Author's response to reviews

Title: Mindfulness-based cognitive therapy for multiple chemical sensitivity: a study protocol for a randomized clinical trial

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Author's response to reviews: see over
Dear editor in chief

Thank you for the opportunity to resubmit our manuscript titled: Mindfulness-based cognitive therapy for multiple chemical sensitivity: a study protocol for a randomized clinical trial. Below you will find a point by point response to the reviewer’s comments.

1. Where is the discussion?

Author response: See discussion in the revised manuscript (Please see page 17).

2. Add ‘Illness perceptions’ to the objectives.

Author response: “Illness perceptions” have been added to the objectives.

3. In the hypotheses, the authors state the following: “we expect a treatment effect will be mediated by the level of mindfulness…”. In addition, they are planning to examine several other possible mediating mechanisms. In which outcomes are you going to examine this?

Author response: Possible mediators that we want to analyze include: The Five Facet Mindfulness Questionnaire, Rumination-reflection Questionnaire, and the Self-compassion Scale. The brief illness perception questionnaire and the perceived stress scale are primarily of interest to us as outcome measures but will also be assessed as possible mediators. We have added the headline “Mediating variables” in the effect measures section to clarify which outcomes will be assessed as such (Please see page 14).
4. The authors should add a third aim about the examination of different mediating variables.

Author response: This aim has been added to the “objectives” section (Please see page 6).

5. Concerning the Inclusion criteria section: What age-range do you apply?

Author response: The age range is 18-65 years, which has been added to the “inclusion criteria” section (Please see page 8).

6. Concerning the Exclusion criteria section: What about meditation techniques that are comparable to mindfulness meditation (i.e., zen meditation)? What about experience with Vipassana meditation?

Author response: We believe that this is a relevant point raised by the reviewer; however, this being a pragmatic trial we want to reduce exclusion criteria to a minimum. Furthermore, we assert that being familiar with meditation is different from engaging in an eight week structured MBCT programme, which in addition to mindfulness contains cognitive behavioural elements and psycho-education on coping with stress, and is taught by an experienced instructor. Many of these elements will likely be novel to individuals who have prior meditation experience. Thus, meditation experience in itself, regardless of the type of meditation, will not exclude individuals from participation.

7. Concerning the Randomization section: At what time point will the baseline assessment take place? Is that after or before the randomization?

Author response: Baseline assessment will take place prior to the randomization. This has been added to the study protocol. (Please see page 9).

8. In which order will the randomization take place? e.g., consecutive?

Author response: Randomization will be conducted in a consecutive order. This point has been added to the protocol (Please see page 10).
9. What type of randomisation will be used? Are there any restrictions, i.e., blocking?

**Author response:** Once every 16 – 20 participants have been recruited, the randomization procedure will be carried out. The randomization will be restricted in the sense that the computer generated allocation sequence will secure equal numbers in both groups. This has been added to the protocol (Please see page 10).

10. Who will inform the participants about the allocation?

**Author response:** The first author will inform participants about the allocation. This has been added to the protocol (Please see page 10).

11. Concerning the Intervention section: Can the authors give an example of the adjustments they have made to the original program of Segal et al.?

**Author response:** The most notable adjustment to the original programme is that we have omitted elements that specifically target relapse of depression. Novel elements that we have included concern applying mindfulness to coping with stress. This has been added to the protocol (Please see page 10).

12. Concerning the Measurements section: Which measurement time points do you apply?

**Author response:** All outcomes will be measured at baseline, post treatment, six months follow-up and at one year follow-up. This has been added to the protocol (Please see page 12).

13. I miss a reference after the statement of the authors that the PSS-10 has proven to be a valid en reliable measure of perceived stress.

**Author response:** A reference has been added to the protocol (Please see ref. number 47).

14. Concerning the Statistical analysis section: What will be the method for the analyses of the mediating mechanisms?
Author response: So far, we are not fixed on any specific statistical analyses of the mediation. A statistician with extensive experience in analysing data from RCT’s will be conducting the analyses.

15. In the power calculation, the authors should take into account patient attrition also.

Author response: While we agree with the reviewer’s comment, we also have to be realistic concerning the amount of participants we are likely to be able to recruit. In our experience, certain factors hinder participant recruitment, such as the fact that the MBCT programme is highly time consuming and the fact that most individuals with MCS have difficulties transporting themselves back and forth from the treatment facilities due to their intolerance. For those reasons, we consider our current estimate to be realistic and would deem it unrealistic to aim to recruit more participants.

