Author's response to reviews

Title: Comparison of embedded and added motor imagery training in patients after stroke: study protocol of a randomised controlled trial using a mixed methods approach

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Author's response to reviews: see over
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Dear Prof. Sandercock

Thank you for your Email from 23th June this year.

We are very grateful about the comments of both reviewers, David M Kent and Valerie M Pomeroy.

In section A) of the attached document we will respond point-by-point to the 1st reviewer’s concerns, David M Kent. In point five, we will respond to all four sub-questions you asked us to specifically address.

In section B) we will comment on the recently published article by Liu et al.:

The manuscript has been checked to conform to the journal formal style. The permission of the responsible ethics committee is attached. However it is in German. Do you require that it should be translated into English?

We would be more than happy if you could accept our responses and the revised manuscript, which has been checked to conform to the journal style. If you have any further questions please do not hesitate to contact me.

Kindest regards,
Corina Schuster and co-authors
A) Response to the 1st reviewer: David M Kent (DKe)

1. **DKe**: Please clarify the primary outcome. It appears that the primary outcome is the time it takes to perform the task. This is measured at several different time points including immediately after therapy and at follow-up. At which time point is the primary outcome ascertained?
   
   If other time points will be used as outcome measures, or if changes in time to perform the task will be used, these should be specified as secondary outcome measures.
   
   An overall count of the number of different secondary outcome measures would also be helpful, since many different scales and many different time points are measured, and each measurement might be performed in different ways (e.g. simple averages over individual or pre-post differences, etc.).

   **CSch**: Figure 1 and Table 1 provide an overview about the measurement time points and all primary and secondary outcome measures. The table has been refined for simplification. A numbering has been added to the description of outcome measures in section ‘Secondary outcome measures’, page 7 to 9. This corresponds to the numbering in Table 1. Additionally, all used scores (total scores or mean values) have been cited in the outcome measure descriptions (Section ‘Secondary outcome measures’, page 7 to 9).

   The following sentences have been included in Section ‘Primary and secondary outcome measures’, page 6:
   
   “Table 1 provides an overview on all study outcome measures. All outcome measures will be assessed at four times: twice during the baseline phase, after the intervention, and after the two week follow-up phase. Changes over time will be calculated by the differences between BL vs. T0, T0 vs. T1 and T1 vs. FU.”

2. **DKe**: What are the inclusion and exclusion criteria for enrollees, including age, time since stroke, comorbidities, etc.

   **CSch**: Table 2 in the appendix provides an overview about all patient inclusion and exclusion criteria. In summary,
   
   - patients have to be older than 18.
   - patients at least 3 months after a first-ever stroke.
   - patients without joint replacements, limiting body pain, range of motion or compromised mental capacity to give written informed consent.

   Section ‘Recruitment process and patient selection criteria’ on page 11 provides a reference to Table 2.

3. **DKe**: Regarding the power calculation, the trial appears to be underpowered. The effect size chosen was based on the effect size of MI versus control. Presumably the effect size of two different MI interventions will be much smaller. Although not previously compared in the stroke setting, an indirect estimate may be available if both types of MI were compared to a similar control, or if the two interventions were compared in another setting. In addition, the one-tail hypothesis testing does not seem appropriate for this study.

   **CSch**: The following sentences have been included in Section ‘Sample size calculation’ on page 18 of the manuscript:
To our knowledge, two MI interventions have not been compared in one study in a stroke setting until now. We are aware of one sports study from Smith et al. [1]. In this study, Hockey players were divided into 4 groups to compare MI based on the PETTLEP approach with ‘traditional MI’, ‘clothing imagery’ and a control group. The results showed that the PETTLEP MI group gained the most whereas the ‘traditional MI group’ gained the least benefits. These results encourage us in our approach, pragmatic sample size estimation for the stroke setting, and choice of a directed one-tailed hypothesis testing. However, as Smith et al. did not investigate stroke patients, their results cannot be used for sample size estimation in this study.

4. **DKe**: The two interventions (added or embedded MI) seem non-comparable in several respects. In particular, with embedded MI, the physiotherapist spends 45 minutes with the patient, while with added MI the physiotherapist is in direct contact with the patient for only 30 minutes per session. This needs to be better defended or addressed as a limitation of the study.

**CSch**: We are aware of this possible limit of the study. Embedded MI (as in EG1) is the novel MI approach investigated in this study. Added MI (as in EG2) is the current MI therapy standard against EG1 will be benchmarked. To compare all groups in this study a methodology was implemented to minimise the effect of different therapist contact times. Our approach is to embed the tape listening (EG2, CG) into times of patient-therapist contact and cue the patient involvement. In particular, the following measures have been taken:

- The tape used in experimental group 2 (EG2) and the control group (CG) has been recorded with the research therapist guiding the patient. Hence patients hear the same voice from the tape as they are used in physiotherapy training.
- While listening to instructions from the tape, patients in EG2 will be asked to imagine the complete motor task and to report the number of motor task imaginations to the research therapist afterwards. That request has been included to remain concentrated and attentive during the added MI session.
- Before and after listening to the tape (EG2, CG), the research therapist will be present in the room, to help patients in sitting up and put on/off cloths. The therapist will ask patients how they liked the tape content.

This paragraph has been added to Section ‘Study intervention’ on page 17.

5. **DKe**: Please describe the process of randomization/concealment.

**Editor**: Please describe the process of randomization/concealment?, please make sure to specify:

a) how the random sequence is generated  
b) whether any stratification or minimisation will be used  
c) how the treatment allocations will be assigned to each participant (e.g. opening envelopes or via some central computer randomisation service)  
d) how the process achieves allocation concealment

**CSch**: The process of randomisation and concealment is described in Section ‘Randomisation and allocation concealment’, page 12, as follows:

a) A randomisation list has been generated with MATLAB 2007b (Mathworks Inc., USA) by a researcher not involved in the study. The generated list has been sent to the
clinic’s pharmacist, who is not involved in the study and will have no contact with study patients.
b) Neither stratification nor a minimisation method during the randomisation process will be used.
c) After both baseline assessments patients will be given the sealed envelop by the treating therapist. The envelope will be provided by the pharmacist, who prepared the envelope based on the randomisation list. Patients will open the envelop themselves.
d) After opening, envelops will be stored with the patient's personal documents in a locked cabinet. Only the treating therapist and the research assistant will have access to the documents. The independent examiner will not have access to the documents. Patients will be told not to talk to the examiner about the group allocation or therapy content during the post-intervention assessments.

6. **DKe**: Pls. specify whether the primary analysis will be based on completers only, or if outcome measures of non-completers will be obtained and included in the primary analysis.

**CSch**: If outcome measures of non-completers can be obtained, they will be included in the primary analysis. Outcome measures of non-completers will be analysed with an intention-to-treat analysis as stated in Section 'Presentation of results', page 18. The following sentence has been added to the manuscript (Section ‘Group comparison’, page 18): Missing values will be replaced by the average trend of all participants of the respective group.

7. **DKe**: It was unclear what the purpose of the qualitative study was and how it might relate to the results of the randomized trial.

**CSch**: Section 'Background' on page 4, provides background information on quantitative and qualitative parts of the study. Aims and research questions of both parts are stated too. In Section ‘Methodology of the qualitative study part’ on page 20, the following paragraph has been added: “Our exploratory approach used in the qualitative part evaluates patient’s prior experience and usage of MI as well experience they have gained during the study intervention. The semi-structured interviews will add an important insight into patient’s experience and attitudes to MI. Additionally, new hypotheses for further investigations can be derived. Embedding MI into physiotherapy is a new therapy approach. The patient’s awareness and positive or negative experience during the embedded MI intervention could be explored in detail during the semi-structured interviews. After finishing the proposed investigation, it is aimed to implement the more beneficial MI approach (quantitative data analyses) into daily therapy practice. Insight gained from the qualitative patient data during interviews can help to adapt the beneficial MI approach to the patient’s needs.”

8. **DKe**: minor point: on page 11, it states that randomization is used to ensure “external validity”. Randomization (of a sufficiently large sample) ensures internal validity (i.e. non-biased comparison). External validity depends on the target of inference.
CSch: Thank you for spotting this error. It has been corrected in the manuscript accordingly.


Thank you for referring to the recently published article from Liu and colleagues. Liu et al. aimed to investigate the effect of a mental imagery intervention versus a conventional occupational therapy to transfer learned activities of daily living in a hospital environment to a novel environment, e.g. at home. Their mental imagery approach contains four aspects: chunking of the activity, self-reflecting on the patient’s abilities, visual feedback, and internal rehearsal of the task. Hence, the individual benefit of internal rehearsal as it is used in motor imagery has not been investigated.

In contrast, our study aims to compare two different motor imagery techniques that could be integrated into daily physiotherapy practice.

Liu’s results confirmed a beneficial effect of the mental imagery intervention during an early phase of the inpatient rehabilitation.

Patients in the mental imagery group showed a better performance on trained tasks in a novel environment than patients in the control group. With respect to our motor imagery investigation, the results of Liu et al. confirm earlier work of Liu and co-authors, as cited in the manuscript.

Reference: