Author's response to reviews

Title: Repetitive Transcranial Magnetic Stimulation (rTMS) for Treatment-Resistant Major Depression (TRMD) Veteran Patients: Study Protocol for a Randomized Controlled Trial

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Author’s response to reviews:

July 5, 2017
RE: Manuscript Trials-TRLS-D-17-00251 entitled "Repetitive Transcranial Magnetic Stimulation (rTMS) for Treatment-Resistant Major Depression (TRMD) Veteran Patients: Study Protocol for a Randomized Controlled Trial"

Dear Editor:

Thank you for considering our revised manuscript to be published in Trials. We did respond to the reviewer’s comments on June 27 and uploaded a cover letter (a copy of which is below) and a revised manuscript addressing the comments on that day. The June 27 version of the cover letter and manuscript were subsequently updated on June 29 to reflect additional comments sent to us on June 28.

We have re-highlighted (now in light blue) the changes made to the manuscript on June 27. The changes made to the manuscript on June 29 remain in yellow.

Please let me know if additional information is needed.

Thank you again for your time and consideration.

Sincerely,

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June 27, 2017
Dear Editor:

Thank you for considering our revised manuscript to be published in Trials. We appreciate the comments about the resubmission and address their specific comments below. Changes to the manuscript are in yellow.

Reviewer reports:

This is a well written manuscript reporting a double blind randomized controlled trials.

Response: Thanks for the comment

The randomization that uses an adaptive randomization scheme is well described.

Response: Thanks for the comment

The double blind procedure is well described.

Response: Thanks for the comment

The description of the intervention seems complete.

Response: Thanks for the comment

The sample size calculation: Why choosing a power of 81% and not 80% or 90%. Please clarify.

Response: The designed study power was 80%. To round up a sample size of 360, the actual power became 81%
The outcomes measures should be more completely reported. Particularly the time frame should be reported for each outcome as well as the metric used and when scale are used the rating of the scales should be detailed (eg 0-10).

Response: We created Table 2a to detail outcome measures for treatment efficacy.

The authors report use of a measure batterie. Please clarify if these measures are separate secondary outcomes and report their time points.

Response: As stated on page 12 and Table 2a, a neuropsychological battery is used to measure a participant’s cognitive function, which is measured at baseline, end of the acute treatment, and the end of follow-up. It is considered as part of the secondary measurements of the study.

The outcome assessment is well described with specific methods to ensure quality.

Response: Thanks for the comment

The analysis: how will missing data be handled?

Response: The multiple imputations will be used to handle missing data using Rubin’s method. (now stated on page 15)

The authors report that "The SPIRIT checklist and the flow diagram (Figure 1) provide an overview of the 166 experimental design and procedures": the spirit checklist is a reporting guidelines, it cannot provide an overview of design and procedure.

Response: On page 5, the sentence has been modified to ‘The flow diagram (Figure 1) provides an overview of the study design and procedures': (Note: ‘166’ is a formatting line number)

Please let me know if additional information is needed.

Thank you again for your time and consideration.

Sincerely,

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