Reviewer’s report

Title: Bias in a protocol for a meta-analysis of 5-HTTLPR, stress, and depression

Version: 3  Date: 3 June 2014

Reviewer: Matthew C Keller

Reviewer’s report:

I have read Moffit & Caspi’s revision and their response to my critique. I understand that they are critiquing the validity of lifetime measures of stress/depression. I continue to believe that my original critique remains valid and unanswered. Say that in 50% of cases, the stress came before the depression and in 50% of cases it came after the depression (and hence stress could not have caused the depression). That measure of stress *still has* a statistical relationship with the prospective measure of stress, and the effect of the correlation (stress_retrospective, stress_prospective) being less than 1 on significance of the G-by-Stress term may or may not be countervailed by larger N. And similarly for depression. (Or are the authors arguing that these correlations = 0? Or that the G-by-Stress_after_dep is of opposite sign of the G-by-Stress_before_dep and causes the overall GxE to not be significant? I find both scenarios extremely improbable). This requires modeling in my opinion, not arguments based on intuition. So I do not think that the authors have addressed this issue. That said, I don’t see how my disagreement with them on this should hold up publication of this MS, which I think fully deserves to be published.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests