Review Article

Dietary inflammatory index and depression: a meta-analysis

Jian Wang†, Yao Zhou†, Kang Chen†, Yuntian Jing, Jiaan He, Hongxiao Sun and Xinhua Hu*

Department of Vascular and Thyroid Surgery, The First Affiliated Hospital, China Medical University, Shenyang 110001, People’s Republic of China

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Abstract

Objective: The purpose of the present meta-analysis was to evaluate the association between the inflammatory potential of diet, determined by the dietary inflammatory index (DII®) score, and depression.

Design: Systematic review and meta-analysis.

Setting: A comprehensive literature search was conducted in PubMed, Web of Science and EMBASE databases up to August 2018. All observational studies that examined the association of the DII score with depression/depressive symptoms were included.

Subjects: Four prospective cohorts and two cross-sectional studies enrolling a total of 49,584 subjects.

Results: Overall, individuals in the highest DII category had a 23% higher risk of depression (risk ratio (RR) = 1.23; 95% CI 1.12, 1.35). When stratified by study design, the pooled RR was 1.25 (95% CI 1.12, 1.40) for the prospective cohort studies and 1.16 (95% CI 0.96, 1.41) for the cross-sectional studies. Gender-specific analysis showed that this association was observed in women (RR = 1.25; 95% CI 1.09, 1.42) but was not statistically significant in men (RR = 1.15; 95% CI 0.83, 1.59).

Conclusions: The meta-analysis suggests that pro-inflammatory diet estimated by a higher DII score is independently associated with an increased risk of depression, particularly in women. However, more well-designed studies are needed to evaluate whether an anti-inflammatory diet can reduce the risk of depression.

Depression is an important public health challenge worldwide. The estimated lifetime prevalence of depression is 3.3–21.4% in the WHO’s World Mental Health Surveys. Depressive disorders not only impose a significant economic burden, but also account for substantial impairments in quality of life and global disability. Therefore, identification of new preventive strategies is crucial.

Low-grade chronic inflammation has been linked to the pathophysiology of depression. Inflammatory cytokines can sometimes trigger depression in human subjects and are often associated with depression. Dietary patterns may have an influence on depression partly through acting on inflammatory pathways. A decline in inflammation was associated with fewer depressive symptoms after a dietary intervention. A well-designed meta-analysis also concluded the antidepressant effects of anti-inflammatory agents. The dietary inflammation index (DII®) is a validated measure of the inflammatory potential of diet partly through acting on inflammatory pathways. This new dietary tool particularly focuses on the inflammatory potential of the overall diet. Lower DII score indicates a more anti-inflammatory diet and higher DII score reflects a more pro-inflammatory diet. There has been an increasing interest in investigating the association of lower DII score with depression. However, results from these available studies are not consistent.

To our knowledge, there is currently no previous meta-analysis to evaluate the association between DII score and depression. Therefore, purpose of the present meta-analysis was to summarize the evidence on the association between the inflammatory potential of diet estimated by the DII score and depression.

*Corresponding author: Email xinhahu@126.com

† Jian Wang, Yao Zhou and Kang Chen contributed equally to this article.
Methods

Data source and searches
The MOOSE (Meta-Analysis of Observational Studies in Epidemiology) guidelines were utilized for the current study. A computerized search strategy was utilized using PubMed, Web of Science and EMBASE databases up to August 2018. Search keywords included (dietary inflammatory index OR anti-inflammatory diet OR pro-inflammatory diet OR inflammatory potential of diet) AND (depression OR depressive symptoms). References of retrieved articles were manually searched to identify any additional study.

Study selection
Included studies had to satisfy the following inclusion criteria: (i) observational study (cohort, case-control or cross-sectional design); (ii) inflammatory potential of the diet estimated by DII score as the exposure; (iii) incident depression/depressive symptoms as the outcome measure; and (iv) provide the multivariable-adjusted hazard ratio or OR and CI of depression/depressive symptoms for the highest DII score (pro-inflammatory diet) v. the lowest DII score (anti-inflammatory diet). Studies were excluded if they: (i) failed to provide multivariable-adjusted risk estimates of depression; and (ii) had recurrence of depressive symptoms as the outcome. For multiple publications from the same participants, we selected the studies with the largest sample size.

Data extraction and quality assessment
Data extraction and quality assessment were conducted from the included studies by two independent authors. Any disagreements were resolved by consensus or consultation with a third author.

The following information was collected from each included study: surname of the first author, year of publication, geographic region, study design, number of participants, proportion of women, mean age or age range of the participants at baseline, diagnosis of depression, DII measure, DII score comparison, most fully multivariable-adjusted risk estimate and length of follow-up for cohort studies. The methodological quality of the included studies was checked using the twenty-two-item STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) score. A study achieving a higher score represented the better methodological quality.

Statistical analyses
Meta-analysis was performed using the statistical software package Stata® version 12.0. To evaluate the relationship between the DII score and depression, the summary risk estimate was pooled for the highest v. the lowest category of DII score. Heterogeneity across studies was examined using the Cochrane Q test and I^2 statistic. Statistical heterogeneity was set at P<0.1 for the Cochrane Q test or I^2 statistic >50%. A random-effects model was applied when pooled analysis resulted in statistical heterogeneity, or a fixed-effects model was used otherwise. Subgroup analyses were performed by study design and gender. Publication bias was examined by Begg’s rank correlation and Egger’s linear regression test. A sensitivity analysis was performed to examine the robustness of the overall risk estimate by removing each single study in each turn.

Results

Search results and study characteristics
Figure 1 shows the flow diagram of the study selection process. Overall, a total of six studies marked the inclusion criteria. Table 1 summarizes the main characteristics of the included studies. Of six studies, four used a prospective cohort design and two were cross-sectional studies. All included studies were published between 2014 and 2017. These studies were conducted in the USA, Spain, France, Ireland and Australia. The sample size ranged from 2047 to 18875, with a total number of 49 584 individuals. The length of follow-up of the prospective cohort studies ranged from 8 to 12.6 years. The DII score was estimated by validated FFQ or dietary records. Depressive symptoms were evaluated by the Center for Epidemiologic Studies Depression Scale (CES-D), the Patient Health Questionnaire (PHQ) or self-reported antidepressant use. The quality assessment based on the STROBE score showed that the prospective cohort studies were grouped...
Table 1  Characteristics of studies included in the current meta-analysis of the association between the inflammatory potential of diet, determined by dietary inflammatory index (DII®) score, and depression

