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Review

Electrical brain stimulation (tES) improves learning more than performance: A meta-analysis

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ABSTRACT

Researchers have recently started evaluating whether stimulating the brain noninvasively with a weak and painless electrical current (*transcranial Electrical Stimulation*, tES) enhances physiological and cognitive processes. Some studies found that tES has weak but positive effects on brain physiology, cognition, or assessment performance, which has attracted massive public interest. We present the first meta-analytic test of the hypothesis that tES in a learning phase is more effective than tES in an assessment phase. The meta-analysis included 246 effect sizes from studies on language or mathematical competence. The effect of tES was stronger when stimulation was administered during a learning phase ($d = 0.712$) as compared to stimulation administered during test performance ($d = 0.207$). The overall effect was stimulation-dosage specific and, as found in a previous meta-analysis, significant only for anodal stimulation and not for cathodal. The results provide evidence for the modulation of long-term synaptic plasticity by tES in the context of practically relevant learning tasks and highlight the need for more systematic evaluations of tES in educational settings.

1. Introduction

The search for more effective learning techniques has been a quest of humanity since time immemorial. Recently, researchers have started evaluating whether stimulating the brain non-invasively with a weak and painless electrical current (*transcranial Electrical Stimulation*, tES) enhances learning and performance. In tES, typically two electrodes are attached to the scalp via saline-soaked sponges. The applied current is usually not higher than 2 mA. In a stimulation session, the current is typically applied from 2 minutes to 20 min. The most common form of tES is transcranial Direct Current Stimulation (tDCS), where anodal and cathodal stimulation can be distinguished. The effects of tES are usually investigated by comparing a tES group with a SHAM control group, in which everything is done the same, including the placement of the electrodes on the skull, but no actual electrical stimulation is given for most of the session. To many, the attractiveness of tES research with healthy participants lies in the promise of achieving performance improvements without investing more time and effort. tES has attracted massive public interest as demonstrated by TED talks and numerous YouTube tutorials for building self-stimulation devices from household items. The physicist Stephen Hawking even raised the question of whether electrical brain stimulation might lead us to the next step of human evolution (Hawking, 2013).

A rapidly increasing (Minarik et al., 2016) number of studies have investigated to what extent these hopes are realistic and tES is actually effective. The results have been summarized in several meta-analyses, but the results of the single studies as well as of the meta-analyses are heterogeneous. One recent meta-analysis analyzed the effects of single-session tDCS on 30 physiological measures (Horvath et al., 2015a). Only the effects of tDCS on motor-evoked potentials reached significance, whereas none of the other 29 variables was reliably affected by tDCS. A second meta-analysis by the same authors investigated tDCS effects on cognitive outcomes, including executive functions, language production, and memory in healthy adults (Horvath et al., 2015b). None of the 59 comparisons was statistically significant. In contrast, more positive evidence comes from a meta-analysis of tDCS effects on language-related cognitive processes, which found a medium strong effect size (Cohen's $d = 0.445$; Price et al., 2015). However, with 8 effect sizes from a total of 119 participants, the database was small and the precision of estimation was low as indicated by the large confidence interval (95% CI [0.176, 0.715]). Three meta-analyses focusing on working memory functioning and including between 8 to 36 effect sizes found only weak and inconsistent effects of tDCS (Brunoni and Vanderhasselt, 2014; Hill et al., 2016; Mancuso et al., 2016). The effect sizes were largely unrelated to current density and stimulation duration (Hill et al., 2016) and partly suffered from publication bias (Mancuso

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et al., 2016). In sum, the meta-analyses so far found mostly low overall effect sizes. However, the heterogeneity of the effect sizes was high, raising the question whether unaccounted variables might moderate the effect of tES on the outcome measures.

In the present meta-analysis, we tested the hypothesis that tES improves learning, that is, the encoding of new information in long-term memory, stronger than processing or recall of already known information from long-term memory. A meta-analytic comparison of these two conditions is possible, because there are basically two types of studies in research on tES. In one type, a psychological construct (e.g., mathematical competence or working memory capacity) is assessed and the participants receive brain stimulation before or during the assessment. In the following, we call this approach *stimulation of test performance*. In the other type of studies, the participants first participate in a learning intervention, for example, they memorize words in a foreign language or practice mental arithmetic. They receive the brain stimulation before or during this learning phase. After the learning phase, the participants complete a learning outcome measure (e.g., assessing how many new words they had learned or how strongly their mental arithmetic competence improved). Usually, there is no separate brain stimulation directly before or during the learning outcome test. In the following, we call this approach *stimulation of learning*.

