An Update on Blinding Practices in tDCS and tACS Research

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Importance of Blinding in Research

Benjamin Franklin

Blindfolded participants during “mesmerism”/sixth sense experiments

Performance worse when blind(fold)ed

Revealed bias and importance of blinding

Claude Bernard

Wrote first seminal essays about blinding participants in order to promote objectivity

Importance of Blinding in Research

Clever Hans

Smartest horse in the world ?

or

“Reading” the investigator ? (tension, facial expression, other unintentional cues)

Recommendations for Blinding in Research

CONSORT

TRANSPARENT REPORTING of TRIALS

THE COCHRANE COLLABORATION®

STROBE Statement

Strengthening the reporting of observational studies in epidemiology

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

Recommendations for Blinding in Research

International Journal of Methods in Psychiatric Research

International Journal of Neuropsychopharmacology (2011), **14**, 1133–1145. © CINP 2011

Brain Stimulation 6 (2013) 690–695

Contents lists available at SciVerse ScienceDirect

Brain Stimulation

Clinical Neurophysiology 127 (2016) 1031–1048

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Review

A technical guide to tDCS, and related non-invasive brain stimulation tools

A.J. Woods [a,*], A. Antal [b], M. Bikson [c], P.S. Boggio [d], A.R. Brunoni [e], P. Celnik [f], L.G. Cohen [g], F. Fregni [h], C.S. Herrmann [i], E.S. Kappenman [j], H. Knotkova [k], D. Liebetanz [b], C. Miniussi [l], P.C. Miranda [m], W. Paulus [b], A. Priori [n], D. Reato [c], C. Stagg [o,p], N. Wenderoth [q], M.A. Nitsche [b,r,s]

Recommendations for Blinding in Research

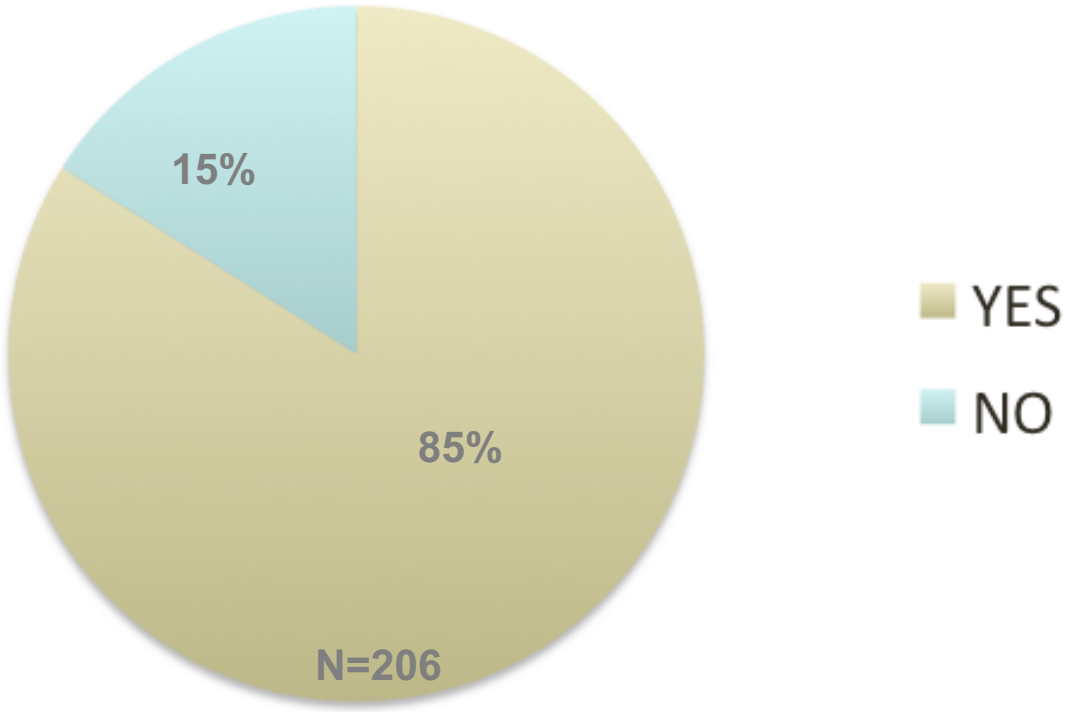
~ **behavioral task** - online, offline, both

~ **voltage** - <1 to 2.5 mA (most common 2, 1, 1.5)

~ **duration** – 1 to 60 min (most common 20, 15, 10)

