Reviewer's report

Title: Transcranial bright light treatment via ear canals in seasonal affective disorder: a randomized, double-blind dose-response study

Version: 3  Date: 3 May 2014

Reviewer: Shadab Rahman

Reviewer's report:

The authors’ clarifications have been very helpful in evaluating the work. Previous work published by the same group (Can transcranial brain-targeted bright light treatment via ear canals be effective in relieving symptoms in seasonal affective disorder? - A pilot study. Med Hypotheses 2012, 78:511-515) suggests that TBL may ameliorate SAD symptoms, but was not placebo controlled. A similar argument as presented in the present manuscript based on response rates was provided in that study as well, negating a placebo effect; however, without a placebo control the argument still remains only a speculation. Without the addition of a placebo control, which would demonstrate that TBL improves SAD symptoms the negative findings of a dose response in the present study are only of marginal significance over the previously published work.

Major:

1. The authors have still not clarified whether the participants and physicians were blinded to receiving active treatment, not just the intensity. If they were, then that may serve to mitigate the concerns of a placebo effect. If this was the case, please clarify and report in the manuscript.

2. While the authors’ argument negating a placebo effect appears reasonable, it is nonetheless very concerning and troubling that the response rates based on SIGH-SAD and HAMA were 35-45% and 47-62%, which fall within the range of placebo response in previous studies, as mentioned by the authors in their response. Please discuss.

3. Please clarify the rationale for using the different doses. Since it appears that the major objective of the current study was to establish a dose response curve, the doses do not appear to be very different. Why did the authors not test a wider range of intensities?

4. The authors should include the following point in their revised manuscript as presented in their response “However, based on the literature on the wavelength-dependent effects of light in humans, we chose to use a blue-enriched light source as this corresponds with the known maximum sensitivity of light-sensitive melanopsin in the retina. Assuming that the potentially light-sensitive opsins found outside of the retina (Blackshaw and Snyder 1999, Kojima et al. 2011, Koyanagi et al. 2013, Tarttelin et al. 2003, Kumbalasiri and Provenzio 2005, Lein et al. 2007) have similar features to the
ones located in the retina, it is not unreasonable to assume that the extra-retinal light opsins may also be maximally sensitive to shorter wavelengths."

5. The authors should elaborate their discussion section on cognitive performance to clarify that the improvement in reaction time is not likely an acute effect, as suggested by the negative findings by Bromundt et al., 2014, but instead likely associated with an improvement in depressive symptomatology.

Minor:


**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I have received research funding from Government of Ontario/ Pharmacia Canada Inc./ Genesis Research Foundation/ OBGYN Graduate Scholarship in Science and Technology at the University of Toronto, Faculty of Medicine and the Frederick Banting and Charles Best Canada Graduate Scholarships Doctoral Award from Canadian Institutes of Health Research. SAR has IP filed for Prevention of Circadian Rhythm Disruption by Using Optical Filters. SAR owns equity in Melcort Inc. and ZircLight Inc. SAR is a co-investigator on studies sponsored by Biological Illuminations LLC.