Effects of Transcranial Electrical Stimulation (tES) in Defence and Security Related Tasks: Meta-Analysis of Findings from Healthy Populations

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ABSTRACT

Introduction: *Transcranial electrical stimulation (tES) techniques have shown promise in both research and applied settings. The diverse applications of tES may prove advantageous to multiple Defence and Security (D&S) related tasks and operational conditions, by enhancing personnel performance beyond baseline abilities. However, a comprehensive review of tES and its applications relevant to D&S is needed to understand its efficacy and safety. In this study we completed a meta-analysis in several domains relevant for D&S (visual search, vigilance, and a sample of studies that covered both working memory and inhibition), in order to evaluate its potential to enhance performance.*

Method: *Applying the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) Statement guidelines, the following databases were searched: PsycINFO (Ovid), Pubmed, Web of Science Core Collection (Web of Knowledge), tDCS Database, CINAHL, and the Defence Science and Technology Lab (DSTL) database, covering the period until October 2020. Inclusion criteria were: healthy adults, and single or multi-session tES protocol (tDCS, tACS, tRNS). Only sham-controlled designs with primary outcome measures of reaction time or accuracy were included. Risk of bias was assessed using the RevMan Cochrane tool.*

Results: *We selected 72 papers with 247 effect sizes. Since there were only few papers that used tACS or tRNS for the chosen domains, we focussed on studies that used tDCS (63 papers with 227 effect sizes) Overall, we report a small effect of tES (Hedges' g=0.112, p=0.002). We split our analysis by domain (Working Memory, Inhibition, Vigilance, and Visual Search) and assessed a range of stimulation parameters to determine which ones yielded a larger Hedges' g, with a focus on Vigilance and Visual Search. We identified six parameters: (i) between participants design, (ii) partly online stimulation where the task is partly completed outside the stimulation period, (iii) stimulation of frontal areas, (iv) stimulation intensity ≥ 2 mA, (v) stimulation duration > 900 s, and (vi) training paradigm. Risk of bias was most prominent in blinding of outcome assessment, blinding of personnel, and selective data reporting.*

Conclusion: *Our quantitative review identified several variables important for the application of tES in D&S settings. This work also highlights the need for replication, more systematicity in outcome reporting, and the necessity for large, well-powered studies prior to application of tES in D&S.*

Keywords: *tES, tDCS, meta-analysis, visual search, working memory, vigilance, inhibition, training*

1.0 PURPOSE AND OBJECTIVES

1.1 Purpose

With a growing body of research suggesting that the application of transcranial Electrical Stimulation (tES) benefits cognitive, perceptual and motor functions [1], it is important to Defence and Security (D&S) to understand and evidence these claims. In line with this, tES has been identified as one method of human augmentation [2] that has potential to change the face of war [3]. Evaluating the effects of tES on performance will contribute to evidence as whether or not there is potential for such techniques to maximise the human component of the military workforce. Doing so will support D&S in maintaining a strategic and tactical advantage during future conflicts.

1.2 Objectives

There is a considerable literature indicating the potential of tES to enhance performance in areas relevant to D&S. However, the case for its use is diminished by the fact that it is unclear how much of the literature can be generalised into D&S situations. This is due to methodological variations and lack of standardised practices. Therefore, we performed a review of tES and its applications relevant to D&S to understand the research, its implications, limitations, and future directions for military forces. Our research aims were to:

- Identify perceptual and cognitive domains, investigated in tES research on healthy participants, that could have implications for D&S applications.
- Select the most promising domains for in-depth meta-analysis.
- Perform a meta-analysis for the selected domains, focusing on parameters that could yield the most successful results in terms of efficacy and effectiveness of tES application in environments relevant to D&S.

2.0 INTRODUCTION

tES is a promising method for modulating brain activity, which can have subsequent effects on cognition and behaviour. tES applies low electrical currents (e.g., 0.5-2.0 mA) via one or more electrodes placed on the head, to target specific brain areas. This technique has the potential to enhance personnel performance beyond baseline abilities. There is evidence to suggest beneficial performance enhancement following tES in cognitive functions that promote decision-making (planning, memory and problem solving), survivability (risk-taking, threat detection, perception and motor performance), and training (accelerated learning, retention and reaction time [4]), all of which are vital for operational success [1]. The very good safety record (non-invasive and limited side effects), low-cost, and relative portability of tES are attractive features for D&S applications [5].

tES also has the potential to be applied at various stages of D&S deployment, depending upon the specific goal and time of administration. For example, tES could be implemented for an assessment to investigate biomarkers and modifications in cortical parameters, such as excitability and brain oscillations, testing personnel before and after missions [6]. Alternatively, tES could be applied to enhance performance in different cognitive and physical domains.

