a wide range of clinical and mental health parameters, including depressive

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symptoms, anxiety and psychological well-being; information on diet and lifestyle factors; and a wide range of confounding factors, including mental health history and use of antidepressant medications. Furthermore, the recently completed follow-up of the Mitchelstown cohort will permit longitudinal analysis of the reported diet-mental health associations to be examined in an ageing population. Despite these strengths, we have identified several limitations. The cross-sectional study design precludes drawing conclusions regarding the temporal direction of the relationship between dietary inflammation and mental health. Mental illness can influence appetite and alter an individual's food choices, for example emotional eating may be characterized by reduced consumption of fruits and vegetables [42] (which, for the most part, are anti-inflammatory) and increased intake of energy-dense fast foods, sweets and confectionary [43,44] (which are more pro-inflammatory). The temporal relationship between E-DII scores and history of depression and use of anti-depressants, which were included as potential confounders, is complicated. The fact that only the association between E-DII and depressive symptoms persisted after control for these historical data may reflect the limitations of this study design. It would be interesting to see if interval changes in dietary factors (which tend to be refractory to change) could affect mental health outcomes [45–47]. Thus, prospective studies investigating whether a more pro-inflammatory diet arises from adverse mental health status or is a causative factor are required. As a structured dietary assessment method, the use of an FFQ can introduce biases related to psychosocial factors (response sets) [48,49] that are known to vary by gender [50] and might distort results [51]. The generalizability of our findings may be limited. The Mitchelstown cohort comprises adult participants recruited from a large primary care centre in Mitchelstown, County Cork, Ireland, which includes 8 general practitioners (GP) and serves an urban and rural catchment area of approximately 20,000. Around 98% of Irish adults are registered with a GP making it possible, even in the absence of a universal patient registration system, to undertake population-based epidemiological studies that are representative of the general population [52]. Finally, another potential limitation of the study includes non-availability of information on the remaining 18 food parameters for DII calculation.

In conclusion, these novel results provide further confirmation regarding the relationship between dietary inflammatory potential and depressive symptoms. Importantly, they expand on the previously described diet-depression associations and highlight the potential of a more anti-inflammatory diet in the context of anxiety and psychological well-being. Mental health disorders have a substantial socio-economic impact [53]. Considering the increasing prevalence and adverse health outcomes associated with poor mental health, there is an unquestionable need for more effective, inexpensive and accessible approaches to diminish the risk of adverse mental health outcomes and their associated burden. Expanding the knowledge base regarding the relationship between dietary inflammatory potential and mental health is warranted, with a view to developing new nutritional therapies or interventions to improve and maintain optimal mental health and emotional well-being.

Author contributions

CMP and IJP contributed to the conception and design of the study, analysis and interpretation of the data, drafting of the manuscript and critical revision of the manuscript for important intellectual input. NS and JRH generated the DII scores, contributed to the interpretation of the data, drafting and critical revision of the manuscript for important intellectual input. All authors approved the final version.

Conflict of interest

We wish to disclose that Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina in order to develop computer and smart phone applications for patient counselling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI. The subject matter of this paper will not have any direct bearing on that work, nor has that activity exerted any influence on this project.

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