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June 29, 2018

**Submission of our revised manuscript:**

**“Vagus nerve stimulation as adjunctive neurostimulation tool in treatment-resistant depression - methodological features and practical advices” (Manuscript ID: JoVE58264R2)**

Dear Alisha DSouza, Ph.D.,

Please find enclosed our revised manuscript, *"* *Vagus nerve stimulation as adjunctive neurostimulation tool in treatment-resistant depression - methodological features and practical advices.”*

The authors are Caroline Lücke, Christian Heinen, Bettina H. Bewernick, Merve Aydin, Alexandra Philomena Lam, Teja W. Grömer, Alexandra Philipsen, Helge H.O. Müller, and Sebastian Moeller.

We appreciate your e-mail from June 15, 2018 and the comments of the editors.

We incorporated the suggestions of the editors in our revised manuscript. All changes were tracked using the Microsoft Word ‘Track Changes’ feature.

The aim of the manuscript is to familiarize the reader of the manuscript or the viewer of the video with the management and adjustment of the vagus nerve stimulator for efficient treatment in patients with therapy-resistant depression. Another important aspect of the manuscript is to present clinical cases and clinical data which show the efficiency of the therapy but also side effects which the treating physician needs to be aware of. We also present parts of the surgery that the viewer or reader can understand what kind of effort has to be made to treat depressive patients with the VNS device. It is beyond the scope of this manuscript to present the details of the surgery to implant the device. Thus, the surgical procedure cannot be part of the video.

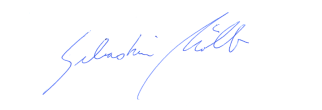
Still, we were able to ask an experienced neurosurgeon (Christian Heinen) to answer the raised questions regarding details of the operation. He is now a co-author of the manuscript.

We believe that the comments significantly improved the manuscript and hope that the article is now acceptable for publication in *JoVE*.

Below, please find our responses to the editors.

Thank you for your consideration.

Sincerely,

  
Dr. Sebastian Moeller (on behalf of the authors)

**Revision of Manuscript JoVE58264R2**

**Editorial comments:**

Please edit the title to focus on the highlight portions of the protocol.

Response:

We edited the title of the manuscript to focus on the highlight portions of the protocol.

We have re-written your steps using imperative voice, and have unhighlighted non-filmable steps. Please verify and approve.

Response:

We verify and approve the changes which were made by the editors.

Please provide anesthetic used, dosage, and also mention any additional drugs. Please add them to the table of materials.

Response:

We now provide the anesthetic including the dosage and also mention additional drugs. The drugs were also added to the table of materials.

Prepare how? Please mention how sterilization is performed.

Response:

In the revised version of the manuscript we describe in detail how the patient has to be prepared for the operation. We now also present how the sterilization is performed.

Mention surgical tools, and depth of the incision.

Response:

We now mention surgical tools and the depth of the incision.

Mention surgical tools used. Please add them to the table of materials.

Response:

We now mention the surgical tools and also added them to the table of materials.

Where are they positioned. Please add them to the table of materials.

Response:

We now describe in detail where the self-retractors are positioned. We also added them to the table of materials.

Of the VNS stimulator?

Response:

We added the former missing information within our revised version of the manuscript.

Where are they placed exactly?

Response:

We now describe in detail where the electrodes are exactly placed.

How is the testing performed? What stimulation frequency, voltage and duration is applied?

Response:

We thank the editor for this important question. We added the missing information within the revised version of our manuscript.

How is the testing performed? Please mention all instruments used and list them in the table of materials.

Response: Testings are performed via a hand-held based digital interface between the implanted VNS and the programming wand. The relevant tuning parameters (mA, Hz, on/off time) for antidepressiive therapy are all metioned within the manuscript and especially in the filmed parts of this manuscript.

We now describe in detail how testing is performed and also mention all instruments.

Mention specifications, also please add it to the table of materials.

Response:

We now mention specifications and added them to the table of materials.

Which loops? Are these provided with the tunnelizer? If not, please mention the suture type used (also add to the materials table).

Response:

We also added information about the loops and the tunnelizer within the revised version of our manuscript.

Needs additional details for clarification. Please add instructions for all actions to be performed.

Response:

We added details to clarify the procedure and also added instructions for all actions to be performed.

Please add additional steps to describe the wound closure.

Response:

In the revised version of our manuscript we added additional steps to describe the wound closure.

Dosage?

Response:

In the revised version of our manuscript we provide the dosage of lithium.

This section overlaps significantly with previous publications, please rewrite using original text.

Response:

We again thank the editor for the constructive criticism. We revised the section. We now use original language throughout the manuscript.

Please report the error bars, and also define them. Please mention the statistical test used, and report the sample sizes.

Response:

We now provide the former missing information.

How many patients?

Response:

We included this information within the revised version of our manuscript.

How many patients?

Response:

We included this information within the revised version of our manuscript.

Define the format of the results. Are these mean (SD)?

Response:

We now define the format of the results.

It seemed like it was implanted in the neck from the protocol. Please check.

Response:

The electrodes are placed in the neck, the pulse generator is placed under the skin of the chest.

Please remove the commercial reference. You can add it to the table of materials.

Response:

We removed the commercial reference.

This section overlaps significantly with previous publications, please rewrite using original text.

Response:

We again thank the editor for the constructive criticism. We revised the section. We now use original language throughout the manuscript.

This section overlaps significantly with previous publications, please rewrite using original text.

Response:

We again thank the editor for the constructive criticism. We revised the section. We now use original language throughout the manuscript.