There are a number of significant gaps in the tES literature in areas relevant to military use. Despite the considerable volume of literature indicating the potential of transcranial Direct Current Stimulation (tDCS) to enhance performance in areas relevant to military organisations, it is unclear how much of the existing literature can be generalised to military applications. For tES to be truly beneficial, more research needs to be conducted, investigating the applied aspects of using tES in military environments. Davis and Smith (2019) broke down the main obstacles into five areas: inter-individual differences, generalisability of research involving general populations to military personnel, whether the effects sizes of tES are large enough to make any practical difference to military capability and mission outcomes, the generalisability of laboratory-based research into operational environments, and how tES could fit into established military personnel enhancement programmes.

The effects of tES are subject to a high amount of inter-individual variability, so stimulation of identical brain regions can have different effects for different people and/or in different situations. While some authors have noted the requirement of relatively predictable and repeatable outcomes for the majority of stimulated individuals to justify tES as a treatment device in clinical settings [7], this requirement might be even more important in the military. Given that military situations have potentially lethal consequences, mean group-level improvements are insufficient if the performance of some personnel is reduced. Therefore, the goal of tES should be enhancement of everyone's performance. Consequently, military tES use should be tailored to each individual in order to achieve optimal results.

It is difficult to predict an individual's response to tES because many of the variables interact in complex ways. The majority of relationships between stimulation parameters and enhancement (or diminution) effects are not linear [8]. For example, even the basic notion that activity tends to increase under the anodal electrode and decrease (or remain stable) under the cathodal electrode depends on the targeted brain region [9]. Additionally, the effects of tDCS can sometimes be completely reversed by factors like current strength [10], gender [11], or by complex interactions between variables, including baseline task performance level [12-14] and psychological traits [15].

Therefore, it is paramount to establish the usefulness of tES for domains that are of interest to D&S. The meta-analysis will allow for direct comparison of the effects of various studies with a multitude of different stimulation parameters and outcome measures. This meta-analysis will guide the selection of the most promising parameters and outcome measures for further research and future experimental work.

3.0 APPROACH

We performed a meta-analysis. Given the scale of the work done on the effects of tES in cognition, we focused on specific cognitive areas relevant to military performance. We applied the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.

3.1 Study selection

We searched several databases between 05/10/2020 and 31/10/2020: PSYCInfo, Medline, CINAHL, EBSCO Host, Web of Knowledge, and the tDCS Database. Our search strategy was as follows. First we created the union of the terms [tDCS], [tACS], and [tRNS] to capture all papers that used tES. We then took the intersection with terms that identified our chosen domains: e.g. [Visual search], [Working Memory], [Endurance]. Originally, there were 24 domains in total. However, since this yielded a very large number of papers, it was decided to focus on four domains in particular, because of their high relevance for D&S settings: Visual Search, Working Memory, Vigilance, Inhibition. The domains of Visual Search and Vigilance were covered exhaustively. For Working Memory and Inhibition however, it was necessary to further limit the number of papers by including only those in our meta-analysis that were members of both the Working Memory set and the Inhibition set. Consequently, these two domains were not covered exhaustively, and the results reported here for Working Memory and Inhibition are only preliminary. In the end, we selected a total of 72 studies, which contained 247 effects that met our inclusion criteria: healthy participants aged 18 or over, and sham-controlled assessment of behavioural outcomes of the application of tES as a primary measure. (see Figure 3-1)

