Reviewer’s report

Title: So depression is an inflammatory disease, but where does the inflammation come from?

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Reviewer: Juan C Leza

Reviewer’s report:

Interesting review about one of the hot topics in translational psychiatry. The senior authors are recognized scientists in the topic.

General: too much information about inflammatory basis of diet, excercise, smoking... and les about the link between these and depression. I would suggest tuning down generalized aspects on these topic (why not age?) and more on relationships between depression in humans with these other pathologies or status os depressive behaviors in animal models.

Similarly, too much is known about cytokines, that is ok, but probably adding more information about other mediators of inflammation (prostaglandins, transcription factors....) will increase impact of the review. Also, commentaries about the breaking in the balance between proinflammatory and antiinflammatory equilibrium are needed

Please, revise the specificity of each reference, i.e, the first one Maes, 1995 is a really important reference, somehow seminal in the topic, but there is no reference in tis work about antiinflamamtory pathways, as stated in the first sentence of the ms.

In general, various of the inflammatory conditions presented in the review have been "related" with depression, but most of these relations are not based in strong statistical analysis taking into account, i.e. possible confounders, so clear statement should be done when strong, sound works are cited. Other cases should be presented as coexisting questions, not totally proved cause-effect connexion.

Of special importance the subheading 7, about gut permeability and the microbiome.

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests