Reviewer's report

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

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Reviewer: Shadab Rahman

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The manuscript by Jurvelin et al., attempts to provide evidence supporting therapeutic effects of light in SAD patients using a novel non-ocular light delivery method. While the novelty of the approach appears to be the strength of the work, this aspect also demands the highest levels of methodological rigor. Several methodological concerns diminish the enthusiasm for the work.

1. The study is described as a “randomized, controlled double-blind dose-response study” (pg. 5 last paragraph). This statement is very misleading as it is not clear what was controlled in this study. The light treatments occurred at home under unsupervised uncontrolled conditions. It is also not clear what aspect was double-blind as there is no placebo control. It appears that the authors are referring to the patients and physicians being blinded to the intensity condition as the double-blind state of the study. It must be noted that both the evaluating physicians and patients groups were aware of receiving a novel treatment for their SAD condition and therefore were not blinded to the treatment.

2. The lack of placebo control is a major confound in the study. Without a placebo control or even a follow-up measurement when the patients did not receive treatment, it is not possible to delineate whether the reduction in depression scores was a direct effect of treatment or a time-into study effect confounded by a placebo effect.

3. In addition, how was treatment compliance monitored? With a sample size of 89 patients and 4 weeks of at-home treatment one can expect considerable inter- and intra-individual variance in treatment compliance, both in terms of the total number of treatments received over 4 weeks and the timing of treatments relative to their wake times.

4. Although the authors propose a saturation effect for the lack of a dose-response it is quite likely that the response is a placebo effect therefore all doses appear to elicit the same response. Since the patients were blinded to the dose but knew that they are receiving treatment for their SAD symptoms they can be expected to show the same level of placebo effect irrespective of the treatment dose.

5. Do we know anything about the regularity of sleep/wake cycles in these patients before and during treatment? Moreover do we know the ambient light intensity at home during treatment? It is possible that patients maintained more regular sleep/wake cycles and therefore light/dark cycles during the treatment
phase coinciding with the timing of transcranial light therapy that helped to stabilize circadian rhythms and likely counteracted the typical phase delay observed in SAD patients. Is there any assessment of circadian phase before and after treatment and the correlation is change in phase and treatment outcome? It is not necessary that the benefits of transcranial light exposure treatment in SAD is mediated by the circadian system but then it needs to be shown that the improvements in depression ratings in this study population is independent of changes in circadian phase alignment.

6. The authors state that “bright light used in this study was visible to the patients, even though it was administered using extra-visual routes” (pg. 14 first paragraph). Please elaborate on this statement providing details on the light levels that the patients may have received via the eyes and how frequently this may have occurred.

7. What is the justification for using a blue-enriched light source? If the photoreceptors responsible for mediating these effects are the deep brain photoreceptors instead of the ocular photoreceptors then the light reaching those photoreceptors are likely the longer wavelengths due to tissue interference. The long wavelength portion of the visual spectrum appears to be minimal in the spectral composition of the light source used in the study. The authors need to construct action spectra to show the spectral sensitivity of this response to demonstrate that the response is truly short-wavelength sensitive that would warrant using short-wavelength enriched light.

8. The authors need to present and discuss the results of Bromundt et al., 2013 (Chronobiology International 2013 Nov. 13) that show a lack of improvement in alertness or reaction time in response to 12-min transcranial light exposure, which contrast the results presented in this current study.

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

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

Declaration of competing interests:

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