There are some findings supporting the view that a stimulation of learning might be more effective than the stimulation of test performance. First, anodal tDCS has been shown to reduce regional levels of the inhibitory neurotransmitter *gamma*-Aminobutyric acid (GABA; Stagg et al., 2009). Levels of this neurotransmitter correlate negatively with learning (Floyer-Lea et al., 2006). Second, anodal tDCS seems to improve learning through neuroplastic alterations of synaptic connections, which share some similarities with long term potentiation and depression (Paulus et al., 2016; Stagg and Nitsche, 2011). In animal studies, for instance, anodal tDCS promoted long-term potentiation in the motor cortex by increasing the secretion of the brain-derived neurotrophic factor (BDNF), which is an important growth factor in synaptic learning (Castillo et al., 2011; Fritsch et al., 2011). Similar mechanisms might underlie tES effects on human learning in motor tasks and cognitive tasks (Krause and Cohen Kadosh, 2013). Finally, the only previous meta-analysis taking this potential moderator into account found a significant effect of tES for the stimulation before or during working memory trainings, that is, learning, but no significant effect of tES for the (online or offline) stimulation before or during working memory assessments (Mancuso et al., 2016). However, the generalizability of the finding is unclear. It is limited to a specific working memory function only, is based on a mere ten effect sizes, and had a fail-safe *N* of seven, meaning that the effect would cease to be significant if only seven unpublished studies with null results would be included in the analyses.

For these reasons, we conducted a meta-analysis designed to provide more comprehensive and generalizable evidence for the effects of tES during learning and test performance. To reduce the heterogeneity of the included studies and to aid the interpretation of the results, we included only studies in the domains of mathematics and language, such as vocabulary learning, sentence comprehension, or arithmetic. Mathematics and language competence are prerequisites of academic achievement in many subjects, professional success, and participation in society (OECD, 2001). Our main research questions were: (1) Does tES affect mathematical and language competence? Based on previous meta-analyses (Brunoni and Vanderhasselt, 2014; Hill et al., 2016; Mancuso et al., 2016; Price et al., 2015), we hypothesized to find a positive effect. (2) Does the stimulation before or during a learning phase have stronger effects than the stimulation before or during test performance? We had the hypothesis that this is the case, because tES has been found to affect processes underlying long-term potentiation, that is, learning (Fritsch et al., 2011; Krause and Cohen Kadosh, 2013). (3) Is anodal but not cathodal stimulation effective in the subset of studies using tDCS? We hypothesized this to be the case, as it had been established in a previous meta-analysis on tES (Jacobson et al., 2012). (4) Are the tES effects dosage-specific? We expected to find a systematic relation between stimulation dosage and learning outcomes, which would demonstrate the systematicity of the effects included in the meta-analysis.

2. Methods

2.1. Inclusion criteria

Studies were included in the meta-analysis when they fulfilled each of the following criteria: (1) The study used any kind of transcranial electrical brain stimulation (i.e., tDCS, HDtDCS, tACS, tPCS, or tRNS, for more details see section Data Coding). (2) The study included at least one measure of mathematical or language competence, for example, mental arithmetic or vocabulary learning. We included effect sizes from any task assessing domain-specific fact knowledge, skills, procedural knowledge, declarative knowledge, or problem solving as a competence measure. Studies using numerical or verbal stimuli were excluded when they included not directly practically relevant tasks (e.g., the Stroop task), assessed basic cognitive functions (e.g., categorization), or domain-general cognitive processes (e.g., executive functions). (3) The study reported information that allowed us to compute a standardized effect size (e.g., group means, standard deviations, and number of participants). If the necessary information was not reported in a publication, we contacted the authors. If the authors gave the missing information, the study was included. (4) The effect size was collected with a sample size greater than three so that we could calculate the respective variance of the effect size (see Formula 8). (5) The majority of the participants was either healthy or had dyslexia, dyscalculia, or math anxiety but did not suffer from any other diagnosed neurological or physical disorders. (6) The study was published in the English language.