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study design</th>
<th>Sample size (n)</th>
<th>Female (%)</th>
<th>Mean age (years)</th>
<th>Diagnosis of depression</th>
<th>DII® measure</th>
<th>DII® score comparison</th>
<th>Depresion events (n)</th>
<th>HR or OR</th>
<th>95% CI</th>
<th>Adjustment for covariates</th>
<th>Follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sánchez-Villegas et al. (2015)</td>
<td>Spain</td>
<td>Prospective cohort</td>
<td>15 093</td>
<td>58.7 (sd 12.1)</td>
<td>38.3</td>
<td>Self-reported physician-provided diagnosis</td>
<td>Twenty-eight-item FFQ</td>
<td>Quintile 5 v. 1; &gt; 0.66 v. &lt; -3.16 (median)</td>
<td>Cases: 1051</td>
<td>1.37</td>
<td>1.09, 1.73</td>
<td>Age, sex, BMI, smoking, PA, vitamin supplements, TEI, presence of CVD, DM, hypertension or dyslipidaemia</td>
<td>8.5</td>
</tr>
<tr>
<td>Shivappa et al. (2017)</td>
<td>Australia</td>
<td>Prospective cohort</td>
<td>6438</td>
<td>100.0 (sd 1.4)</td>
<td>52</td>
<td>CES-D ≥ 10</td>
<td>101-item FFQ</td>
<td>Quartile 4 v. 1; &gt;2.88 v. ≤-0.88 (median)</td>
<td>Cases: 1156</td>
<td>1.23</td>
<td>1.05, 1.45</td>
<td>TEI, highest qualification completed, marital status, menopause, night sweats, major personal illness or injury, lifestyle factors, smoking, PA, BMI, depression diagnosis or treatment</td>
<td>12</td>
</tr>
<tr>
<td>Adjibade et al. (2017)</td>
<td>France</td>
<td>Prospective cohort</td>
<td>3523</td>
<td>42.3 (sd 6.2)</td>
<td>49.5</td>
<td>CES-D ≥ 23 (W) CES-D ≥ 17 (M)</td>
<td>24 h dietary records</td>
<td>Quartile 4 v. 1; &gt;1.77 v. &lt; -0.76</td>
<td>Cases: 172</td>
<td>1.07</td>
<td>0.66, 1.72</td>
<td>Age, sex, intervention group during the trial phase, education, energy intake, marital status, socio-professional status, number of 24 h dietary records, interval between two CES-D measures, smoking, PA, BMI</td>
<td>12.6</td>
</tr>
<tr>
<td>Phillips et al. (2017)</td>
<td>Ireland</td>
<td>Cross-sectional</td>
<td>2047</td>
<td>50.8 (sd 5.4)</td>
<td>59.7</td>
<td>CES-D &gt; 16</td>
<td>Forty-five-item FFQ</td>
<td>Tertile 3 v. 1</td>
<td>Cases: NP</td>
<td>1.36</td>
<td>0.83, 2.24</td>
<td>Age, BMI, PA, smoking, alcohol consumption, antidepressant use, history of depression</td>
<td>–</td>
</tr>
<tr>
<td>Wirth et al. (2017)</td>
<td>USA</td>
<td>Cross-sectional</td>
<td>18 875</td>
<td>50.7 (sd 6.9)</td>
<td>46.9</td>
<td>PHQ-9 ≥ 10</td>
<td>Food items in 24 h dietary recalls</td>
<td>Quartile 4 v. 1; &gt;1.99 v. &lt; -0.84</td>
<td>Cases: 1648</td>
<td>1.13</td>
<td>0.92, 1.39</td>
<td>Age, race, education, marital status, perceived health, current infection status, family history of smoking, smoking, past cancer diagnosis, arthritis, mean nightly sleep duration</td>
<td>–</td>
</tr>
<tr>
<td>Shivappa et al. (2018)</td>
<td>USA</td>
<td>Prospective cohort</td>
<td>3608</td>
<td>56.5 (sd 9.2)</td>
<td>61.4</td>
<td>CES-D ≥ 16</td>
<td>Twenty-four single food parameters from the FFQ</td>
<td>Quartile 4 v. 1</td>
<td>Cases: 837</td>
<td>1.24</td>
<td>1.01, 1.53</td>
<td>Age, sex, race, BMI, education, smoking habits, yearly income, PA, Charlson comorbidity index, baseline CES-D, statins use, NSAID or cortisone use</td>
<td>8</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CES-D, Center for Epidemiologic Studies Depression Scale; W, women; M, men; PHQ-9, nine-item Patient Health Questionnaire; NP, not provided; PA, physical activity; TEI, total energy intake; DM, diabetes mellitus; NSAID, non-steroidal anti-inflammatory drug.
among women. Overall, individuals with the highest DII associated with an increased risk of depression, especially when stratified by gender the association was stronger in women than men. Women contribute more strongly to depressive symptoms among those with the highest DII score (representing the greatest pro-inflammatory dietary potential) had a 23% higher risk of depression. This finding reveals that modifications of diet inflammatory potential may offer a feasible strategy for preventing depression.

The included epidemiological studies that investigated the association between DII score and depression applied the cross-sectional and prospective cohort designs. Subgroup analysis by study design showed that a significant association of DII score with depression was noted from the prospective cohort studies but it failed to detect an association among the cross-sectional studies. Nevertheless, in cross-sectional studies it is difficult to differentiate a causal association between diet inflammatory potential and depression. Given that the best evidence on this association came from prospective cohort studies, the positive association of the DII score with depression should be robust.

