Author’s response to reviews

Title: Personalized objects can optimize the diagnosis of EMCS in the assessment of functional object use in the CRS-R: a double blind, randomized clinical trial

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Author’s response to reviews:

Dear Editor, Dear reviewers

Thank you for your attention and for the reviewers’ comments concerning our manuscript entitled “Personalized Objects can Optimize the Diagnosis of EMCS in the Assessment of Functional Object Use in the CRS-R: A double blind, randomized clinical trial” (ID: NURL-D-17-00458R1)”. We thank the reviewers for the time and effort that they have put into reviewing the previous version of the manuscript. Their suggestions have enabled us to improve our work. Based on the instructions provided in your letter, we have studied comments carefully and have made correction which we hope meet with approval. We uploaded the file of the revised manuscript. Accordingly, we have uploaded a copy of the original manuscript with all the changes highlighted by using the track changes mode in MS Word.
Appended to this letter is our point-by-point response to the comments raised by the reviewers. The comments are reproduced and our responses are given directly afterward in a different color (red).

We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

We hope that the revised manuscript is accepted for publication in the BMC Neurology.

Thank you and best regards.

Yours Sincerely,

Haibo Di

Responds to the reviewer’s comments:

Reviewer #1:

Peter Charles Watson (Reviewer 1): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

I am happy that my original comments have now been satisfactorily addressed. Basically the McNemar test is saying that of the five changed re-diagnoses involving personal objects all five were from MCS to EMCS.

Reply: We would like to thank the reviewer for his agreement.
Reviewer #2:

Luigi Trojano, M.D. (Reviewer 2): In the revised version of their paper the authors addressed several issues raised after reading the original manuscript. The paper is improved, but I believe that several changes are still necessary to improve it.

1) The authors provided some details about assessment of presence of motor responses in their patients. However, in doing so the authors did not specify whether they selected patients on the basis of this clinical feature. Moreover, it could be useful for the clinicians to have more details about the behaviour with personalized vs. non-personalized objects in the five patients who improved with personalized objects.

Reply: We thank the reviewer for his second careful revision. Yes, we indeed based on some clinical features when we recruited patients from hospital. We have adapted the previous manuscript, with the exclusion criteria of dyskinesia of the upper limbs, and hope this makes the patient selection more clearly (Lines 48 to 52, page 6).

We have adapted the discussion on the specific reactions patients showed to include the patient numbers, and hope this gives a clearer image of which patient showed which behavior (Lines 24 to 35, page 10). But for the non-personalized objects, the behaviors of these patients were inconsistent with the function of objects and were therefore not scored. We added a sentence in the discussion to make this clear (Lines 35 to 37, page 10).

2) The authors specified that order of administration of the two versions of CRS-R was counterbalanced across subjects. However, they did not specify how long time intervened between assessment sessions (they only stated that the delay was 'as short as possible'. Do they mean in the range of hours, days?) Moreover, the authors did not specify whether motor responses were consistent across repeated examinations.

Reply: We are very sorry for our ambiguous expression. Considering the patients’ instability and the risk of fatigue, the interval between the two assessors was as short as possible within 2 hours. The manuscript has been revised accordingly in the text (Lines 31 to 33, page 7).

Motor responses were indeed consistent across the examinations, as can be deduced from the motor scores in the CRS-R. We have made this clearer in the text of the discussion (Lines 23 to 29, page 11).
3) The authors did not specify whether objects were selected among actual patients' personal belongings.

Reply: Yes, the personalized objects were selected among actual patients’ personal belongings. Specifically, they were all chosen from patients’ bedsides in hospital under the help of family member and nurse. The revised has been made accordingly in the text (Lines 15 to 19, page 7 and Lines 33 to 36, page 7).

4) Data about features of the patient sample are presented twice, in the method and in the result section. The authors should emend the text. By the same token, in the discussion the authors reported summary statistics already presented in the result section.

Reply: Thanks for suggestions to the method, result and discussion section. We have amended it in methods section (Lines 25 to 26, page 6) and deleted ” And Table 1 shows the clinical data for each of the 21 patients diagnosed as MCS using CRS-R (15 male, 6 female; 11 MCS+, 10 MCS--; mean age 54.67 ± 13.58 years old; mean time between injury and assessment was 6 ± 3.81 months). Etiology was traumatic in 11 (52%) and non-traumatic in 10 (48%) patients” in the result section. In addition, we have deleted “The incidence of Functional Object Use was significantly higher using personalized objects than non-personalized objects in the CRS-R (χ² = 5, df = 1, p < 0.05)” in the discussion section.

5) The authors stated that a patient diagnosed as MCS- showed 'object use to both the personalized objects and non-personalized objects (the comb and mobile phone)'. This finding might cast doubt on the diagnosis in this patient.

Reply: According to standard CRS-R guidelines: “Movements executed are generally compatible with both object's specific function “, they can get the maximum score of motor sub-scale (i.e., diagnosis of EMCS). This MCS patient, he can only use one object when using the non-personalized object, thus, he cannot be diagnosed as EMCS. This phenomenon indicates the importance of using personalized objects during CRS-R assessment process. We have amended it in the discussion section (Lines 48 to 52, page 10 and Lines 8 to 12, page 11).
6) The discussion section might briefly outline putative mechanisms of the improvement described in this study. The authors might cite further data about improvements in responses with familiar/personal stimuli. Moreover, the authors might comment on the fact that some patients showed a parallel improvement on the motor and on the arousal scale during the 'personalized' examination. This finding could suggest that the improvement on motor scale was related to enhanced arousal.

Reply: We have discussed the different response generated by personal stimuli and non-personal stimuli in present study and cited further research (Lines 45 to 53, page 9 and Lines 7 to 16, page 10).

To ensure the sufficient arousal level and a credible evaluation result, this behavioral scale was accessed while patients were under eye opening state. Besides, during the assessment process, we implement the arousal facilitation protocol according to the guideline of CRS-R. We can conclude that emotional stimuli (such as music, familiar faces, ownname and so on) can evoke the active response. In this study, some patients showed a parallel improvement on the motor and on the arousal scale by using personalized objects, which indicated personalized objects may improve the arousal of patients and promote the use of objects during the CRS-R assessment, possibly related to the mood and arousal hypothesis. We have amended the discussion in the text (Lines 13 to 29, page 11).

7) Data about follow-up should be presented in the result section, and commented upon in the discussion section. Since all patients are reported (by family members) to be still in EMCS at follow-up, this finding could suggest a misdiagnosis at the baseline, or alternatively a change in clinical status intervened during the assessment period. Both alternatives might be problematic for interpretation of findings and should be discussed.

Reply: We thank the reviewer for this interesting reflection. We do not expect any misdiagnoses at baseline, as multiple initial CRS-R exams were performed before start of this study.

We have changed the paragraph in the discussion about the follow-up (Lines 31 to 48, page 11). We now point out that is unlikely that patients improved their state during the short period of this study, and the stability of the diagnosis 6 months after the study.
8) Several typos and English usage mistakes are still present throughout the manuscript. A very very careful editing is mandatory. Below only a few instances.

Abstract, line 13: The rest assessments were performed..

P5, line 11: sound stimuli when patients are scaned with PET [7]

P7, line 8: The order of the two assessor patients was randomized

P9, lines : effective behaviors like smiling, laughing, frowning, crying (affective?)

P10, lines 1-2: All of the 5 EMCS patients are still in EMCS which reported by their family members.

Reply: We are so sorry for our incorrect writing. And we have modified the English usage mistakes and typos throughout text.