2.2. Literature search

The literature search is visualized in Fig. 1. We searched title, abstract, heading, table of contents, key concepts, original title, tests, and measures of all articles in the electronic database PsycINFO in May 2016. The search included articles from peer-reviewed journals as well as grey literature. The search terms included the types of electrical brain stimulation and mathematical or language competencies. The exact search was conducted in the database PsycINFO with the following search string: ((tDCS or tACS or tPCS or tRNS or transcranial direct current stimulation or transcranial alternating current stimulation or transcranial random noise stimulation or transcranial pulsed current stimulation or brainstimulation) and (math* or num* or arith* or magnitude* or language or linguistic* or comprehension or vocab*)). We also conducted an exploratory internet search and used several mailing lists of relevant research communities to request any unpublished studies or published studies not yet included in the search results. Only one person responded to this request and sent four additional effect sizes with the respective values of the moderator variables.

A trained coder excluded studies with titles and abstracts not fulfilling the inclusion criteria. Subsequently, forty-two full-text articles were obtained for further examination by two trained and independent raters. The inter-rater agreement (100% * *number of agreements/number of all full-texts*) for the inclusion of full-texts was 83%. Disagreements were resolved by discussion. All studies except one, authored by Sarkar et al. (2014), tested healthy participants. This particular study did not find a significant effect regarding brain stimulation on mathematical achievement for participants with math anxiety. To maximize the interpretability of the results, we excluded the study. A total of 35 studies could finally be included in the meta-analysis (see Appendix for more details).

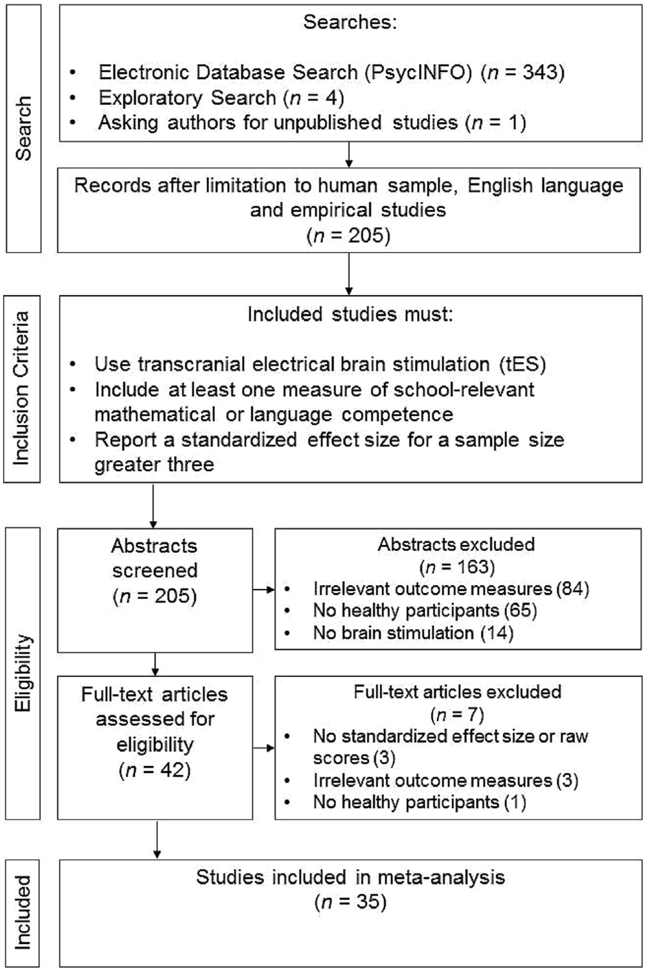

Fig. 1. Flow chart of the literature search.

Table 1
Summary of coded characteristics, number of coded studies (*j*), and effect sizes (*k*).

