Author's response to reviews

Title: Diet, a new target to prevent depression?

Authors:

A Sanchez-Villegas (asanchez@dcc.ulpgc.es)
MA Martínez González (mamartinez@unav.es)

Version: 3 Date: 9 September 2012

Author's response to reviews: see over
Reviewer's report
Title: Diet, a new target to prevent and treat depression?
Version: 2 Date: 21 August 2012
Reviewer: Ryoichi Nagatomi

Reviewer's report:
The paper by Sanchez-Villegas and Martinez-Gonzalez is a mini-review of current studies regarding diet and depression. They suggest that although epidemiological evidence is not sufficient, diet and its pattern may be considered as a risk factor for major depression from longitudinal observational studies, and that diet involvement in the development of major depression may have common etiology with cardiovascular diseases.

1. Major compulsory Revisions
I agree with the importance of nutrition and dietary pattern on progression or prevention of diseases, but as the authors have mentioned evidence regarding the contribution of dietary pattern to the prevention or progression of depression is still not sufficient. Since the conclusion the authors drew largely depend upon epidemiological studies both cross-sectional and cohort studies, the authors should discuss about the confounding factors that may influence the interpretation of previous epidemiological data. For example, the presence of serious disease is considered to be a major risk factor for depression. So, even though epidemiological data may show similar association of the prevalence of depression and CVD with dietary patterns, it is possible that the presence of CVD may have lead to major depression.

Following your suggestion we have included a new paragraph in the discussion section regarding the possible presence of confounding factors when observational studies are conducted to assess the association between diet and depression.

Regarding the possible contribution of CVD on depression as an alternative causal mechanism that may confound the relationship between diet and depression we admit this possibility, and now have included a sentence about the necessity to adjust for the presence of CVD in the multivariate models. We also have added that an even better procedure (at least as a sensitivity analysis) would be to exclude all cases of prevalent cardiovascular disease (i.e. to apply restriction) from the data base before assessing the role of diet on incident depression. Restriction is an excellent technique in epidemiology to prevent or at least to reduce confounding by known risk factors.
Reviewer's report
Title: Diet, a new target to prevent and treat depression?
Version: 2 Date: 17 August 2012
Reviewer: Miguel Roca

Reviewer's report:
The manuscript is a review of the role of diet and depression. The topic is an important and a promising field of research. The author’s conclusion is that further observational studies as well as randomized studies are needed to confirm preliminary findings.

There are some major and minor questions regarding the publication of the paper in BMC Medicine.

The design of the paper is confuse between “prevention” and “treatment” of depression. The relation with diet as a prevention is clear in cardiovascular disease but not in affective disorders. “Truly causal relationship” in psychiatry is a question without scientific answers. “Risk of developing depression” it’s different than “primary prevention of depression”. At the background section the authors said: “relatively little etiological longitudinal research has been conducted....” The term “etiological” induces here more confusion about the question, as well as the considerations on the metabolic syndrome and cardiovascular disease. Metabolic and inflammatory processes are one of the factors related and studied.

Following your comments we have changed the title of our manuscript. The aim of our manuscript was to assess the role of diet as a component cause in only some of the potential mechanisms that may contribute to cause the onset of depression. We were not meaning at all diet as a means for treatment. We did not consider any factor that may act after the onset of disease. Our conceptual framework was a multicausal model, separating component causes and sufficient causes (please, check Rothman, Greenland and Lash. Modern Epidemiology, 3rd ed. Philadelphia: Lippincott, Williams and Wilkins, 2008; pages 5-18 and 25-30). Our research is relevant only for depression risk/depression prevention from a public health perspective, i.e. what is the diet that can be recommended in anticipation to a general population exempt from depression in order to reduce the future population burden of depression. This is very different from the clinical context of the medical treatment of the depressive patient.