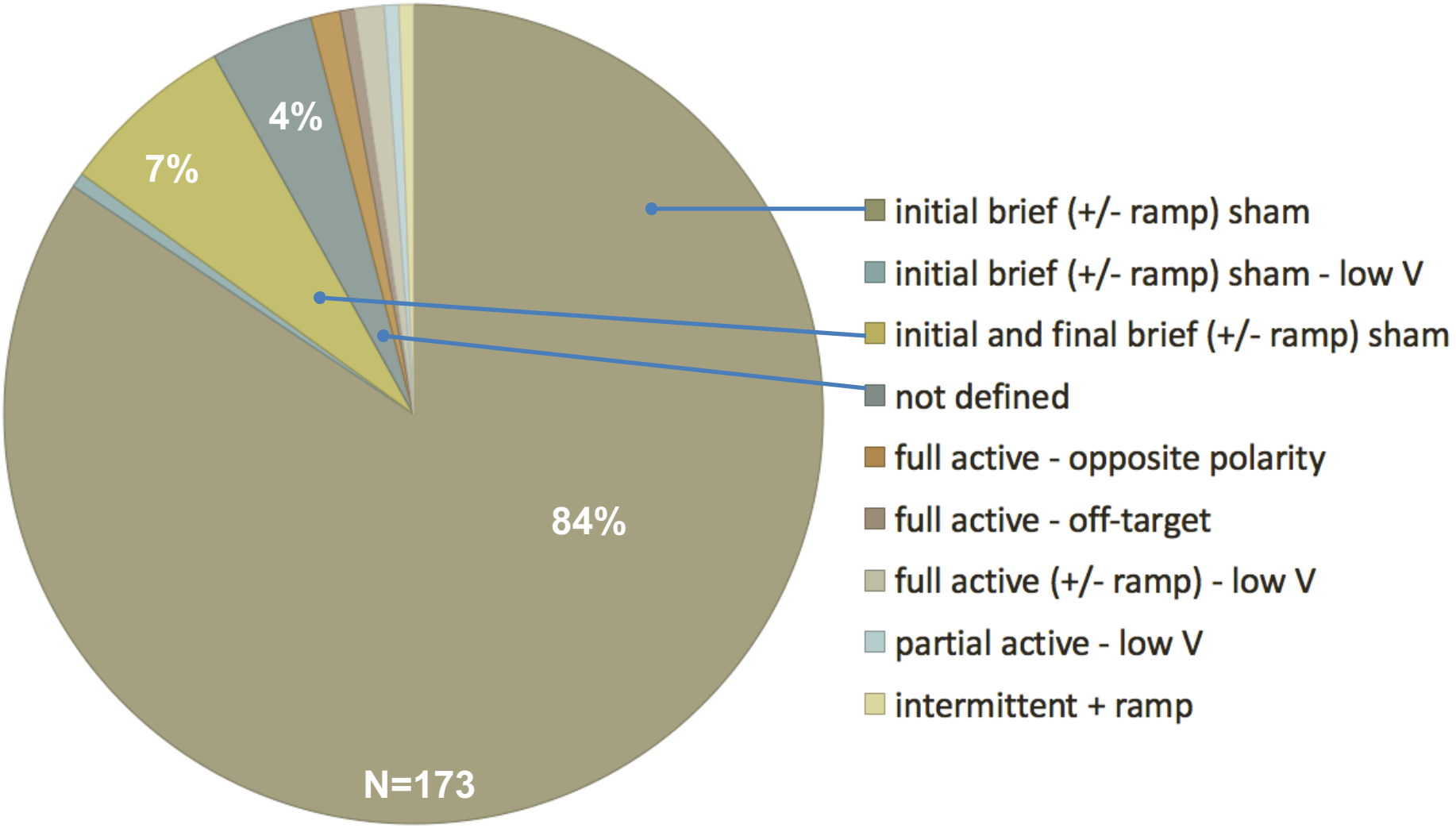
~ **montage** – highly variable, study-specific