	No. of studies *j*	No. of effect sizes *k*
Overall	35	246
Stimulation		
Timing of stimulation		
Test performance	25	186
Learning	9	51
Both	4	9
Stimulation Method		
tDCS	29	213
HDtDCS	1	8
tACS	0	0
tPCS	1	2
tRNS	4	23
Active Electrode		
Anodal stimulation	24	167
Cathodal stimulation	11	41
Alternating current	4	23
Hemisphere – anode		
Left	28	168
Right	14	44
Right and left	4	20
Central	1	4
Hemisphere – cathode		
Left	16	74
Right	22	108
Right and left	4	20
Central	3	18
Area of stimulation – anode		
Frontal cortex	14	74
Central cortex	3	10
Parietal cortex	16	98
Temporal cortex	2	20
Occipital cortex	2	14
Supraorbital cortex	6	17
Shoulder	2	7
Area of stimulation – cathode		
Frontal cortex	12	53
Central cortex	5	24
Parietal cortex	9	33
Temporal cortex	1	2
Occipital cortex	1	12
Supraorbital cortex	10	72
Ear	1	1
Cheek	1	12
Shoulder	3	23
Number of stimulation sessions	16	98
Duration of stimulation/session [min]	15	96
Current density anode [mA/cm^2]		
$0 \le J < .04$	12	86
$.04 \le J < .08$	19	93
$J \ge .08$	9	65
Current density cathode [mA/cm2]		
$0 \le \mathrm{J} < .04$	14	91
$.04 \le \mathrm{J} < .08$	18	92
$\mathrm{J} \ge .08$	7	41
Electrode size – anode [cm^2]	33	243
Electrode size – cathode [cm2]	31	223
Electrode sizes		
Same	23	144
Different	9	79
Competence test		
Domain		
Mathematics	17	85
Language	18	161
Measure		
Solution accuracy	25	121
Solution time	21	109
Other	5	16
Stimulus novelty		
Familiar	29	205
Unfamiliar	3	30
Stimulus type		
Pictures	8	71
Numbers	12	58

(*continued on next page*)

2.3. Data coding

We coded all effects reported in the included studies that resulted from a comparison of a brain-stimulation condition with a no-stimulation control condition (SHAM) or from a pre-test/post-test comparison involving stimulation. We did not limit the number of effects included from each study because studies using several groups, competence measures, or measurement points frequently reported several relevant comparisons. To maximize comparability over the studies, we coded the raw data (i.e., the means and standard deviations of the competence measures) instead of the reported effect sizes and then computed a standardized effect size the same way for each study, as described in the next subsection.

For each included effect, the values of the moderator analyses were coded. An overview of all moderators with their levels and the numbers of studies and effect sizes on each level is given in Table 1. We included moderators relating to the stimulation (stimulation type, timing of stimulation, active electrode, hemisphere of the electrodes, area of the electrodes, size of the electrodes, amperage, current density, number of stimulation sessions, duration of stimulation sessions, time between stimulation sessions), the competence test (time from learning phase, test domain, stimulus novelty, stimulus type, task type, measure), the sample (age, gender, university students), and the study (publication type, research group, randomization, control group, comparison).

In coding the stimulation type, we distinguished among the five most common types of transcranial electrical brain stimulation (tES), namely tDCS, HDtDCS, tACS, tPCS, and tRNS (Nitsche & Paulus, 2000). Including all types of tES in our analysis allowed us to test whether the

Table 1 (*continued*)

	No. of studies *j*	No. of effect sizes *k*
Words	5	55
Words and pictures	4	46
Other	3	5
Task type		
Picture naming	5	54
Sentence comprehension	2	27
Vocabulary	2	26
Fact recall	2	13
Verbal fluency	3	11
Grammar	1	2
Other language task	4	29
Mental arithmetic	7	33
Vocabulary	2	26
Magnitude comparison	5	24
Number line estimation (number to space)	2	13
Other mathematics task	5	14
Time from learning phase	6	45
Learner Characteristics		
Age [years]	32	231
University students		
Yes	11	63
No	7	31
Gender [%]	32	225
Study characteristics		
Randomization		
Yes	26	163
No	4	37
Control group		
Sham	34	232
Nothing	1	2
No control	1	11
Comparison		
Pre-post gains	12	64
Post-post	24	171
Pre-post	1	11
Publication type		
Peer-reviewed	34	242
Unpublished	1	4
Research group		
Cohen Kadosh	5	15
Grabner	4	27
Other	26	204