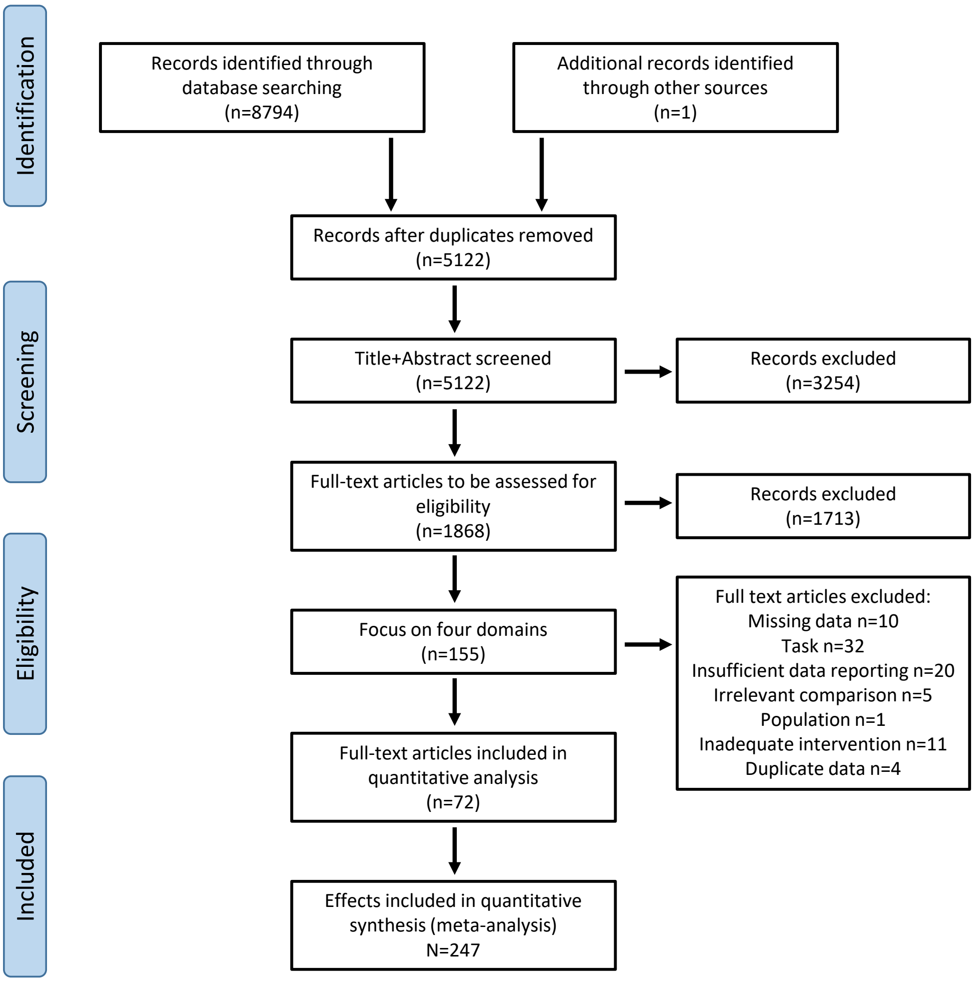

Figure 3-1: Flow chart for selection process of papers

3.2 Study Quality Assessment

The selected studies were rated for their methodological quality [16]. Seven specific areas were considered: random sequence generation, allocation concealment, blinding of participants, blinding of personnel, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. The risk of bias was either rated as low, unclear or high. An ‘unclear’ rating was given when (i) insufficient detail was reported, (ii) sufficient detail was reported, but an assessment of bias was not possible, or (iii) when no measurement was made of the bias that was rated. As can been seen from Figure 3-2, the areas with highest risk of bias are blinding of personnal and blinding of outcome assessment.

