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OPTIMIZING TDCS PROTOCOLS BY LOOKING FOR THE MOST EFFECTIVE TIMING OF STIMULATION WITH RESPECT TO TASK EXECUTION

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BACKGROUND

- Neurophysiological effects of tDCS on cortical excitability
 - ➤ at rest:
 - > a-tDCS increased cortical excitability in a widespread network
 - c-tDCS failed to modulate cortical excitability
 - tDCS+task:
 - a-tDCS induced increase in cortical excitability is confined to functionally activated network
 - c-tDCS decreased cortical excitability.

State dependency

- Studies heterogeneity concerning tDCS + task:
 - > priming
 - > synergistic
 - consolidator



Bikson & Rahman, 2013; Siebner, et al., 2009; Tatti et al., 2022; Pisoni et al., 2018; Romero Lauro et al., 2014; 2016; Varoli et al., 2018; Vergallito et al., 2023



AIM

This study aims to investigate how different coupling of the stimulation induced by tDCS with the endogenous stimulation induced by a concurrent task execution might result in stronger behavioral effects for both polarities.







STUDY DESIGN



SHAM

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in one of these configurations, counterbalanced between participants



STUDY 1: ANODAL-tDCS

PARTICIPANTS	28 healthy right-handed (21 F; 7 M)
AGE	22.6 ± 1.9 (range 19 - 27)
EDUCATION	16.5 ± 1.7 (range 13 - 18)

STUDY 2: CATHODAL-tDCS

PARTICIPANTS	14 healthy right-handed (10 F; 4 M)
AGE	27 ± 8.7 (range 19 - 55)
EDUCATION	16.5 ± 2.6 (range 13 - 21)

tDCS PARAMETERS:

Target electrode: rPPC (25 cm²)

Reference electrode: left SO area (35 cm²)

1.5 mA for 20 minutes









TASK 1: PCT POSNER CUEING TASK

3 blocks x 96 trials each CUE: valid vs. invalid

TASK 2: ANT ATTENTION NETWORK TEST

3 blocks x 96 trials each CUE: valid, invalid, null, double TARGET: congruent, incongruent, neutral





Statistical Analysis

- Study 1 and 2 were analyzed separately
- two mixed models (ACC and RTs)
- fixed effects in ANT: stimulation timing (4 levels), target (3 levels), and cue (4 levels)
- random effect: subjects' intercept





ACCURACY \sim (stimulation*cue*target) + trial + (1|ID)

STUDY 1: ANODAL-tDCS

STUDY 2: CATHODAL-tDCS

 \uparrow for congruent target $(\chi^2(2) = 1216.03; p < .001)$

 \uparrow for valid cue ($\chi^2(3)$ = 16.22; p<.01)

 \uparrow with trial ($\chi^2(1)$ = 25.65; p<.001)

No main effect of stimulation timing (p=0.34)

Interaction stimulation timing*cue $(\chi^2(9)=17.36; p<.05)$

 \uparrow for congruent target $(\chi^2(2) = 962.21; p < .001)$

 \uparrow for valid cue ($\chi^2(3)$ = 39.1; p<.01)

No main effect of trial (p=0.68)

No main effect of stimulation timing (p=0.93)





Interaction stimulation*cue ($\chi^2(9)$ = 17.36; p<.05)



ACCURACY

Società Italiana di Psicofisiologia e Neuroscienze Cognitive



RTs ~ (stimulation*cue*target) + trial + (1|ID)

STUDY 1: ANODAL-tDCS

STUDY 2: CATHODAL-tDCS

Interaction target*cue $(\chi^2(6)=5.24; p<.001)$

 \downarrow for congruent target ($\chi^2(2)$ = 6594.56; p<.001)

 \downarrow for valid cue (χ^2 (3)= 933.22; p<.001)

 \uparrow with trial ($\chi^2(1)$ = 11.33; p<.001)

 \uparrow for stimulation timing ($\chi^2(3)$ = 39.18; p<.001)



Interaction target*cue $(\chi^2(6)= 12.8; p<.05)$

 \downarrow for congruent target ($\chi^2(2)$ = 3541.74; p<.001)

 \downarrow for valid cue (χ^2 (3)= 504.56; p<.001)

 \uparrow with trial ($\chi^2(1)$ = 6.92; p<.005)

 \uparrow for stimulation timing ($\chi^2(3)$ = 52.01; p<.001)



RTs ~ (stimulation*cue*target) + trial + (1|ID)





Statistical Analysis

- Study 1 and 2 were analyzed separately
- two mixed models (ACC and RTs)
- fixed effects in PPC: stimulation timing (4 levels) and cue (2 levels)
- random effect: subjects' intercept





ACCURACY ~ (stimulation*cue) + trial + (1|ID)

STUDY 1: ANODAL-tDCS

STUDY 2: CATHODAL-tDCS

 \uparrow for valid cue (χ^2 (1)= 259.85; p<.001).

