Reviewer's report

Title: Homeopathy for mental fatigue: lessons from a randomized, triple blind, placebo-controlled cross-over clinical trial

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Reviewer: Jonathan Davidson

Reviewer's report:

The objectives are fairly well covered but one important issue relates to the authors' conflation of ADHD and the symptom of inattention, which is not in any way specific to ADHD. Depression, schizophrenia, PTSD and a host of other disorders are accompanied by this symptom and it is doubtful if they all can be reduced to a common final pathway - maybe, but the case needs to be made that it is so. Thus the reference to Kaplan (#10) either needs more elaboration or dropping from the text. So a re-focusing away from ADHD towards fatigue and its related symptom of inattention is necessary throughout the paper.

Other comments follow:

Crossover trials in psychiatry have a poor track record and rarely deliver what we hope for - regression to the mean, improvement over time of the disorder under study and subject attrition are all factors - here the retention rate was excellent but the other two factors appear to have been a problem. It is recommended that the main analysis focus on phase 1 only and that subsequent studies not adopt a crossover design. I disagree with the statement on page 3 that a positive outcome from this trial would encourage further work in ADHD - for that, you need to start out with ADHD.

Not sure if you'd expect much effect from one single dose of the remedy. Has this model been used with success in other trials - i.e. Stroop protocols in healthy volunteers with allopathic drugs? Would pre-treatment for a week or longer have been a superior design?

Page 4 - was a minimum cutoff score required on the Chalder scale to qualify for entry? This might have obviated the problem of having some subjects with no fatigue at baseline (page 10).

Besides expressing the dose in traditional homeopathic terms as a dilution, it should also be expressed in mg, ng, picograms, femtograms or whatever amount it was. How much Kali phos was in the mother tincture and in the 6X dilution?

It is disturbing that the amounts of potassium were the same in both drug groups - it means then that the only difference would be the succussion process in the "active" arm. Maybe the comparability of the two substances explained the lack of difference in outcome.
Page 13 para 2. A type II error could have occurred but it equally likely that the outcomes were representative of the real story.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare I have no competing interests.