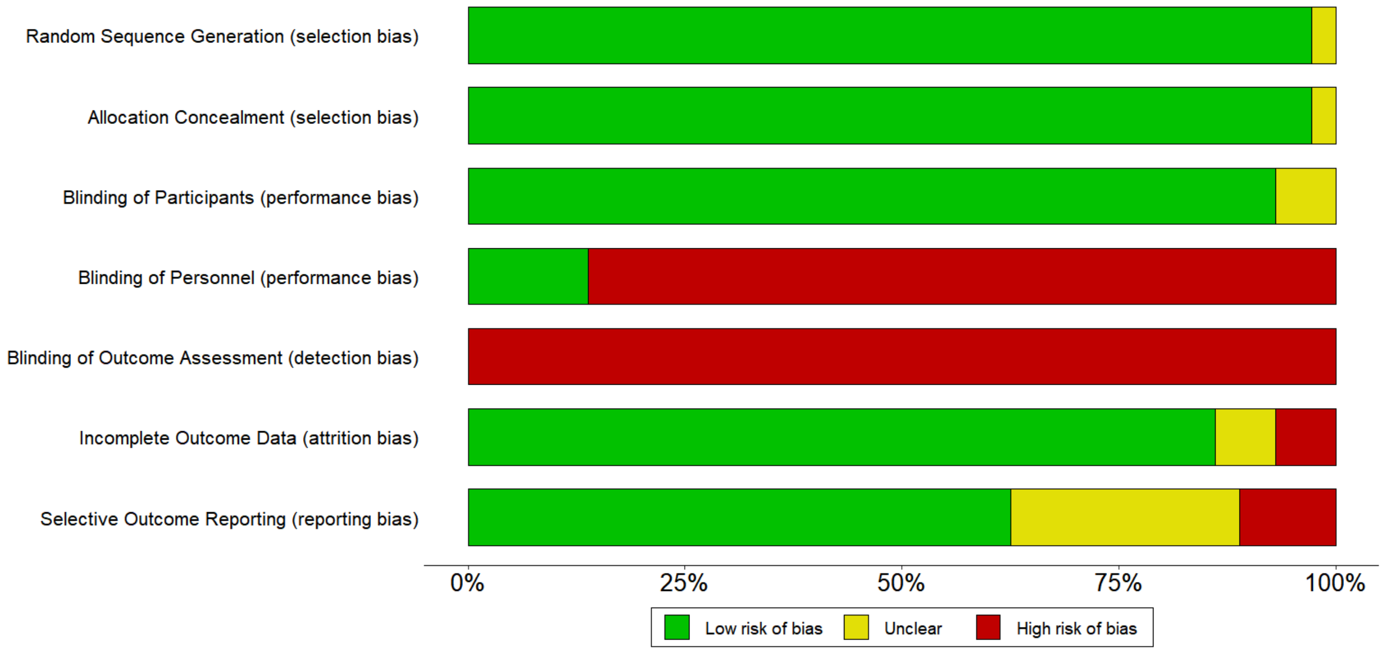

Figure 3-2: Risk of Bias assessments

3.3 Quantitative analyses

Our meta-analysis used the comparison between an active condition and a sham condition as its basic unit. For each of these comparisons the value of Hedges' g was computed, taking into account whether the comparison was within participant or between participants. The sign of Hedges' g values was given based on whether performance improved or deteriorated: faster reaction times for the active condition relative to sham, and higher accuracy rates for the active condition relative to sham, would both yield a positive Hedges' g. Slower reaction times and lower accuracy rates would yield a negative Hedges' g.

To compute Hedges' g, means and standard deviations were acquired from the selected studies. It should be noted that only very few studies presented these values in a table. Most studies only reported their results in graphs. Consequently, the majority of the means and standard deviations were obtained from these graphs with WebPlotDigitizer [17]. Since many of the studies selected used designs with several independent variables, data were pooled across blocks and conditions where necessary.

Most studies in the meta-analysis used complicated designs, rather than a simple two group comparison between active stimulation and sham. Also, around half of the effects were measured within-participant. Consequently, many of the effects violated the assumption of independence underlying fixed-effect meta-analysis. We therefore used three-level meta-analytic approach [18], since it allows the inclusion of various effect sizes derived from the same study. This approach has two random intercepts: one to capture variance at the level of individual effect sizes, and one to capture variance at the level of individual studies.

The analysis was run in R with the package *metafor* [19], in particular the function *rma.rv*. We included two random intercepts to define the three-level structure: one for each indvidual effect size (Level 1) and one for each individual study (Level 2). *Rma.rv* fits the model using numerical methods. Usually, a single solution is reached within a few iterations but occasionally the model fails to converge.

4.0 RESULTS AND DISCUSSION

Figure 4-1 shows the sizes of all 247 effects included in the meta-analysis split by stimulation protocol. The overall effect sizes found were .212, .064, .129, and -.040 for tRNS, tACS, anodal tDCS and cathodal tDCS, respectively. It is clear that the vast majority of studies and effects used a tDCS protocol. Hence, we focused on the 227 effects from 63 studies where this protocol was used.

