Reviewer's report

Title: Cortisol levels and genetic polymorphisms relationship with antidepressant response to placebo and fluoxetine, in patients with major depressive disorder. A prospective study

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Reviewer: Jon-Kar Zubieta

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This is an interesting manuscript examining measures of HPA function, including relevant genetic polymorphisms, in a 1-week placebo lead in, followed by 2 months of fluoxetine. Associations between HPA axis dysfunction measures, responses to the placebo lead in, early response and later response to fluoxetine were examined. Potential confounding factors and limitations are adequately explained. Minor comments are noted below.

Abstract: “Euthyroid patients with fluoxetine”. All patients were euthyroid that were included in the study, please modify the phrasing to “Euthyroid patients were treated with placebo (one week) and…."

Methods: Please indicate the laboratory cut-offs for diagnosing thyroid dysfunction?

Results:
1. Was there any relationship with chronicity, number of prior episodes of MDD, and/or stressors, early adverse events, and placebo and fluoxetine responses?
2. Was there any relationship between the results obtained and the use of benzodiazepines during the trial?
3. Page 12: “This strongly suggest(s) that previous episodes significantly reduced the possibility of responding to placebo (p=0.019). What is the statistic applied to obtain this p value? Please describe in its entirety.
4. The same comment applies throughout the manuscript. For each p value, please report the test utilized, T, F or Chi values, as well as the p value.

Discussion: Low cortisol levels in the placebo responder group may also indicate a lesser biological disturbance in stress regulatory mechanisms. Please comment on this issue in the Discussion.

Minor editing to conform to English grammar is suggested throughout.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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