Reviewer’s report

Title: Telomere shortening in leukocyte subpopulations in depression

Version: 5 Date: 21 April 2014

Reviewer: Owen M Wolkowitz

Reviewer’s report:

Minor essential revisions:

Overall, this is an important study that adds useful and important information to the growing examination of cell aging in depression. The article is well written and the analyses are well done. The figures usefully augment the text and are impressive. There are a number of methodological limitations, but the authors have been careful to acknowledge most of them in the “Limitations” section of their Discussion. There are a few remaining points to consider:

1. Although the authors acknowledge this in the Discussion, I believe they should temper their diagnoses of unipolar major depressive disorder in the Methods section by referring to it as “as determined by standard clinical evaluation.”

2. How were these 44 depressed individuals identified for inclusion? Had they all been inpatients when they received their diagnose?

3. What time of day were the blood samples obtained? Were the subjects fasted? Had any subjects had recent colds or infections or immunizations? Did any have significant elevations in the WBC?

4. How was “age at first depressive episode” and total number of episodes determined? How reliable are those? Do they have any information as to the combined duration of each subject’s episodes?

5. The authors report on antidepressant use. Is this just current use or also lifetime use? Was this quantified over the subjects lifetime? Are there records on other medications that are relevant: lithium, antipsychotics, statins, insulin sensitizers, omega-3 fatty acids, vitamins, etc? Are data available on BMI? I recognize that the authors do comment on several of these limitations.

6. Were all samples run in the same batch?

7. If post hoc comparisons of individual groups were performed after the overall ANOVA significance, this should be presented on p. 7.

8. What metric do they use for calculating an average acceleration of cell aging of 25-28 years?

9. How long were the IR subjects in remission?

10. On p. 8, it is difficult to infer that the IR groups did not recover, since we do not know their pre-depression baseline. Perhaps they started with a lower telomere length. However, another study, which could be cited, also found no difference in telomere length between current and remitted depressives.
(Verhoeven et al., 2013).

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.