Examining the Efficacy of Combining Cognitive Training and Non-Invasive Brain Stimulation: A Transdiagnostic Systematic Review and Meta-Analysis

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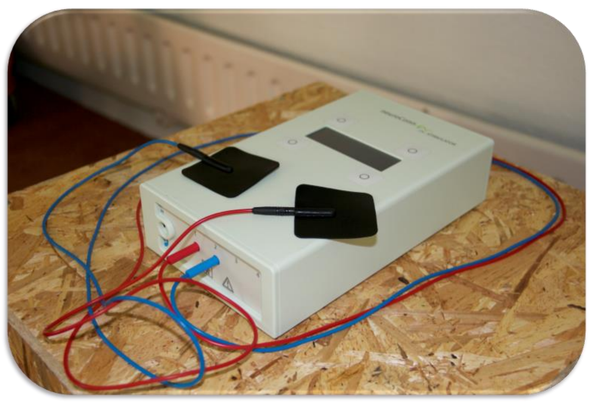
Introduction

Cognitive impairments are related to impaired everyday functioning across disorders. Cognitive training (CT) can help overcome these impairments. Non-invasive brain stimulation (NIBS) may increase the learning potential during CT by facilitating long-term potentiation.

Objective: To investigate whether combining CT with NIBS is more effective in improving cognitive, clinical and functional outcomes compared to CT on its own.



Commonly used NIBS:
Transcranial electrical current stimulation (tES)

tES combined with
computerized cognitive training

Method

Search

- Electronic databases (PubMed, PsycINFO, MEDLINE, Web of Science)
- Grey literature (registries, mails to authors, dissertations)

Inclusion Criteria

- Randomized controlled trial in clinical or healthy populations
- Comparing [CT + NIBS vs. CT only] or [CT + NIBS vs. CT + Sham NIBS]

Statistical Analysis

- Random-effects meta-analysis with robust variance estimation
- Moderator analysis (participant characteristics, characteristics of cognitive training, intervention design)
- Sensitivity analyses (impact of methodological choices, risk of bias, publication bias)

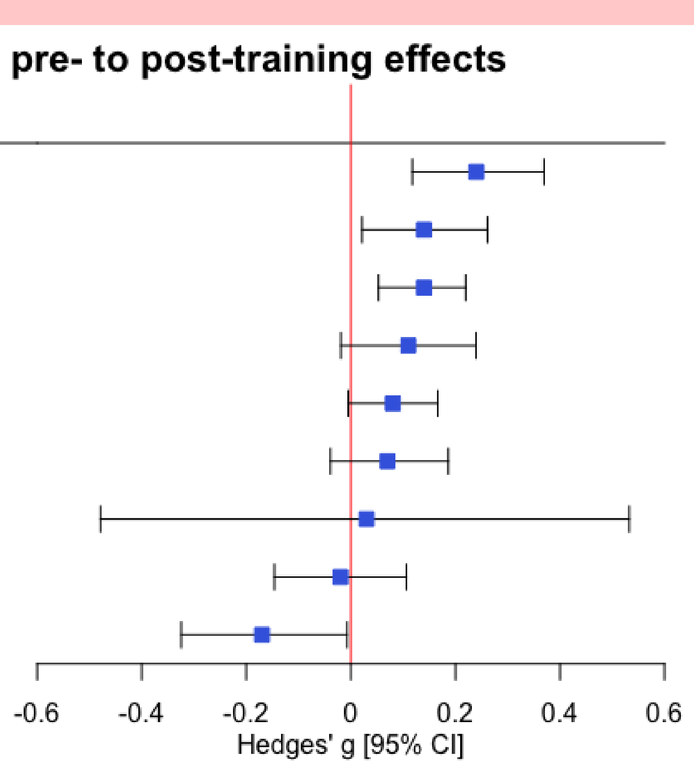
Results

Post-training effects (62 studies, 651 outcome measures)

- **Clinical populations** (27 studies)**:** Schizophrenia, mild cognitive impairment, Alzheimer's disease, HIV+, MS, Parkinson's disease, fibromyalgia, morbid obesity, ADHD, substance-use disorder

Forest plot: Meta-analysis pre- to post-training effects

Outcome domain	k (n)	g
Global Cognition	16 (28)	0.24
Learning/ Memory	29 (121)	0.14
Working Memory	36 (156)	0.14
Language	12 (21)	0.11
Executive Function	40 (182)	0.08
Complex Attention	39 (120)	0.07
Perceptual Motor	12 (23)	0.03
Clinical Outcome	18 (63)	-0.02
Functional Outcome	9 (14)	-0.17



Note. The forest plot shows the standardized mean effect size from pre- to post-training for each domain. A larger effect size is in favor of CT + NIBS over CT + sham NIBS or CT only. (k = number of studies, n = number of outcome measures, g = Hedges' *g)*

Moderator analysis

- No significant moderators

Risk of bias (per study)

Domain	L	UC	H
Sequence generation	21	38	3
Allocation concealment	7	47	8
Baseline differences	57	2	3
Missing data	28	34	0
Selective reporting	56	4	2

Note. L = low, UC = unclear, H = high

- Excluding studies at high risk of bias did not change the results

Follow-up effects

(22 studies, 223 outcome measures)

- Working memory
  (*g* = 0.28, 95% CI 0.14-0.42)
- Other domains not statistically distinct from zero

Conclusion

Combining NIBS and CT can lead to **additional improvements in cognitive functioning** compared to CT only or CT combined with sham NIBS

Additional improvements were **not found for clinical outcomes and everyday functioning.**

Recommendations for Future Research

Assess clinical relevance of the treatment combination by:

1) **designing cognitive training focusing on improving everyday functioning (e.g., add strategies, generalization procedures and a trained therapist)**
2) **adding functional outcome measures**
3) **assessing long-term effects and**
4) **using validated cognitive outcome measures**

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