stimulation method moderates the effect on learning outcomes. In transcranial direct current stimulation (tDCS), a low-intensity (0.5–2 mA) constant current is used. The direction of current is determined by the active electrode, which can either be the anode or the cathode. Previous results suggest that anodal stimulation increases cortical excitability (Boros et al., 2008; Nitsche et al., 2003) and cathodal stimulation decreases cortical excitability (Ardolino et al., 2005). High-definition tDCS (HDtDCS) works in a similar way but makes use of smaller gel-based electrodes instead of large sponges. For the constant-current stimulation (tDCS and HDtDCS), we coded the electrode characteristics (active electrode, size and density of the electrode, hemisphere, area) separately for the anode and the cathode. Transcranial alternating current stimulation (tACS) is also similar to tDCS but uses a low-intensity (0.25–1 mA) bidirectional, biphasic current and can be applied at different frequencies. Transcranial pulsed current stimulation (tPCS) uses repeated bursts of low-intensity (0.6–1 mA) pulses. Transcranial random noise stimulation (tRNS) employs very low-intensity (−500 to 500 μA) alternating current with random amplitudes and frequencies (Moreno-Duarte et al., 2014). Implementation of tES may further vary in parameters of dosage, describing the amount of current delivered (in mA), the size of the electrodes (in cm^2), the resulting average density of the current (in $\mathrm{mA/cm}^2$), the duration of the stimulation (in min), and the placement of the electrode. It is suggested that difference in the stimulation dosage may lead to changes and inversion of the direction of effects of tES (Moreno-Duarte et al., 2014).

All competence test means, *SD*s, and moderator variables were independently coded by two trained raters. The inter-rater agreement (100% * number of agreeing values/number of all coded values) for the coded variables ranged from 72% to 100%, with an average of 93%. Disagreements were resolved by discussion. If relevant information was missing or was reported in an ambiguous way, we contacted the authors via e-mail.

2.4. Data preparation

For each effect, we computed the effect size as Cohen's *d* from the coded raw data using syntax. For one study (Flöel et al., 2008) the raw data was not available. Instead, we included two *t*-values for dependent measures reported in that study and transformed them into Cohen's *d*. In the following, we present the formulas used for the calculation of Cohen's *d* that were derived from various sources (Borenstein, 2009; Cohen, 1988; Morris, 2008; Morris and DeShon, 2002). We use the term *treatment* to refer to the stimulation (i.e., tES) and we use the notation *M* for Mean, *SD* for standard deviation, *T1* for the pre-test, *T2* for the post-test, and *n* for sample size.

For studies reporting pre-post comparisons for a treatment condition, we computed the effect sizes as the following:

$$d = \frac{M_{Treatmen,T2} - M_{Treatment,T1}}{SD_{Treatment,T1}} \tag{1}$$

To calculate effect sizes from a post-post comparison between a treatment group and a control group at T2, we used the following formula:

$$d = \frac{M_{Treatment,T2} - M_{Control,T2}}{\sqrt{\frac{(n_{Treatment,T2}-1)\times SD^2_{Treatment,T2} + (n_{Control,T2}-1)\times SD^2_{Control,T2}}{n_{Treatment,T2} + n_{Control,T2} - 2}}} \tag{2}$$

If the study reported descriptive data for a treatment condition and a control condition at T1 and T2 which allows calculation of pre-post gains, we calculated effect sizes for within-subjects designs as the following:

$$d = \frac{(M_{Treatment,T2} - M_{Treatment,T1}) - (M_{Control,T2} - M_{Control,T1})}{\frac{SD_{Treatment,T1} + SD_{Control,T1}}{2}} \tag{3}$$

For effects on pre-post gains for between-subjects designs, we used the following formula:

$$d = \frac{(M_{Treatment,T2} - M_{Treatment,T1}) - (M_{Control,T2} - M_{Control,T1})}{\sqrt{\frac{(n_{Treatment,T1}-1)\times SD^2_{Treatment,T1} + (n_{Control,T1}-1)\times SD^2_{Control,T1}}{n_{Treatment,T1} + n_{Control,T1} - 2}}} \tag{4}$$