16. Page 4 (background): the first time you use the word CNS, write it in full.

Author response: “Central nervous system” in has been added to the protocol (Please see page 4).

17. Page 5 (background): a comma instead of a dot after ‘example’ in the sentence “…a high degree of co-morbidity to MCS, for example, …”

Author response: The sentence has been corrected (Please see page 6).

18. Page 6: the aims and hypotheses should be put in a separate section, called ‘Aims’ and not in the methods section.

Author response: The sections “objectives” and “hypotheses” have been moved outside the “methods” section (Please see page 6).

19. Page 9 (intervention): write RCT in full or put the abbreviation in brackets after the full written word the first time you use it.

Author response: The above has been added to the protocol (Please see page 2).

20. Page 11 (measurements): “into Danish” instead of “in to Danish”

Author response: The sentence has been corrected (Please see page 13).
21. Page 15 (ethical considerations): two small mistakes, namely 1) “a” MBCT programme instead of “an”; 2) “Any adverse events reported by the participants will be registered and reported in future publications”.

Author response: Regarding 1) the consonant letter in “an MBCT program” starts with a vowel sound, and therefore we maintain that above is correct. The latter sentence has been corrected in the protocol (Please see page 16).

23. The formulation of the concept “commonly experienced symptoms” in the ‘objectives’ is a bit vague. In addition, “the degree to which chemical tolerance affects participants’ lives” is vague because it is very broad. Perhaps you can state (in brackets) the domains or examples of the domains which the QEESI will assess.

Author response: Some examples of what the QEESI measures have been added in the “objectives” section (Please see page 6).

24. The difference between ‘psychological distress’ and ‘perceived distress’ in the objectives is vague. Perhaps the authors can state the exact concepts they want to measure instead of the general term ‘psychological distress’ (like the authors already did in their hypotheses).

Author response: The exact concepts we are intending to measure have been have been added in brackets to the protocol (Please see page 6).

25. In the section ‘Empirical design’, the authors state that the trial will be undertaken at suitable locations. Can the authors be clearer what they mean with suitable locations?

Author response: To avoid any misunderstandings we have removed the phrase “suitable locations” from the protocol. The term simply referred to facilities fit for group therapy in terms of space etc.

26. The authors state: “…we will use this information to verify whether symptoms reported in the SCAN can be attributed to an illness of known physical cause other than MCS.” Will this be done by a medical doctor? And what will be done with the information?

Author response: We have removed the sentence from the protocol given that a verification of symptoms as part of any diagnosis would require a proper medical examination. The primary
purpose of utilizing the SCAN interview is to obtain an overview of the participants’ symptoms, both psychological and physical, which the protocol also states (Please see page 9).

27. Will the participants in the no treatment group receive the programme at a later moment? If not, how are you going to keep these participants motivated?

Author response: We recently conducted a pilot trial (Skovbjerg et al., 2012) with the same setup as described in the protocol. Participant attrition in the control group did not prove to be a major problem in that trial. We have chosen, however, to rename the control condition to “treatment as usual”, as was the original name given to the control condition in the pilot trial. We have done this given that the label “no-treatment” could give the impression that the controls are prevented from seeking out treatment while enrolled in the study and also due to the fact that, in our experience a significant proportion of the controls do receive treatment for their symptoms in one way or another. Treatment as usual is, thus, in our opinion a more appropriate.

28. The statement “The authors found the scale to have acceptable psychometric properties” is vague.

Author response: This statement has been clarified in the protocol (Please see page 14).

29. The authors want to use the method of multiple imputation to address missing data. In our own trial we eventually decided to do this in a sensitivity analysis only. Because it can be questioned if you can reliable estimate the outcomes when for example only one assessment of a particular patient is available. In most cases you have demographic and clinical information about the patient, but there is still so much information that you miss. To date, there is no consensus about what to do. There are many other trials that use multiple imputations before performing their analyses. Nevertheless, if the authors have not done this already, I advice them to discuss this issue with a statistician.

Author response: We intend to consult a statistician in the analyses of the results.

30. The authors state that they believe that a 25% reduction on the QEESI will represent a clinically meaningful reduction in the impact of MCS. Can you underpin this?

Author response: Given the fact that the QEESI has never been used in an intervention study, identifying what will amount to a clinical meaningful change is a challenge. We have chosen a 25% percent reduction as a clinical meaningful change, which corresponds to a Cohen’s d of 0.61,
regarded as a medium effect size. A reduction of this magnitude will be, in our minds, of clinical importance to our participants.