When stratified by gender the association was stronger in women. While suggestive of a positive association between DII score and depression, results in men were not statistically significant. Similar to the current findings with respect to gender differences, data from the Whitehall II Study (27) also displayed a gender-specific association between DII and recurrence of depressive symptoms. These results suggest that dietary sources of inflammation contribute more strongly to depressive symptoms among women than men. Women’s susceptibility to inflammation and its mood effects may account for gender differences in depressive symptoms. To clarify the gender-specific inflammatory potential of the diet–depression relationship, more prospective longitudinal studies are needed before a definitive conclusion can be drawn.

### Discussion

The current meta-analysis suggests that a pro-inflammatory diet as estimated by a higher DII score is independently associated with an increased risk of depression, especially among women. Overall, individuals with the highest DII score (representing the greatest pro-inflammatory dietary potential) had a 23% higher risk of depression. This finding reveals that modifications of diet inflammatory potential may offer a feasible strategy for preventing depression.

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Our findings generally are in line with previous meta-analyses\(^29,30\) and support that healthy and Mediterranean dietary patterns could reduce depression risk. The healthy dietary pattern is mainly characterized by high intakes of fruits and vegetables, fish, seafood and wholegrain products. The Mediterranean dietary pattern is characterized by high intakes of fruits, vegetables, legumes, wholegrain products and fish, low to moderate intakes of meat, dairy products and alcohol, and consumption of olive oil. Several foods in these two dietary patterns have anti-inflammatory properties. The DII score is a novel dietary quality tool that specifically focuses on the dietary inflammatory potential. The anti-inflammatory effect of the healthy and Mediterranean dietary patterns is at least partly owing to the effect of specific food parameters on influencing inflammatory pathways\(^31\). The pro-inflammatory effect of the diet may increase activation of the inflammatory response system. In addition, mechanisms underlying diet that may influence depression or depressive symptoms include effects on neurotransmitters, oxidative stress and the gut–brain axis\(^32,33\).

In practice, it is important to know whether depression can be prevented by changing dietary patterns. Our meta-analysis holds important implications for clinical practice. With diet as a modifiable factor, limiting pro-inflammatory diets and/or favouring anti-inflammatory diets may be an approach for preventing depression and reducing depressive symptoms. For example, dietary supplementation with PUFA could improve inflammation-associated depressive symptoms\(^34\). In addition, nutritional interventions targeting the gut microbiota also could modulate depression\(^35\). Substantial evidence from animal and human research supports a beneficial effect of anti-inflammatory add-on therapy in depression\(^36\). However, the National Institute for Health and Care Excellence (UK) did not recommend anti-inflammatory diets alone or add-on therapy in depression\(^37\). More well-designed interventional trials are needed to investigate the efficacy of anti-inflammatory diets for the management of depression.

Some potential limitations of the current review should be mentioned. First, the use of various measures of depression is a potential limitation. The included studies applied the CES-D, PHQ-9 or self-reported antidepressant use to determine depression, which may have led to misclassification of participants with depression at enrolment. Second, the DII score was computed by self-report from FFQ or 24 h dietary records, which carries an inherent recall bias. Third, the included studies used different cut-off values of DII score for their comparisons of inflammatory diets, which may lead to overestimate or underestimate the pooled risk summary. Fourth, we did not perform subgroup analyses due to the small number of studies included and the results may be unreliable. Finally, generalizability of our findings to diverse populations should be taken with caution because most of the analysed participants were of European descent.

**Conclusion**

The current meta-analysis suggests that pro-inflammatory diet, as estimated by the DII score, is independently associated with an increased risk of depression, particularly...
in women. This finding highlights the potential of limiting pro-inflammatory diets and/or favouring anti-inflammatory diets in decreasing depression risk. However, more prospective longitudinal studies with improved methodology are warranted confirm the current findings.

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Supplementary material

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