When only *t*-values were reported, we transformed the *t*-values (t) to d for within designs as follows:

$$d = \frac{t}{\sqrt{n}} \tag{5}$$

We transformed t-values for between designs with:

$$d = t \times \sqrt{\frac{n_{Treatment} + n_{Control}}{n_{Treatment} \times n_{Control}}} \tag{6}$$

When studies reported *F*-values for univariate ANOVAs we transformed the *F*-values to Cohen's *d* by:

$$d = \sqrt{F \times \frac{n_{Treatment} + n_{Control}}{n_{Treatment} \times n_{Control}}} \tag{7}$$

After computing Cohen's *d*, we used the following equation to compute the variance of each effect size (Schmidt and Hunter, 2015):

$$Var(d) = \left(\frac{N-1}{N-3}\right)\left(\frac{4}{N}\right)\left(\frac{1+d^2}{8}\right) \tag{8}$$

A problem in averaging the effect sizes found with tDCS is that anodal stimulation tends to enhance cognition whereas cathodal stimulation might inhibit cognition or have no effect (Jacobson et al., 2012). Averaging over these positive and negative effects would incorrectly result in an effect size close to zero. To avoid this problem, we recoded the signs of all effect sizes so that lower competence in a cathodal-simulation condition and higher competence in an anodal-stimulation condition had positive signs because they were in line with the expectations. Higher competence in a cathodal-simulation condition and lower competence in an anodal-stimulation condition had negative signs to indicate that they were not in line with the expectations. Thus, a positive overall effect size for tDCS in our meta-analysis indicates that cathodal stimulation decreases competence and/or anodal stimulation increases competence. For other stimulation types, this issue did not arise because there was no constant current.

In meta-analyses, it is generally possible to correct the results for measurement error (Schmidt and Hunter, 2015). However, because only one of the included studies reported the reliability of the outcome measure, we could not correct for measurement errors in our meta-analysis. We detected and removed outlier effect sizes (effect sizes with a z-score greater than 3.29; Tabachnick and Fidell, 2014) before the meta-analytic aggregation. There were only two outliers.

2.5. Statistical analysis

Most of the included studies had more than one relevant effect size. Effect sizes from the same study are statistically dependent and thus cannot be handled by conventional meta-analytic techniques (Hedges et al., 2010). Therefore, we employed robust variance estimation (RVE; Hedges et al., 2010; Tanner-Smith and Tipton, 2014; Tanner-Smith et al., 2016), because it allows for the inclusion of statistically dependent effect sizes in a meta-analysis without requiring information about the inter-correlation between effect sizes within studies. Given the expected heterogeneity, we used random-effects models for all analyses (Raudenbush, 2009). Mean effect sizes and meta-regression models using robust variance estimation were estimated using a weighted least squares approach (Hedges et al., 2010; Tanner-Smith & Tipton, 2014). To estimate the overall effect of tES on mathematical and language competence, we estimated a simple RVE meta-regression model, as follows:

$$y_{ij} = \beta_0 + u_j + e_{ij} \tag{9}$$

where y_{ij} is the ith effect size in the jth study, β_0 is the average population effect of the effect size, u_j is the study level random effect such that $\mathrm{Var}(u_j) = \tau^2$ is the between-study variance component, and e_{ij} is the residual for the ith effect size in the jth study. To estimate the variability in the effect size due to moderator variables, we estimated the following mixed-effects RVE meta-regression model:

$$y_{ij} = \beta_0 + \beta_1(Moderator_1)_{ij} + \ldots + \beta_k(Moderator_k)_{ij} + u_j \tag{10}$$

In this model, the moderator represents a continuous variable (e.g., age) or specific dummy-coded levels (e.g., the three levels of current density) of an included moderator variable.

We used the *robumeta* package (Fisher and Tipton, 2014) in the R statistical environment (R Core Team, 2014) for the statistical analyses. To estimate the proportion of explained variance R^2 for the multiple regression models with categorical moderators with more than two levels, we used the following formula (Tabachnick and Fidell, 2014):

$$R^2 = \sum_{i=1}^{k} r_{yi}\beta_i \tag{11}$$

with the bivariate correlation r and the regression coefficient β.

A common problem of meta-analyses is publication bias (Hunter and Schmidt, 2004; Rothstein et al., 2005). We approached this problem by analyzing the symmetry of the distribution around the mean through visual inspection of the funnel plots, computing Egger regressions (Egger et al., 1997), using the trim-and-fill method (Duval and Tweedie, 2000), and estimating HC intervals, representing confidence intervals with robustness to publication bias (Henmi and Copas, 2010).

3. Results

3.1. Characteristics of the included studies

A total of 35 studies reporting 246 effect sizes obtained with 885 participants were included in the meta-analysis. The studies were published between 2008 and 2016. Of the reported effect sizes, 65% related to language and 35% related to mathematics. The studies used various language tasks (22% picture naming, 11% sentence comprehension, 11% vocabulary, 5% fact recall, 5% verbal fluency, 12% other behavioral competence measures) or mathematical tasks (14% mental arithmetic, 10% magnitude comparison, 5% number line estimation, 6% other behavioral competence measures). They were also representative of the research literature in that they included wide ranges of stimulation types, locations, timings, current densities, and numbers of stimulation sessions.

3.2. Overall effectiveness of tES

The meta-analytic results are listed in Table 2. The overall result supported the hypothesis that tES positively affects mathematical and language competence. The overall Cohen's d was 0.343. The 95% confidence interval [0.173, 0.513] did not include the zero, thus indicating that the effect size was significantly different from zero with $p < 0.05$. The I^2 of 51.8 indicated a moderate heterogeneity of the effect sizes (Higgins and Thompson, 2002) implying that the effectiveness of tES is moderated by third variables.

3.3. Moderator analyses

The results also supported our main hypothesis, that tES effects are stronger for the stimulation of learning than for the stimulation of test performance. The effect size was $d = 0.211$ for the stimulation of test performance. With $d = 0.712$, the effect was three times stronger for the stimulation in a learning phase. A stimulation in both phases was descriptively even stronger with $d = 0.763$. All three effect sizes are statistically significant, but it should be noted that the lower bound of the confidence interval of the effect size for the stimulation of test performance is close to zero. Whether learning or test performance was stimulated had a highly significant effect ($p < 0.01$), explained a variance proportion of .163 of the effect sizes, and was the strongest moderator in the meta-analysis.

Further moderator analyses showed that the effect of tES significantly varied under different stimulation conditions. Descriptively, the effect was much stronger for tRNS than for tDCS, but the small number of studies with tRNS combined with the non-independence of many effect sizes did not permit testing the statistical significance of this difference. In tDCS and HDtDCS, a significant effect was only found for anodal but not for cathodal stimulation. Anodal stimulation was effective with $d = 0.343$, whereas cathodal stimulation did not influence learning outcomes with $d = 0.053$. Similarly, hemispheres and areas of the stimulation differed descriptively in their mean effect sizes, but these differences reached significance only for the hemisphere of the cathode. When the cathode was on the right hemisphere, effect sizes were significantly larger as compared to when it was placed on the left hemisphere.

The effect of tES was dosage-specific. The effect sizes increased with the number of stimulation sessions and were highest for a current density between 0.04 and 0.08 mA/cm^2 and a current of 1 mA. The effect of tES was significant for mathematical as well as for language measures and for solution accuracy as well as solution time. In line with

Table 2
Number of studies (*j*), number of effect sizes (*k*), effect size (*d*), 95% confidence interval, measure of heterogeneity τ^2 for the levels of the moderator variables, and significance and R^2 for the moderator analyses