Blinding in tDCS Research - 2016

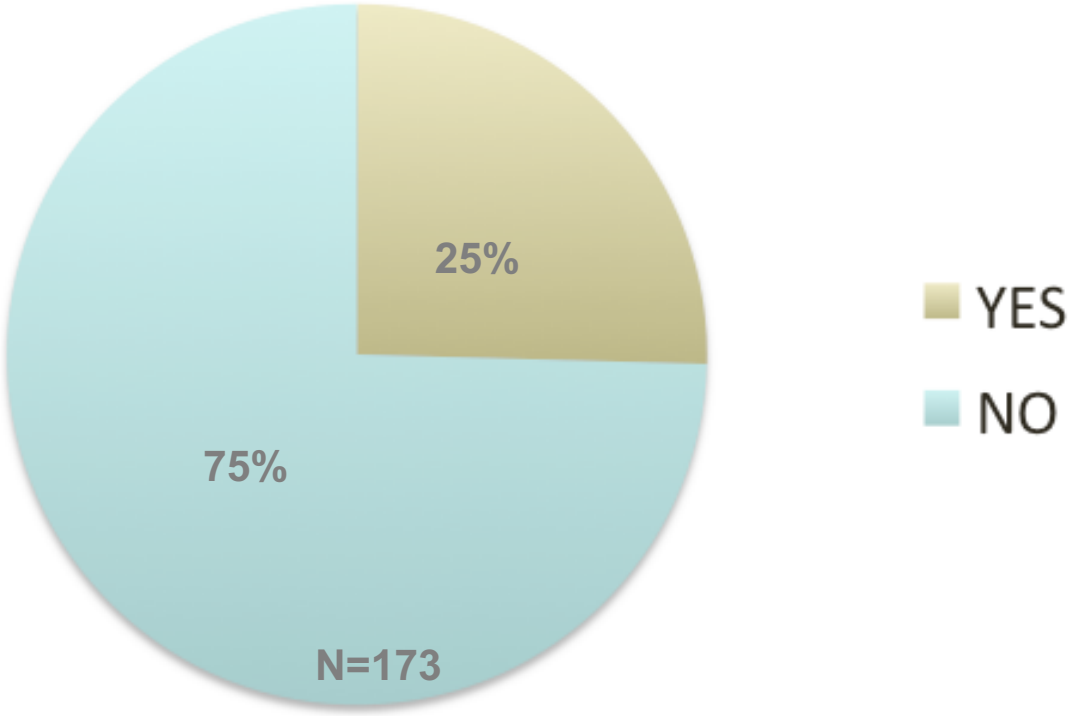


Did the study use a sham/placebo condition?

Blinding in tDCS Research - 2016



Blinding in tDCS Research - 2016



How?

-sensation/AE questionnaire

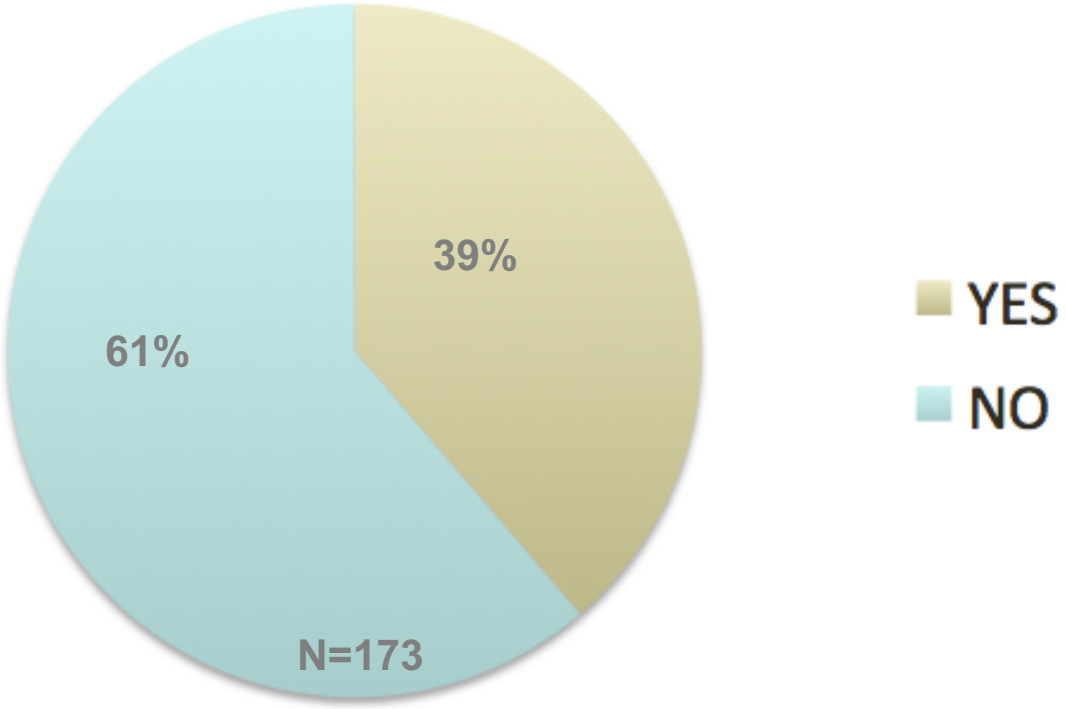
-interview/briefing

-3-choice questionnaire
(+/- confidence rating)

-method not specified

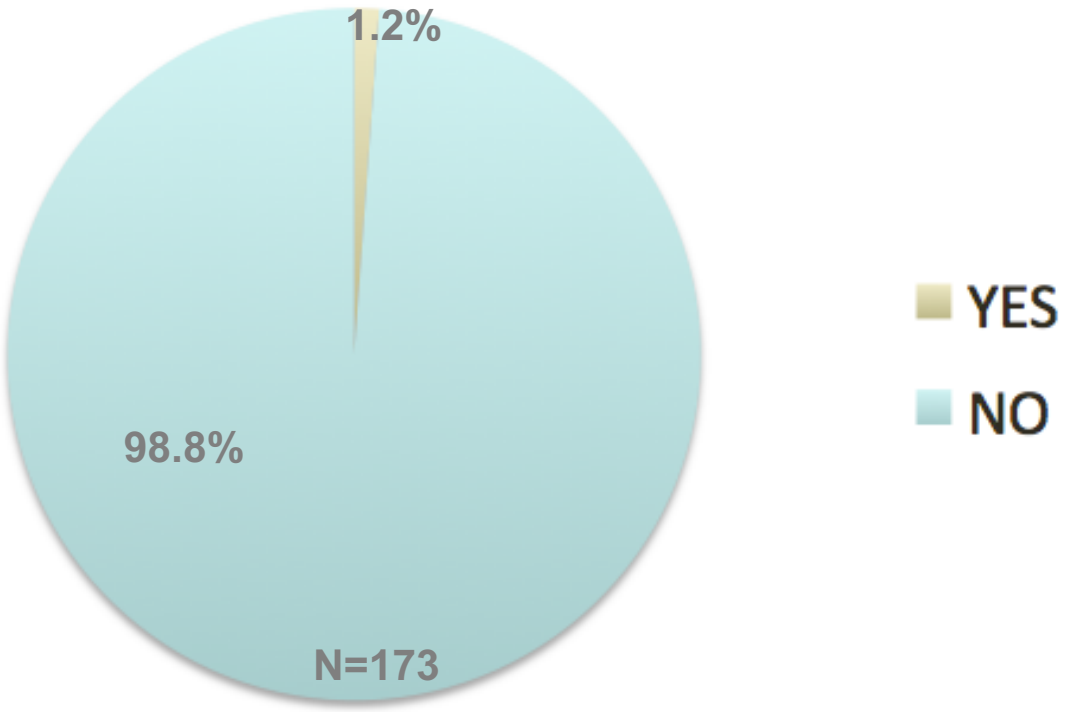
Did the study assess effectiveness of sham condition?

Blinding in tDCS Research - 2016



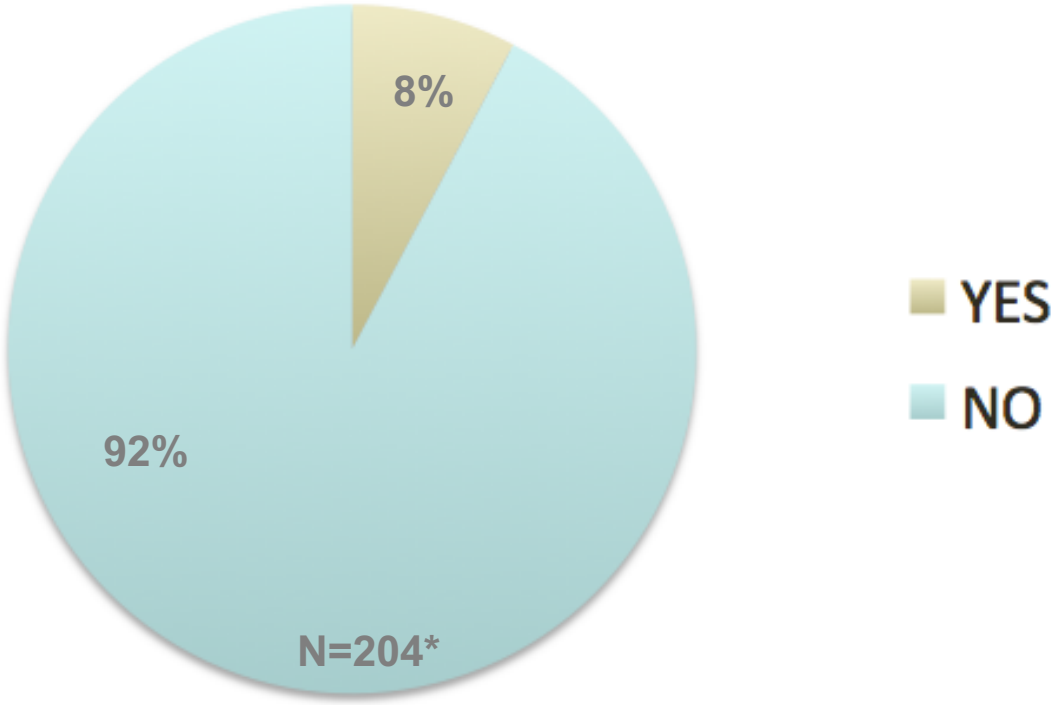
Did the study report administrator blinding?

Blinding in tDCS Research - 2016



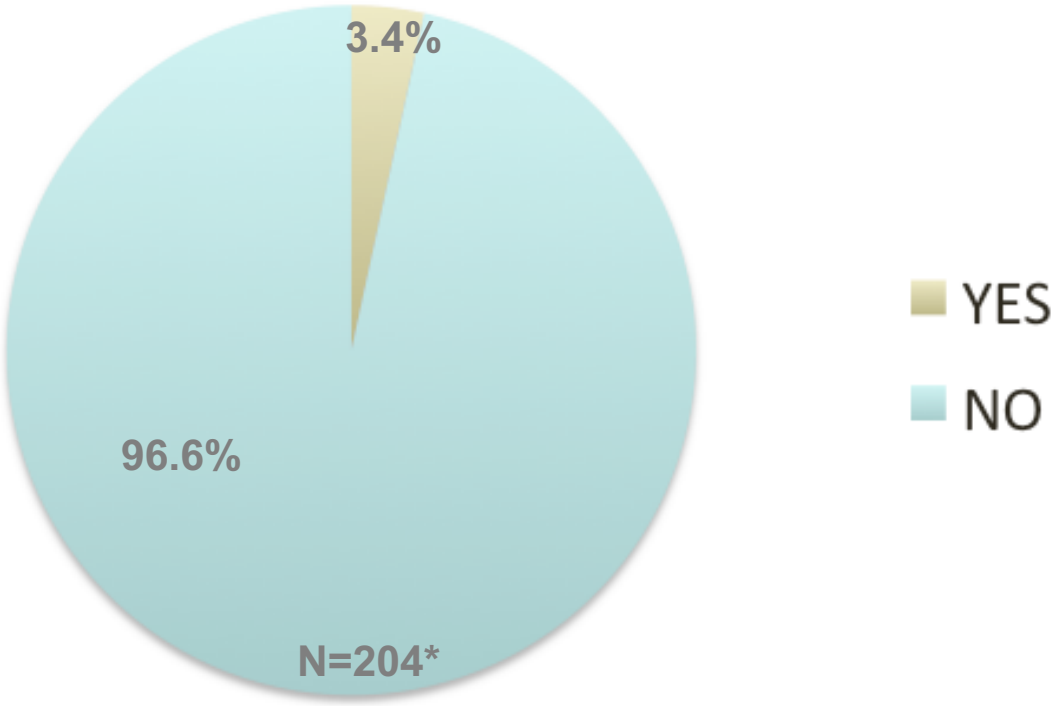
Did the study assess administrator blinding?

Blinding in tDCS Research - 2016



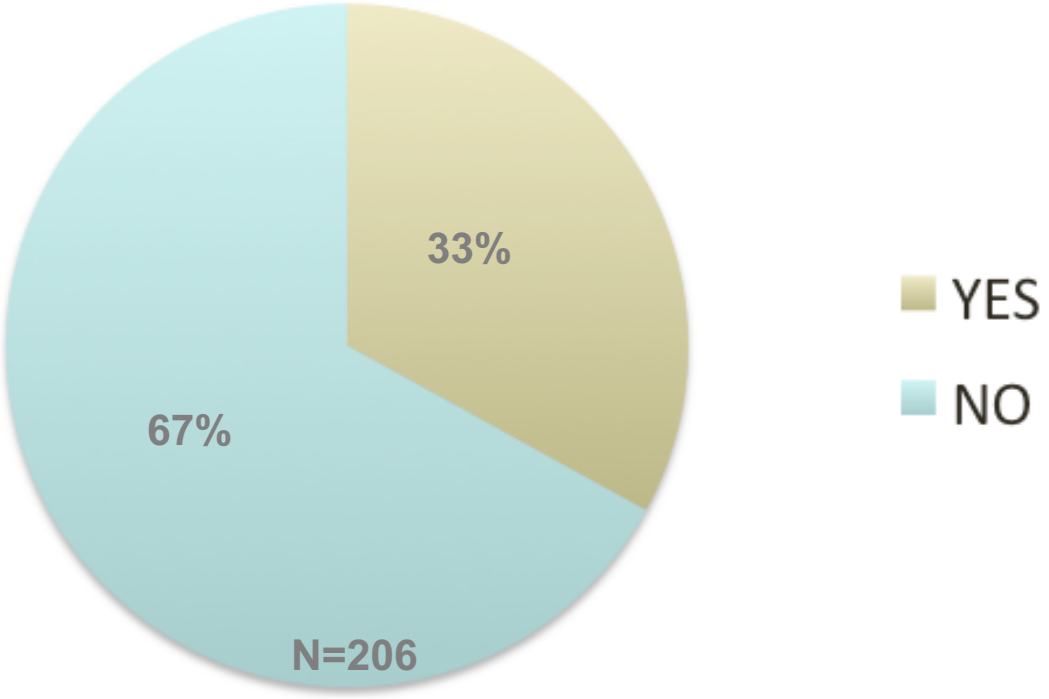
*Did the study report assessor blinding?**

Blinding in tDCS Research - 2016



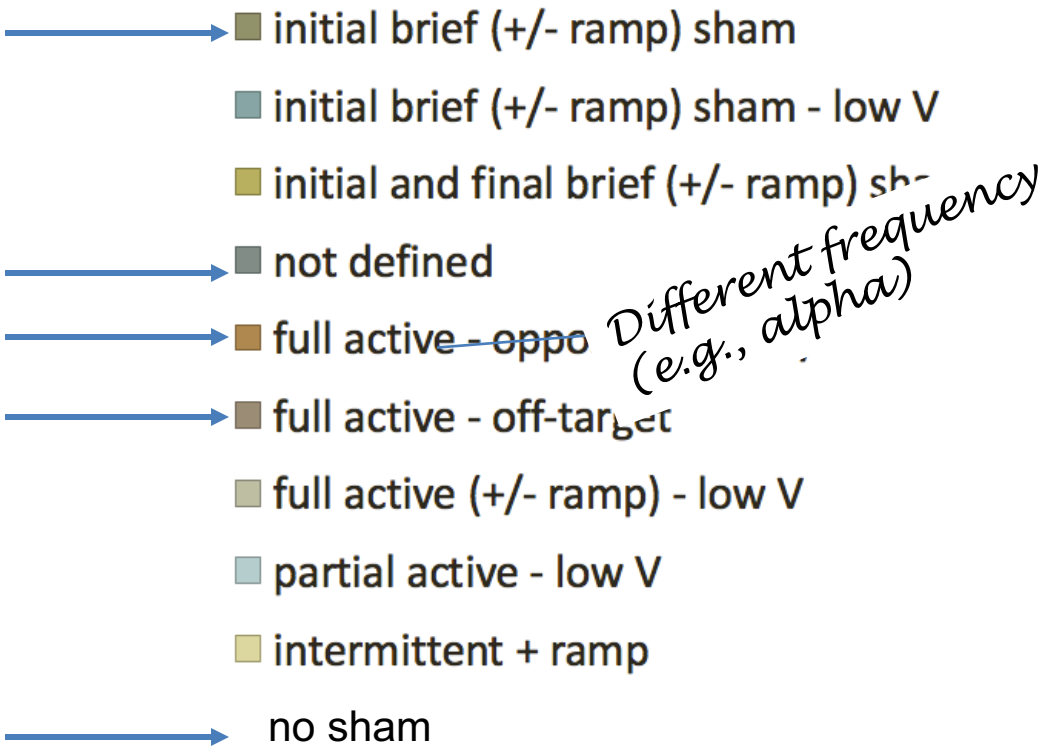
Did the study report rater blinding?