 \downarrow with trial ($\chi^2(1)$ = 6.32; p<.05).

No main effect of stimulation timing (p=0.30)

 \uparrow for valid cue (χ^2 (1)= 275.59; p<.001)

No main effect of trial (p=0.56)

 \uparrow with stimulation ($\chi^2(3)$ = 11.95; p<.005)





ACCURACY ~ (stimulation*cue) + trial + (1|ID)

STUDY 2: CATHODAL-tDCS





RTs ~ (stimulation*cue) + trial + (1|ID)

STUDY 1: ANODAL-tDCS

STUDY 2: CATHODAL-tDCS

 \downarrow for valid cue (χ^2 (1)= 3652.86; p<.001)

No main effect of trial.

 \downarrow for stimulation timing ($\chi^2(3)$ = 86.14; p<.001)

 \downarrow for valid cue (χ^2 (1)= 3275.09; p<.001)

 \uparrow for trial ($\chi^2(1)$ = 17.81; p<.001)

 \uparrow for stimulation timing ($\chi^2(3)$ = 17.38; p<.001)





RTs ~ (stimulation*cue) + trial + (1|ID)

STUDY 1: ANODAL-tDCS

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STUDY 2: CATHODAL-tDCS





GENERAL CONCLUSION

Behavioral effects depend on the stimulation timing.

Greater modulation in online condition or after preactivating the network. Our results further confirm the **state dependency** of tDCS' behavioral effect.

> Timing matters

The polarity-dependent effect emerges only in online conditions.

Obtaining more evidence could pave the way to optimize tDCS use in clinical protocols.





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ABSTRACT

- Previous studies from our group showed how the neurophysiological effects of tDCS depend on the background activity of the stimulated area: at rest anodal tDCS increased cortical excitability in a widespread network (Romero Lauro et al., 2014; 2016), while participants' involvement in a task during tDCS restricted such increment along the functionally activated network (Pisoni et al., 2018).
- This study aims at investigating how different coupling of the stimulation induced by tDCS with the endogenous stimulation induced by a concurrent task execution might result in stronger behavioral effects.
- We applied anodal tDCS for 20 minutes to the right posterior parietal cortex before, after, or during a visuospatial attention task (Posner task, PT) to find the most effective coupling between stimulation and task execution to induce greater changes in participants' performance on a second visuospatial task (Attention Network Task, ANT).
- This resulted in a within-subject study in which 26 healthy adults participated in four experimental sessions, one sham and three anodal, counterbalanced between participants.
- Statistical analyses were carried out using a mixed-model regression inserting accuracy and reaction times (RTs) as dependent variables and the subjects' intercept as a random factor.
- In line with previous literature, participants were more accurate and faster for congruent targets or valid cues.
- We found an interaction between stimulation and target condition ($\Box 2(6) = 12.31$; p=.055): in particular, stimulation applied after PT improved accuracy when the target is neutral in the ANT, compared to online stimulation (p<.05).
- Stimulation had a main effect on RTs ($\Box 2(3) = 56,48$; p<.001), and, interestingly, the stimulation both during-PT and pre-PT resulted in prolonged RTs in the ANT compared to post-PT and sham conditions (p<.05).
- Our preliminary results further confirm the dependence of anodal tDCS behavioral effect on the background activity of the targeted brain area, showing an advantage of pre-activating the targeted brain area with a similar task before the stimulation compared to not pre-activate.



BACKGROUND

- Several studies converge in suggesting that tDCS effects might depend on the background activity of the stimulated area [1, 2, 3].
- Nevertheless, studies are typically heterogeneous considering the coupling of brain stimulation and cognitive tasks, sometimes delivering tDCS before the task (as priming), sometimes during (as synergistic), and sometimes after (as consolidator) [4].
- Previous studies from our group showed how the neurophysiological effects of tDCS depend on the background activity of the stimulated area: at rest anodal tDCS increased cortical excitability in a widespread network (Romero Lauro et al., 2014; 2016), while participants' involvement in a task during tDCS restricted such increment along the functionally activated network (Pisoni et al., 2018).



[1] Bikson & Rahman, 2013; [2] Pisoni et al., 2018; [3] Siebner, et al., 2009;[4] Tatti et al., 2022.