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Is the "end-of-study guess" a valid measure of sham blinding during tDCS?

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1. Rationale

Most tDCS experiments include a *sham* (placebo) protocol, involving a very short period of active stimulation.

Sham tDCS is assumed to be perceptually indistinct on the scalp compared to longer periods of active stimulation. This is important to ensure that behavioural outcome measures are not influenced by placebo effects.

However, we showed in Greinacher et al. (2019) that people *are* able to track the presence and absence of stimulation during active and sham protocols, even at 1mA. This indicates a failure of placebo control.

In this study, we aimed to identify whether the standard method of assessing sham blinding (the "*end of study guess*" questionnaire) corresponded with how well participants could track the presence and absence of stimulation during the course of 1mA and 2mA active and sham tDCS. We hypothesised that the participants who were best at tracking the presence of stimulation should show the highest levels of end-of-study guess accuracy.

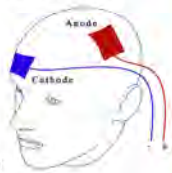
2. Methods

Participants

64 right-handed adults were tested. All were naïve to electrical stimulation. Half received 1mA tDCS and half received 2mA tDCS.

tDCS

Two tDCS protocols were applied in a double-blinded within-subjects design ≥24hrs apart: *Active anodal* (10 min) and *Sham* (20 sec), both with 30s ramp-up/down

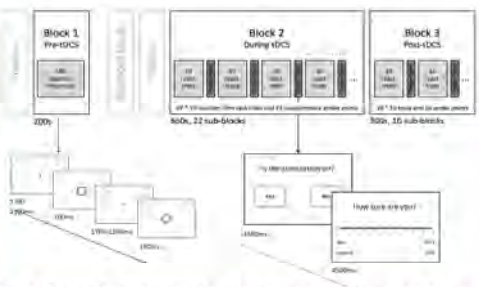


In both protocols, the anode was placed vertically over the left primary motor cortex (C3) to target the right hand, and the cathode horizontally over the right forehead (both 5x7cm in 0.9% saline-soaked sponges).

Reaction time task

Adapted from Minarik et al. (2016) a simple forced-choice RT task was performed with the right hand, before, during and after tDCS. After the initiation of tDCS, 2 probe questions were asked every 30 seconds for the remaining 15 mins (Blocks 2&3) resulting in 32 probe points for each protocol:

1) Is the stimulation on? (yes/no)
2) How sure are you (scale = 0-10)



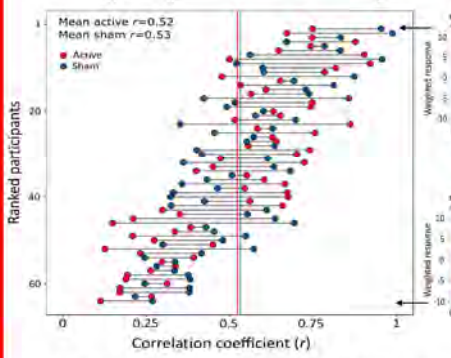
Finally, at the end of the study, participants were asked to guess which of their two sessions had involved sham.

3. Analysis

Weighted response curves were calculated for each of the 32 time points, per participant (and separately for each tDCS protocol) where +10 = *the tDCS is definitely switched on*, and -10 = *the tDCS is definitely switched off*. These weighted response curves were then cross-correlated with the "ideal" response curve for that protocol (i.e. the response that we would expect if the participant was 100% correct at identifying the presence/absence of stimulation at each time point).

4. Results

Q1. Were participants able to track the presence of stimulation?

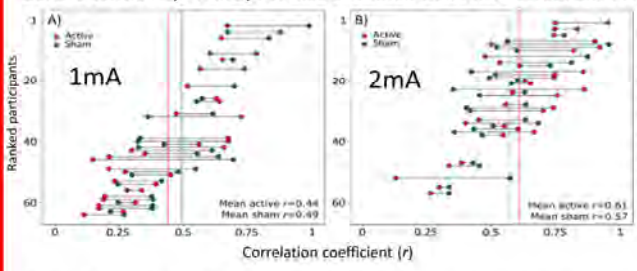


Cross-correlations

Left panel: Cross-correlation coefficients for each participant (active=red, sham=blue). Ranked by mean correlation strength. There was a wide range of sensitivities across participants, with a mean of r=0.52.

Right panels show 2 individual participants' sensitivity curves. Participant 1 was most sensitive in tracking the presence of stimulation overall, and Participant 64 the least sensitive.

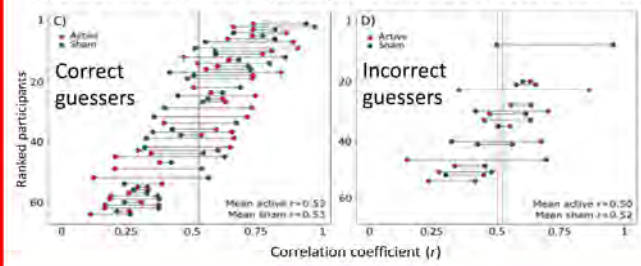
Q2. Did sensitivity to the presence of stimulation differ across 1mA and 2mA?



Current strength

Cross-correlations were generally higher during 2mA relative to 1mA tDCS (i.e. it was easier to track the presence of tDCS during higher intensity stimulation) [F(1,62)=10.62, p=0.002]. Sensitivity was not higher during active stimulation relative to sham [F(1,62)=0.07, p=0.79].

Q3. Did sensitivity differ in participants who were correct vs incorrect in their end of study guess?



End of study guess accuracy

Contrary to our expectations, there was no difference in the sensitivity of participants who guessed correctly compared to those who were incorrect, during either active [t(32.1)=0.47, p=0.64] or during sham stimulation [t(29.9)=0.22, p=0.83].

5. Conclusions

As a group, participants were fairly good at tracking the presence and absence of stimulation during the course of a 10min active and a 20s sham tDCS protocol (mean r=0.52). However there was high variability in sensitivity across participants, with a min r=0.11 and max r=0.95. Sensitivity was generally higher during 2mA than 1mA stimulation. Importantly, sensitivity to the presence of stimulation did not correspond with the accuracy of the end-of-study guess (i.e. the standard post-study questionnaire method of determining whether participants can dissociate the active from the sham session). Our results indicate that the end-of-study guess questionnaire poorly reflects the sensitivity of participants to stimulation during the course of an experiment, and may not be a valid method of assessing sham blinding. Future studies should identify what cues participants use to make their end-of-study-guess decision.

Greinacher, R., Buhôt, L., Möller, L., & Learmonth, G. (2019). The Time Course of Ineffective Sham Blinding During Low-Intensity (1mA) Transcranial Direct Current Stimulation. *European Journal of Neuroscience*.
Minarik, T., Berger, B., Althaus, L., Bader, V., Biebl, B., Brotzeller, F., ... & Sauseng, P. (2016). The importance of sample size for reproducibility of tDCS effects. *Frontiers in human neuroscience*, *10*, 453.