Blinding in tDCS Research - 2016



Did the study collect and report sensation/AE data?

Blinding in tACS



Recommendation – Checklist

	Absent/Minimal Consideration or Reporting	Moderate Consideration or Reporting	Extensive Consideration or Reporting
Blinding			
1. Rationale for sham condition provided.	0	1	2
2. Participant characteristics relevant to sham effectiveness reported (e.g., naïve v. experienced, old v. young, etc.).	0	1	2
3a. Participant blinding described.	0	1	2
3b. Participant blinding/unblinding monitored.	0	1	2
4a. Administrator blinding described.	0	1	2
4b. Administrator blinding/unblinding monitored.	0	1	2
5a. Assessor blinding described.	0	1	2
5b. Assessor blinding/unblinding monitored.	0	1	2
6a. Rater blinding described.	0	1	2
6b. Rater blinding/unblinding monitored.	0	1	2
7. Report when/for whom unblinding occurred, and why.	0	1	2

Adapted from Richardson et al., in press and Gearing et al., 2011

Protocol

Optimizing Rehabilitation for Phantom Limb Pain Using Mirror Therapy and Transcranial Direct Current Stimulation: A Randomized, Double–Blind Clinical Trial Study Protocol

STUDY PROTOCOL Open Access

Stroke Treatment Associated with Rehabilitation Therapy and Transcranial DC Stimulation (START-tDCS): a study protocol for a randomized controlled trial

Suellen M. Andrade[1*], Natanael A. Santos[2], Bernardino Fernández-Calvo[3], Paulo S. Boggio[4], Eliane A. Oliveira[5], José J. Ferreira[6], Amanda Sobreira[5], Felipe Morgan[5], Germana Medeiros[6], Gyovanna S. Cavalcanti[5], Ingrid D. Gadelha[5], Jader Duarte[6], Joercia Marrocos[5], Michele A. Silva[5], Thatiana Rufino[6] and Sanmy R. Nóbrega[7]

Recommendation – Checklist/Questionnaire

Appendix A. (revised questionnaire, English version)

Fertonani et al., 2011

Subject code: _____ **Date:** __/__/_____

Experiment: _____

Did you experience any discomfort or annoyance during the electrical stimulation? Please answer the following questions regarding the different sensations and indicate the degree of intensity of your discomfort according to the following scale:

- ***None*** **= I did not feel the described sensation (0)**
- ***Mild*** **= I mildly felt the described sensation (1)**
- ***Moderate*** **= I felt the described sensation (2)**
- ***Considerable*** **= I felt the described sensation to a considerable degree (3)**
- ***Strong*** **= I strongly felt the described sensation (4)**

In the first stimulation block

Itching:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Pain:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Burning:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Warmth/Heat:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Pinching:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Metallic/Iron taste:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Fatigue:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Other_____:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong

When did the discomfort begin?

☐ At the beginning of the block ☐ At approximately the middle of the block ☐ Towards the end of the block

How long did it last?

☐ It stopped quickly ☐ It stopped in the middle of the block ☐ It stopped at the end of the block

How much did these sensations affect your performance?

☐ Not at all ☐ Slightly ☐ Considerably ☐ Much ☐ Very much

Identify whether these sensations were located over the head or in a different location

☐ On the head _____ ☐ Other _____

In the second stimulation block

. . ..(if there is more than one condition, repeat the list above here based on the block numbers)

If you would like to provide more details, please briefly describe the experimented sensations in relation to the 'Other' or "Fatigue" response:

To be administered at the end of the entire experiment

Do you believe that you received a real or placebo stimulation?

In the first stimulation block/day/week:	☐ real	☐ placebo	☐ I don't know
In the second stimulation block/day/week:	☐ real	☐ placebo	☐ I don't know

. . ..

For the researcher/clinician:

Please report any adverse event/problem (e.g., skin irritation, headache, scalp pain, dizziness, or others, please specify) that occurred and rate the event/problem on a scale from 1 to 4 as previously described.