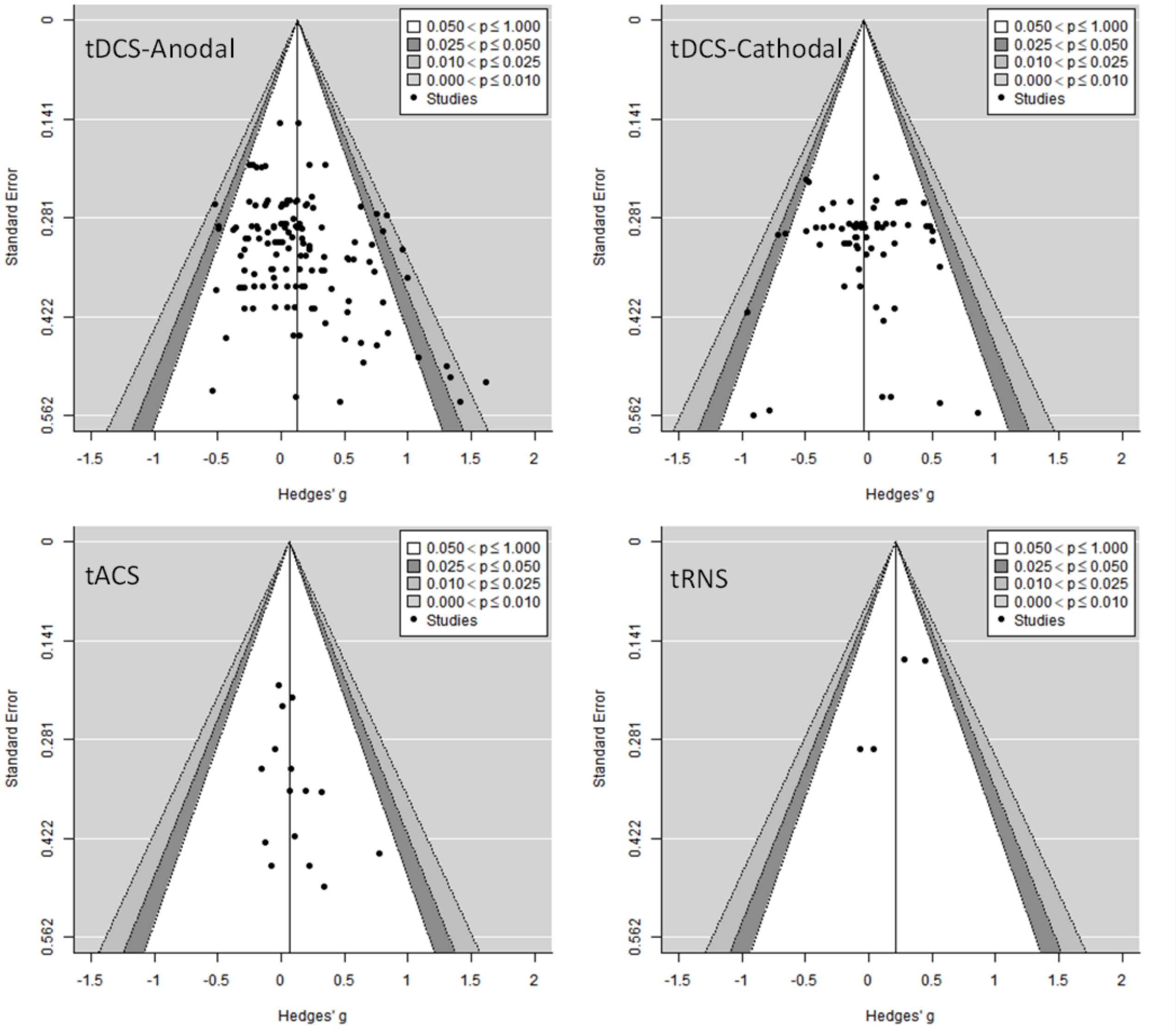

Figure 4-1: Funnel plots of the overall effects of the various tES protocols found in the meta-analysis. Top Left: Anodal tDCS; Top Right: Cathodal tDCS; Bottom Right: tRNS; Bottom Left: tACS

Our main interest was in the domains of Working Memory, Visual Search, Inhibition, and Vigilance, so we ran separate analyses for each. Figure 4-2 shows the funnel plots. The overall effect sizes for tDCS were: Inhibition .056, Vigilance: .146, Working Memory: .184, and Visual Search: .147. However, the various studies used a wide variety of protocols in terms of stimulus parameters.