The paper not includes works on the use of toxics, lifestyle, etc of the depressive patients or the psychological symptoms (depressive, anxiety, adjustment symptoms) related to the diagnosis of a medical condition in a non-depressive patient.

Our focus was not on patients who already have experienced a depressive episode. Instead, the specific aim of our manuscript was to assess the role of diet (as an antecedent factor) in the future risk of depression: Therefore, we have not described the role of other variables different than diet. However, we have included a new paragraph in the discussion section regarding the possible role of confounding factors (such as physical activity or the use of illicit drugs) in the association between diet and depression.
At the “Prevention or treatment” section, the manuscript said: “…. Clinical trials have been generally designed to assess the impact of nutritional interventions on the clinical course of depression…… Moreover, none of these trials has analyzed the effect of an overall dietary pattern”. In the paper of Garcia-Toro et al (J Affective Disorders, 2012, 140(2):200-3) eighty non seasonal depressive outpatients on antidepressant treatment were randomly assigned either to the active or control group and four hygienic-dietary recommendations were prescribed together. Outcome measures were assessed before and after the six month intervention period. The results show a better evolution of depressive symptoms in the active group, suggesting lifestyle recommendations as an effective antidepressant complementary strategy in daily practice. Maybe the paper was not published before the redaction of the current manuscript.

Following your suggestion, we have included this new reference in the last version of the manuscript.

At page 4, the sentence “the intake of trans fatty acids or the consumption of food rich in this kind of fats like fast food or commercial bakery have been recently reported as contributors to higher depression risk” is based just in one association study: consumers of fast food and socioeconomic levels need to be considered as a bias in this sample. Although this association needs to be confirmed by other observational studies, a new line of research has been open and we feel that it should be mentioned. We have included a new reference in the last version of the manuscript including another epidemiological study that reported similar findings. Moreover, it is unlikely that socioeconomic level could explain in any way the results obtained in the SUN project as this large cohort study is based only on university graduates with similar educational level. It is exactly the opposite: a variable cannot induce confounding if it is prohibited from varying (please check Rothman et al, page 169).

We understand that it might be thought that a potential weakness of a cohort study fully composed of university graduates is that it is not representative of the general population. We admit that this feature may have affected the generalizability of those findings, but it could also have actually enhanced the validity of the study because the high level of education and homogeneity of the cohort reduced the potential confounding related to socioeconomic status. In addition, the high educational level of professional participants allowed the investigators to collect high-quality information with questionnaires. In fact, several of the most influential cohort studies in public health (British Medical doctors, Nurses’ Health Study I and II, Physicians study, Health Professionals Follow-up study) are only composed of highly-selected health professionals. Also, some other important cohorts (Framingham health study, Adventist cohorts) are also far from being representative in the statistical sense of the term. However, their results have not incurred in any substantial bias, because they have used the classical method known as “restriction” in epidemiology to reduce the potential for confounding. Restriction is acknowledged in epidemiologic literature as an excellent technique to reduce confounding by known factors (as educational level).
Finally, the limitations included in the “strengths and limitations” section regarding to depression assessment (scales, cut-off points, self-reported evaluations, …) are not especially relevant for this topic. The diagnosis and assessment of severity of a mental disorder is a methodological problem for all the studies with psychiatric patients. The definition of the outcome is essential in epidemiology to avoid misclassification biases that could invalidate the reported results in each study. Moreover, the use of different criteria between studies does not permit conducting comparisons between studies carried out in different populations.

Minor questions.

-Abstract. What are the “similar results” of the cardiovascular studies?. We have changed this sentence in the new version of the manuscript. In the new version of the manuscript the following sentence has been included in the summary subheading of the abstract: “Only a few cohort studies have analyzed the relationship between overall dietary patterns such as the Mediterranean diet and primary prevention of depression. They have found similar results to those obtained for the role of this dietary pattern in cardiovascular disease”

-Some of the sentences in different sections are not followed by bibliography. The number of references is limited due to the journal’s specifications.