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Comments and objections to:

Jurvelin, Heidi: Transcranial bright light : the effect on human psychophysiology

(Thesis, Oulun yliopisto 2018)

Study 4

Violation of the Declaration of Helsinki

The study was approved by the ethics commission responsible for the university hospital of Oulu, i.e. the ethics commission for the Northern Ostrobothnia hospital district. Professor Räsänen, who was responsible for the study, was vice chair of this commission for many years; before, after and during the handling of the application for this study. Räsänen was even present at the meeting where the study was approved. According to the meeting minutes (attached to this message) she left the room as the other members decided about her study.

This is obviously a serious violation of the Declaration of Helsinki, which mandates in art. 23:

"This committee must be transparent in its functioning, must be **independent of the researcher, the sponsor and any other undue influence** and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must **not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration**."[1]

I am aware of the fact, that finnish legislation (only) requires the researcher not to be involved in the decision, and Räsänen complied with this. However, the Declaration of Helsinki clearly states that national laws shall not reduce its rules.

The ethics commission was not independent from the responsible researcher. One can assume, that also the moment of decision was influenced, as the person who collaborates long-term with the other commission members just leaves the room – to wait how her colleagues decide about her project, and to be directly informed about the decision when she will re-enter the room.

The statement in the published study, that it was approved according to the Declaration of Helsinki, is obviously incorrect. The doctoral candidate cannot be blamed for that, and in my opinion has acted in good faith. However, this is a serious (and hopefully exceptional) issue, which has to be addressed by the faculty.

Removal of the placebo control

The study was registered and conducted as a placebo-controlled trial. This is documented in the clinical trial register, which also shows that the placebo group was declared as an active treatment group after the results came in.[2]

This was also confirmed by the candidate during the thesis defense, and by the custos, who was very well aware of the fact. The change is neither mentioned in the publication nor the synopsis as part of the thesis. The study authors commented off-the-record, that the effect in the placebo group was too impressive to be a placebo effect.

Also in the publication, the Discussion part says:

"Assuming that the placebo response of transcranial bright light is in line with the placebo effect found in earlier antidepressant studies, it is not likely that the alleviation of the symptoms in this study would be entirely explained by means of placebo effect."

This is incorrect. The candidate cites an article by Walsh et al., an important and much-cited review of the placebo response in antidepressant trials. It showed a mean placebo response of ~30%. Response is defined as the percentage of participants which achieve a 50% or more reduction on the Hamilton Depression Rating Scale (HDRS, or equivalents, as the Montgomery-Asberg scale MADRS). In Walsh et al. the reviewed studies had a response rate between 10 and 50%. This finding was confirmed by the recent meta-analysis of Furukawa et al., which included 252 trials and found a mean **placebo response of 35-40%.**[3][4]

The corresponding value in the publication of study 4, measured by the HDRS variant SIGH-SAD, is **39%.** That is exactly the placebo response shown in the earlier articles. The 50% response definition is an international standard and used for inter-trial comparisons, as demonstrated before. It is inconsequential, if there were high effects on the BDI scale (Beck Depression Inventory) in study 4, because it is a self-rating instrument which can easily be influenced by circumstances, as for example the expectations of the participants. The clinician-rated HDRS is the gold standard.

In consequence, there has been no reason and particularly no justification to declare the placebo group as an active treatment. Instead, it changed the message of the study results totally: It would have been a demonstration, that the earlight treatment has only a placebo effect. Now it is claimed, that it possibly has a positive effect, at least that it cannot be ruled out because of the lack of a placebo group.

This particular act of declaring placebo as active treatment, has been discussed extensively in the public. It has been called a "**scientific misconduct**" by professor Timo Partonen of the National Institute for Health and Welfare (the THL).[5]

In my opinion, too, this is not acceptable within good scientific practice.

Study 3

In study 3, the primary outcome analysis was negative for all measures, and only after (post-hoc data dredging?) adjusting for age, one of the several scales had a positive result. That was correctly noted by the opponent.

It also should be clear, that this was not a double-blind study. The participants were ice hockey players of the Oulun Kärpät team, whose primary qualification is not physiology or physics. The only "blinding" was to tell them, that the radiation from their earlight device is not necessarily visible. It can be assumed, that they simply saw whose device was emitting light, and which were "placebo" devices. The players have had many intense contacts during that time and surely spoke about their devices, and the group allocation.

The correct or unbiased conclusion would have been, that even with an open design, the earlight device did not produce meaningful effects on psychomotorics. It is really far-fetched to claim, that it improved reaction time.

The opponent noted correctly, that the publisher does not adhere to standard peer-review. Frontiers is also listed as a potentially predatory publisher according to current guidance by the University of Oulu.[6]

Study 1

Study 1 found that earlight had no effect on melatonin or cortisol excretion in a crossover design. The conclusion in the publication, however, is that earlight exerts its effects through another pathway. That it exerts an effect is a given fact for the authors. They base this on just the trials above, which in fact have not demonstrated more than a placebo response.

Additionally, throughout the study 1 and the rest of the thesis, the authors cite questionable sources and predatory journals as suggesting an effect for the earlight. That is, mostly, the "World Journal of Neuroscience" by SCIRP (Scientific Research Publishing), a classic predatory publisher which is identified as such by all sources.[7][8]

One of the repeatedly cited sources is an article by Michael Persinger, a parascientist from Sudbury, Canada. Persinger's experiment found among other things, "that light penetrates the skull" – but the velocity measured for that light was 0,6 km/h. This is barely a trustable finding and no base for further research or publication. Other articles by Persinger are collected online and give a good picture of that person's scientific work.[9]

Therefore, the conclusion that earlight exerts effects through another pathway, is not credible. The correct conclusion should have been simply, that it does not affect melatonin or cortisol secretion in any way.

Study 2

Study 2 will not be discussed here, as it would be too complex. It is probably of higher quality than the other findings.

Conclusion

The publications used in this thesis showed 1) that earlight has no effect on SAD; 2) earlight has no effect on psychomotoric measures; 3) earlight has no effect on melatonin or cortisol secretion.

That means, earlight lacks most of the effects which are characteristic for real bright light treatment. It did not hint on possible effects on these parametres.

The opponent was correct, when he finally noted during the thesis defense, that "at least it did not rule out that earlight might have an effect". However, with a correct reporting of the placebo results in study 4, it would clearly point at that. This should unequivocally be said in the thesis.

Joensuu, 14.3.2018 Philipp-Robert Schulz

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