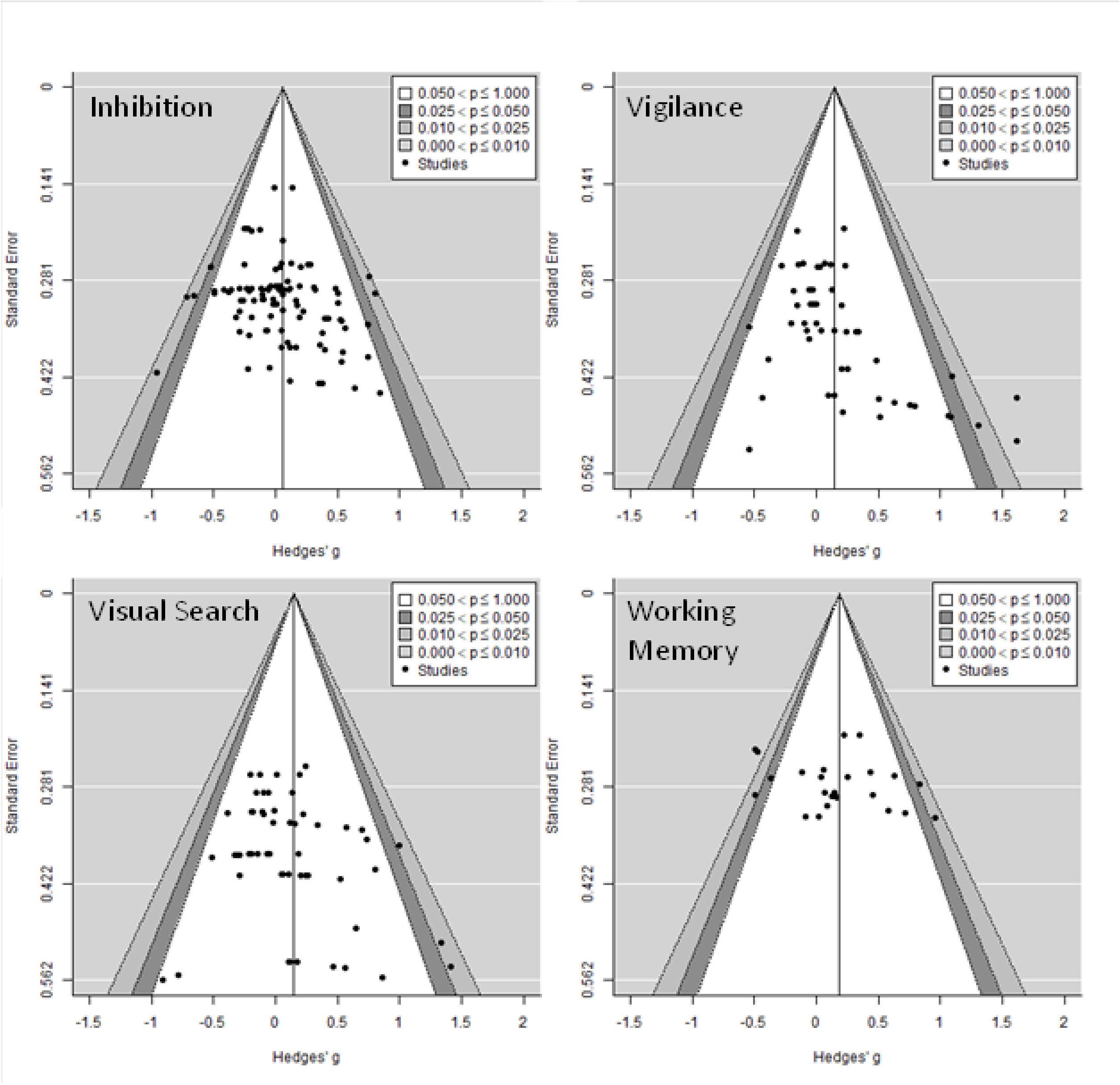

Figure 4-2: Funnel plots of the overall effects of tDCS for the four specific domains. Top Left: Inhibition; Top Right: Vigilance; Bottom Right: Working Memory; Bottom Left: Visual Search

To get a better understanding of which stimulus parameters are the most promising in terms of effect size, we used a set of these parameters as moderators in our multi-level model. The results of these analyses can be found in Table 4-1.

Table 4-1: Results for the moderator analysis across the four domains for each stimulation parameter where p<.050 for at least one of the domains. Dark grey shading: p<.050, Light grey shading: Hedges' g with moderator larger than Hedges' g without moderator. *No studies*: none of the studies selected for this domain used this parameter. Partly online stimulation: task completed partly outside stimulation period. Training: stimulation during skill acquisition