Additional comments: .....

Appendix *Brunoni et al., 2011*

Proposal of a questionnaire surveying for tDC

tDCS Adverse Effects Questionnaire – Ses

Do you experience any of the following symptoms or side-effects?	Enter a value (1– in the space belo (1, absent; 2, mil 3, moderate; 4, severe)
Headache	
Neck pain	
Scalp pain	
Tingling	
Itching	
Burning sensation	
Skin redness	
Sleepiness	

Recommendation – Checklist/Questionnaire

Fertonani et al., 2011

Appendix A. (revised questionnaire, English version)

Subject code: _____ Date: __/__/_____

Experiment: _____

Did you experience any discomfort or annoyance during the electrical stimulation? Please answer the following questions regarding the different sensations and indicate the degree of intensity of your discomfort according to the following scale:

- *None* = I did not feel the described sensation (0)
- *Mild* = I mildly felt the described sensation (1)
- *Moderate* = I felt the described sensation (2)
- *Considerable* = I felt the described sensation to a considerable degree (3)
- *Strong* = I strongly felt the described sensation (4)

In the first stimulation block

Itching:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Pain:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Burning:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Warmth/Heat:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Pinching:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Metallic/Iron taste:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Fatigue:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong
Other _____:	☐ None	☐ Mild	☐ Moderate	☐ Considerable	☐ Strong

When did the discomfort begin?
☐ At the beginning ☐ At approximately the middle of the block ☐ Towards the end of the block

How long did it last?
☐ It stopped quickly ☐ It stopped in the middle of the block ☐ It stopped at the end of the block

How much did these sensations affect your performance?
☐ Not at all ☐ Slightly ☐ Considerably ☐ Much ☐ Very much

Identify whether these sensations were located over the head or in a different location
☐ On the head ☐ Other _____

In the second stimulation block

….(*if there is more than one condition, repeat the list above here based on the block numbers*)

If you would like to provide more details, please briefly describe the experimented sensations in relation to the 'Other' or "Fatigue" response:

To be administered at the end of the entire experiment

Do you believe that you received a real or placebo stimulation?

In the first stimulation block/day/week:	☐ real	☐ placebo	☐ I don't know
In the second stimulation block/day/week:	☐ real	☐ placebo	☐ I don't know

…..

For the researcher/clinician:

Please report any adverse event/problem (e.g., skin irritation, headache, scalp pain, dizziness, or others, please specify) that occurred and rate the event/problem on a scale from 1 to 4 as previously described.

Additional comments: .....

Appendix

Brunoni et al., 2011

Proposal of a questionnaire surveying for tDCS adverse effects

tDCS Adverse Effects Questionnaire – Session _____

Do you experience any of the following symptoms or side-effects?	Enter a value (1–4) in the space below (1, absent; 2, mild; 3, moderate; 4, severe)
Headache	
Neck pain	
Scalp pain	
Tingling	
Itching	
Burning sensation	
Skin redness	
Sleepiness	

___ Phosphenes

___ Dizziness

___ Pressure

___ Skin sensations (other)

(Raco et al., 2014)

Recommendation – Questionnaire

5.1). Which treatment condition do you believe you received?

a) **New treatment (active/full dose stimulation)**

b) **Placebo (sham stimulation)**

c) **Don't know**

5.2). If you answered 'Don't know' above, can you please provide your best (or random) guess of a treatment you received anyway? *(Please skip this question if you answered 'a' or 'b' above).*

a). New/Active treatment

b). Placebo

5.3). On a scale of **0 to 10**, *how confident are you that you received (your selection)*?

Adapted from Bang et al., 2010, Brinjikji et al., 2010, O'Connell et al., 2012, Zhang et al., 2013

Recommendation – Questionnaire

7.1). Which treatment condition do you believe this participant received?

a) **New treatment (active/full dose stimulation)**

b) **Placebo (sham stimulation)**

c) **Don't know**

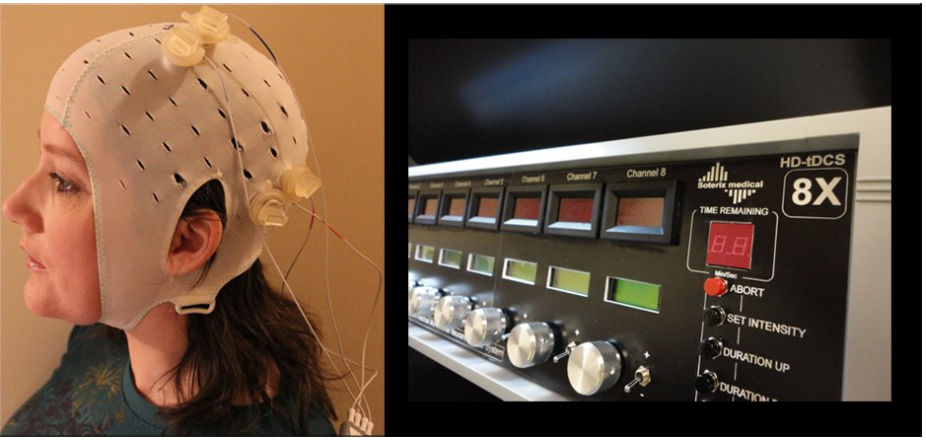
7.2). If you answered 'Don't know' above, can you please provide your best (or random) guess of a treatment the participant received anyway? *(Please skip this question if you answered 'a' or 'b' above).*

