Author's response to reviews

Title: The effect of Transcranial Direct Current Stimulation in addition to tinnitus Retraining Therapy for treatment of chronic tinnitus patients

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Review: The effect of Transcranial Direct Current Stimulation in addition to tinnitus Retraining Therapy for treatment of chronic tinnitus patients: a study protocol for a double-blind controlled randomised trial

Review 1 Tobias Kleinjung

1. Abstract
The sentence ‘evaluations took place’ is replaced by the sentence ‘evaluations will take place’
Evaluations will take place at baseline before therapy started, at the end of the TRT and finally three months after therapy started.

2. Methods
- The acoustic neuroma and psychiatric disorders are evaluated at the ENT consultation. Only the patients that are suitable for the study will be contacted based on the patient file. Patients treated by a psychiatrist for the treatment of a psychosis or psychiatric disorder are excluded from the study.
  • Patients treated by a psychiatrist for a psychosis or psychiatric disorder

The method of measuring hearing thresholds is explained in the section outcome measurements. All patients with hearing thresholds up to 70 dBHL are included. After the trial, the impact of hearing threshold can be evaluated.
A patient is excluded to the study to the following reasons:
  • Auditory thresholds > 70 dBHL

The interaction between test moment, intervention group and hearing thresholds on the outcome measurements will also be calculated

The tDICS will be performed during the counselling. This decision is based on the literature. Martin stated that a cognitive task simultaneously presented with tDICS leads to better within session skills.
3. Sample size

The minimum sample size of 24 is the overall sample size. The article of Meikle stated that the TFI in a treatment group of improvement has a moderate to high effect size. Therefore the calculations based on the programme Glimmpse are accepted.

A reduction of 13 points is considered the minimum to obtain a meaningful reduction in TFI outcome scores. To measure an improvement, the effect size of the TFI is moderate to high [13]. Based on this information, an overall sample size of 24 was needed to reach a desired power of 0.8 assuming a type-I error rate of 0.05 and a standard deviation of 20.

Review 2 Martin Anders

1. Inclusion and exclusion criteria

• maximum length of tinnitus: We will include chronic tinnitus patient with tinnitus duration between 3 months and 3 years. This decision is based on the article of Schlee et al 2014. The stated that more than 3 years tinnitus resulted in less variability of their auditory alpha activity which can be an indicator for reduced adaptability of the auditory cortex in chronic tinnitus.

The inclusion criteria are as follow:

• Duration of (worsening of) tinnitus between 3 months and 4 years

• medication: If the patients take any medication, the use of the medication has to stay stable during the study. I added this comment to the exclusion criteria.

• Change of medication use

• Psychiatric disorders: Patients treated by a psychiatrist for the treatment of a psychosis or psychiatric disorder are excluded from the study. Patients were evaluated at the ENT-consultation and only the patients that are suitable for the study will be contacted based on the patient file.

• Patients treated by a psychiatrist for a psychosis or psychiatric disorder

• Double-blind controlled study?

The patient and the investigator are both blinded to the intervention type as a result of the third party that randomised the 5-digit codes.

Both the patient and investigator are blinded to the intervention type due to a 5-digit-code that can be entered in the study mode of the tDCS device that will be encoded sham or active tDCS stimulation. The 5-digit-codes were randomised and supervised by a third party.

• FUV after 84 days: We are also interested in the long-term effect of tDCS. Therefore outcome measurements are taken after the last session TRT and tDCS and also 84 days after the start of the therapy (approximately 8 weeks after the last session of TRT).

Review 3 : In Seok Moon
1. Inclusion criteria
Hearing thresholds cannot exceed 70 dBHL. After the trial, the impact of hearing threshold can be evaluated. Our experience learns that persons with a hearing loss also experience benefit from the noise masker.
A patient is excluded to the study to the following reasons:
• Auditory thresholds < 70 dBHL
The interaction between test moment, intervention group and hearing thresholds on the outcome measurements will also be calculated.

2. Method
In tinnitus patients mostly bifrontal tDCS is used, but the risk is that the current just flows from one electrode to the other and not reaches the brain. That’s the reason why the cathode for this trial is placed extracephalic.

The extracephalic placement of the cathode was chosen because of the reduced risk of current flowing from one electrode to the other and as a consequence the actual current could stimulate a deeper and wider brain area.

3. Double-Blind study
The patient and the investigator are both blinded to the intervention type as a result of the third party that randomised the 5-digit codes.

Both the patient and investigator are blinded to the intervention type due to a 5-digit-code that can be entered in the study mode of the tDCS device that will be encoded sham or active tDCS stimulation. The 5-digit-codes were randomised and supervised by a third party.

Review 4: Jay Piccirillo

1. Study design
Outcome measurements were taken after the sessions TRT & tDCS and after 84 days after the start of the therapy. We think that maybe the group who receives the real tDCS shows already improvement after the last session instead at the last follow-up visit. This would capture the faster relief.

2. Statistical analyses:
If the data is not normally distributed, than the data will be logarithmic transformed. Normality will be checked again.

To compare the results of both intervention arms, repeated measures will computed if the data is normally distributed. If not, the data will be logarithmic transformed first.

Sample size: The minimum sample size of 24 is the overall sample size. The article of Meikle stated that the TFI in a treatment group of improvement has a moderate to high effect size. Therefore the calculations based on the programme Glimmpse are accepted.
A reduction of 13 points is considered the minimum to obtain a meaningful reduction in TFI outcome scores. To measure an improvement, the effect size of the TFI is moderate to high [13]. Based on this information, an overall sample size of 24 was needed to reach a desired power of 0.8 assuming a type-I error rate of 0.05 and a standard deviation of 20.

Primary effect:
I added that we will analyse the percentage of responder besides to the amount of change.

The primary outcome measurements will be assessed at every test moment. We are interested in the difference in the amount of change between both groups and the percentage of responders in each group.

Furthermore, the percentage of responders with a minimum reduction of 13 point on the TFI, will be calculated by descriptive analyses and also the confidence interval of the observed difference.

3. A native speaker reviewed the article and changes were made where necessary.