Stimulation Parameter	Working Memory	Inhibition	Vigilance	Visual Search
No Moderator	g=.184, p=.180 $n_{studies}$=7, $n_{effects}$=24	g=.056, p=.197 $n_{studies}$=29, $n_{effects}$=99	g=.146, p=.077 $n_{studies}$=17, $n_{effects}$=51	g=.147, p=.072 $n_{studies}$=20, $n_{effects}$=55
Between Participants Design	**g=.322, p=.008** $n_{studies}$=5, $n_{effects}$=14	g=.031, p=.659 $n_{studies}$=14, $n_{effects}$=58	g=.208, p=.214 $n_{studies}$=7, $n_{effects}$=19	g=.256, p=.119 $n_{studies}$=10, $n_{effects}$=24
Anodal Stimulation	**g=.325, p=.011** $n_{studies}$=6, $n_{effects}$=14	g=.003, p=.953 $n_{studies}$=25, $n_{effects}$=60	g=.123, p=.140 $n_{studies}$=14, $n_{effects}$=31	**g=.244, p=.020** $n_{studies}$=20, $n_{effects}$=55
Bilateral Stimulation	*No studies*	**g=.361, p=.006** $\mathrm{n}_{studies}$=4, $\mathrm{n}_{effects}$=12	g=.349, p=.262 $n_{studies}$=3, $n_{effects}$=12	*No studies*
Online Stimulation	**g=.426, p=.014** $n_{studies}$=3, $n_{effects}$=6	g=-.005, p=.938 $n_{studies}$=13, $n_{effects}$=47	g=.155, p=.090 $n_{studies}$=10, $n_{effects}$=28	Failure to converge $n_{studies}$=5, $n_{effects}$=15
Partly Online Stimulation	g=.215, p=.249 $n_{studies}$=2, $n_{effects}$=8	g=-.016, p=.821 $n_{studies}$=4, $n_{effects}$=16	g=.249, p=.317 $n_{studies}$=5, $n_{effects}$=14	**g=.472, p=.020** $n_{studies}$=7, $n_{effects}$=14
Offline Stimulation	g=-.202, p=.756 $n_{studies}$=2, $n_{effects}$=10	**g=.136, p=.037** $n_{studies}$=14, $n_{effects}$=36	g=-.031, p=.753 $n_{studies}$=3, $n_{effects}$=9	g=.040, p=.607 $n_{studies}$=9, $n_{effects}$=26
Stimulation Left Hemisphere	**g=.260, p=.021** $n_{studies}$=6, $n_{effects}$=20	g=.047, p=.408 $n_{studies}$=20, $n_{effects}$=55	g=.145, p=.119 $n_{studies}$=14, $n_{effects}$=32	g=-.038, p=.595 $n_{studies}$=9, $n_{effects}$=22
Stimulation Frontal Areas	**g=.207, p=.029** $n_{studies}$=5, $n_{effects}$=20	g=.070, p=.147 $n_{studies}$=25, $n_{effects}$=89	**g=.199, p=.036** $n_{studies}$=15, $n_{effects}$=37	**g=.410, p=.003** $n_{studies}$=11, $n_{effects}$=21
Stimulation Intensity<2 mA	g=.194, p=.085 $n_{studies}$=4, $n_{effects}$=18	**g=.116, p=.013** $n_{studies}$=18, $n_{effects}$=56	g=.083, p=.329 $n_{studies}$=10, $n_{effects}$=29	g=-.027, p=.684 $n_{studies}$=12, $n_{effects}$=31
Stimulation Intensity≥2 mA	g=.139, p=.692 $n_{studies}$=3, $n_{effects}$=6	g=-.055, p=.415 $n_{studies}$=11, $n_{effects}$=43	g=.205, p=.184 $n_{studies}$=8, $n_{effects}$=22	**g=.377, p=.021** $n_{studies}$=9, $n_{effects}$=24
Stimulation Duration>900 s	g=.213, p=.201 $n_{studies}$=6, $n_{effects}$=20	g=.034, p=.472 $n_{studies}$=23, $n_{effects}$=85	g=.115, p=.148 $n_{studies}$=16, $n_{effects}$=47	**g=.312, p=.021** $n_{studies}$=9, $n_{effects}$=24
Cephalic Reference Electrode	g=.316, p=.312 $n_{studies}$=2, $n_{effects}$=10	**g=.093, p=.037** $n_{studies}$=21, $n_{effects}$=57	g=.075, p=.363 $n_{studies}$=12, $n_{effects}$=37	g=.128, p=.193 $n_{studies}$=8, $n_{effects}$=20
Training	g=.647, p=.212 $n_{studies}$=1, $n_{effects}$=2	g=.381, p=.286 $n_{studies}$=2, $n_{effects}$=3	*No studies*	g=.417, p=.105 $n_{studies}$=6, $n_{effects}$=14