a). New/Active treatment

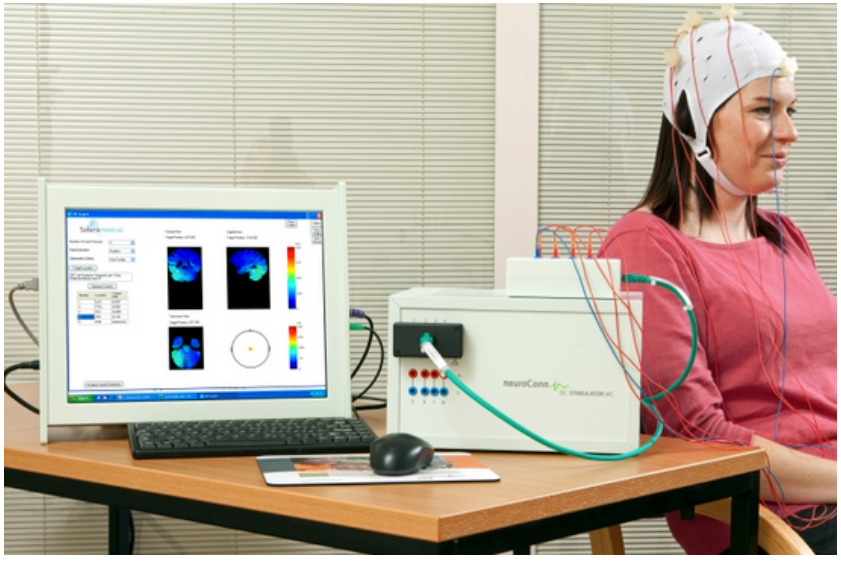
b). Placebo

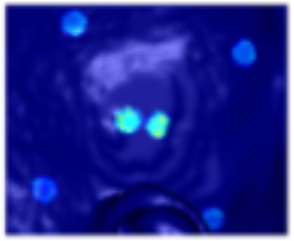
7.3). On a scale of **0 to 10**, *how confident are you that the participant received (your selection)*?

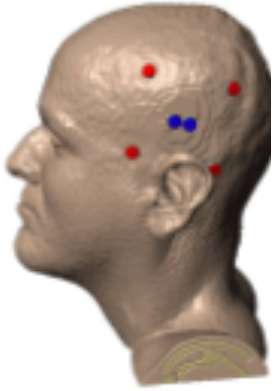
Recommendation – Devices, HD



Dmochowski et al., 2013
Richardson et al., 2015







Garnett & den Ouden, 2015

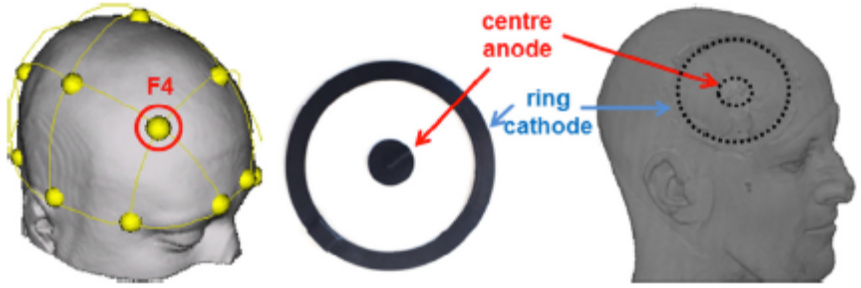


Figure 2. tDCS was administered to the right dorsolateral prefrontal cortex (F4 of the 10–20 EEG system) during both conventional- and HD-tDCS (left panel). The middle and right panels show the electrodes used during HD-tDCS and their location on the head of a healthy volunteer during MRI scanning (dashed line highlights ring and centre electrodes).

Gbadeyan et al., 2016

Recommendation – Design and Analysis

- Recruitment/Participant Characteristics
- Consent
  - De Facto Masking?
    - participants, administrators, assessors
- Between groups instead of crossover
  - (does not free you from sham concerns)
- If crossover, analyze first-period data only
- Complementary active control and sham conditions

Recommendation – Sham Development

- A sham condition should be "indistinguishable"
  - equivalence testing instead of null-hypothesis testing?
- Sham development with investigators
  - If it works for a seasoned investigator, it should work for everyone

Thank You

Lab Members

Sarah Grace Dalton

Holly Stewart

Michaella Maddry

Departmental Collaborators

THE UNIVERSITY of NEW MEXICO
DEPARTMENT OF SPEECH AND HEARING SCIENCES

Rick Arenas

Mentors and Collaborators

UNM CENTER FOR BRAIN RECOVERY AND REPAIR

Center for Brain Recovery and Repair

NIH