From the meta-analysis, several conclusions can be drawn (please keep in mind that only the domains of Visual Search and Vigilance were covered exhaustively, so care should be taken with the interpretation of the results for Working Memory and Inhibition). First, in our four chosen domains, inhibition seems to be in a league of its own. Effect sizes tend to be lower than for the other domains, and parameter settings that create significant Hedges' g values in other domains do not work for inhibition. Second, effect sizes for the Working Memory domain tend to be highest across the board for the stimulation parameters listed. Third, the Vigilance and Visual Search domains look like they are reacting similarly to particular parameter settings. Parameters that increase Hedges' g values for one also tend to increase them for the other (and vice versa). Fourth, it is possible to derive some general advice about stimulation parameters and study design that will yield higher effect sizes. For instance: 1) the stimulation of frontal brain areas seems to be successful across domains (with the notable exception of inhibition); 2) It is also advisable to use a between-participants design; 3) Partly online stimulation (where the task is completed partly outside the stimulation period) also yields good results for all domains except inhibition; 4) A stimulation duration longer than 900 seconds and a stimulation intensity of 2mA or higher also seem preferable. One of the most interesting aspects of the meta-analysis involves (and justifies the inclusion of) training. Even though very few studies used a training protocol, and its inclusion as a moderator did not yield any significant Hedges' g values, it is notable that the Hedges' g values for training are amongst the highest in Table 4-1. This suggests that training is an arena where the application of tDCS might yield tangible improvements in performance. From a D&S point of view this is promising, since training is integral to the job of defence and security personnel.

5.0 LESSONS LEARNED

The application of tES in the cognitive domain is a relatively young field of inquiry. Although we did not use year of publication as a selection criterion, all of the papers included in our meta-analysis were published after 2010. The novelty of the field is reflected in an almost complete lack of standardization. Although individual labs are internally consistent in the type of task they use and the dependent variables they measure, this consistency is almost non-existent between labs. Although, for the purpose of this meta-analysis, we have expressed all results in Hedges' g, this underlying variability should be kept in mind when interpreting the results. A further issue is the lack of power of many of the studies. This is not a bias that is included in the risk of bias tool that we used (probably because it assumes that the study is sufficiently powered), but it is nonetheless another factor that demands that care is taken when interpreting the results. The use of real-world tasks is another area where papers included in this meta-analysis are lacking. Almost all tasks examined were laboratory-based, motivated more by basic theoretical questions than by a desire to improve performance. Interestingly, some of the largest effect sizes in this meta-analysis were reported by studies that did use real-world tasks performed by participants from the D&S community whose job description includes that particular task. In combination with the promising effects of training and tDCS, it does seem that using real world tasks have potential for attaining cognitive enhancement.

6.0 FUTURE WORK

We will use the stimulation parameters that were identified in our meta-analysis for an experiment that involves real-world tasks that combine visual search and vigilance: between-subject design, partly online stimulation, stimulation of frontal brain areas, stimulation intensity ≥ 2 mA, stimulation duration > 900 s, and a training paradigm. Moreover, we will recruit enough participants to have an a priori power of 0.8 at an α-level of .05 to be able to detect an effect size 0.4-0.5. The latter is a reasonable estimate of the effect that we expect to find, since we will be using optimized stimulation parameters.

7.0 CONCLUSIONS

This meta-analysis shows that there is an effect of tDCS stimulation on cognitive performance. However, the effect clearly depends on the domain investigated and the stimulation parameters used. We identified several stimulation parameters that seem to yield larger effect sizes across several domains. However, given the current state of the field, it is still too early to make firm recommendations for D&S applications, and further research is very much needed.

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10.0 AUTHORS' BIOGRAPHIES

Gorana Pobric is a cognitive neuroscientist and a director of the University of Manchester Brain Stimulation Lab. She holds a BSc in Neuroscience from the University of Toronto, a BA in Psychology from the University of Belgrade and a PhD in Cognitive Neuroscience from SISSA, Trieste. Following a post-doc post at the ICN, UCL, Gorana joined faculty at the University of Manchester in 2006. Her research programme focuses on applications of non-invasive brain stimulation in translational research focusing on patient rehabilitation protocols and cognitive enhancement. Her group has active collaborations with labs in the UK, Japan, Canada, US and Brazil.

Johan Hulleman is a vision scientist, specialising in visual search. He obtained a BSc in Medical Biology from the University of Utrecht and a PhD in Experimental Psychology from the University of Nijmegen. After working as a post-doc in Glyn Humphreys' lab in Birmingham for several years, he joined faculty at the University of Hull (2004) and moved to the University of Manchester in 2011. He is a director of the Eye-movement lab where his research focuses on functional visual field (FVF) in eye movements as well as applied visual search (early detection of cancers, rehabilitation in neglect patients). After a sabbatical at Harvard in Jeremy Wolfe's lab, he has an active collaboration (and some theoretical disagreements) with Jeremy, as well as collaborations with labs in Amsterdam, Padova and Birmingham.