	j	*k*	*d*	*95% CI*	τ^2	Moderator	
						Sign.	R^2
Overall	35	246	0.343	[0.173, 0.513]	.200		
Stimulation							
Time of Stimulation						**	.163
Test performance	25	186	0.207	[0.021, 0.393]	.197		
Learning	9	51	0.712	[0.387, 1.040]	.035		
Both	4	9	0.763	-[a]	-[a]		
Stimulation method						–	–
tDCS	29	213	0.267	[0.100, 0.434]	.171		
tRNS	4	23	1.190	-[a]	-[a]		
Active electrode						*ns*	.033
Anodal stimulation	24	167	0.343	[0.143, 0.543]	.005		
Cathodal stimulation	11	41	0.053	[-0.150, 0.256]	.005		
Alternating current	4	23	1.190	-[a]	-[a]		
Hemisphere – anode						*ns*	.022
Left	28	168	0.395	[0.191, 0.589]	.215		
Right	14	44	0.177	[0.016, 0.337]	.116		
Right and left	4	20	0.406	-[a]	-[a]		
Hemisphere – cathode						*	.063
Left	16	74	0.111	[-0.043, 0.264]	.118		
Right	22	108	0.407	[0.163-0.650]	.252		
Right and left	4	20	0.406	-[a]	-[a]		
Central	3	18	0.517	-[a]	-[a]		
Area of stimulation – anode						*ns*	.017
Frontal cortex	14	74	0.353	[0.020, 0.687]	.229		
Central cortex	3	10	0.320	-[a]	-[a]		
Parietal cortex	16	98	0.385	[0.117, 0.654]	.120		
Temporal cortex	2	20	0.184	-[a]	-[a]		
Occipital cortex	2	14	-0.140	-[a]	-[a]		
Supraorbital cortex	6	17	0.186	[-0.130, 0.504]	.010		
Right Shoulder	2	7	-0.188	-[a]	-[a]		
Area of stimulation – cathode						*ns*	.088
Frontal cortex	12	53	0.169	[-0.125, 0.463]	.116		
Central cortex	5	24	0.468	-[a]	-[a]		
Parietal cortex	9	33	0.325	[-0.092, 0.742]	.148		
Supraorbital cortex	10	72	0.451	[0.006, 0.897]	.371		
Right Shoulder	3	23	0.103	-[a]	-[a]		
Number of stimulation sessions	16	98	–	–	–	**	.095
Duration of stimulation/session [min]	15	96	–	–	–	*ns*	.146
Current density anode [mA/cm^2]						**	.099
$0 \le J < .04$	12	86	0.329	[0.150, 0.635]	.026		
$.04 \le J < .08$	19	93	0.434	[0.141, 0.728]	.368		
$J \ge .08$	9	65	0.041	[-0.143, 0.225]	.000		
Current density cathode [mA/cm^2]						**	.094
$0 \le \mathrm{J} < .04$	14	91	0.360	[0.124, 0.596]	.096		
$.04 \le \mathrm{J} < .08$	18	92	0.455	[0.158, 0.751]	.282		
$\mathrm{J} \ge .08$	7	41	0.068	[-0.201, 0.337]	.000		
Amperage [mA]						*	.054
1.0	16	103	0.481	[0.212, 0.750]	.102		
1.5	7	34	0.445	[-0.249, 1.140]	.598		
2.0	12	108	0.145	[-0.006, 0.356]	.133		
Electrode size – anode [cm^2]	33	243				*ns*	.001
Electrode size – cathode [cm2]	31	223				*ns*	.012
Electrode sizes						*ns*	.001
Same	23	144	0.457	[0.201, 0.713]	.300		
Different	9	79	0.232	[-0.029, 0.493]	.065		
Competence test							
Domain						*ns*	.004
Mathematics	17	85	0.289	[0.040, 0.538]	.120		
Language	18	161	0.395	[0.139, 0.652]	.311		
Measure						*ns*	.020
Solution accuracy	25	121	0.280	[0.043, 0.516]	.219		
Solution time	21	109	0.260	[0.036, 0.485]	.210		
Other	5	16	0.488	-[a]	-[a]		
Stimulus novelty						-[a]	-[a]
Familiar	29	205	0.301	[0.106, 0.495]	.199		
Unfamiliar	3	30	0.593	-[a]	-[a]		
Stimulus type						*ns*	.020
Pictures	8	71	0.457	[0.131, 0.783]	.393		
Numbers	12	58	0.218	[-0.092, 0.528]	.121		
Words	5	55	0.066	-[a]	-[a]		

(*continued on next page*)

Table 2 (*continued*)

	j	*k*	*d*	*95% CI*	τ^2	Moderator	
						Sign.	R^2
Words and pictures	4	46	0.362	-[a]	-[a]		
Other	3	5	0.925	-[a]	-[a]		
Task type						-[a]	-[a]
Picture naming	5	54	0.171	-[a]	-[a]		
Sentence comprehension	2	27	0.009	-[a]	-[a]		
Vocabulary	2	26	0.652	-[a]	-[a]		
Fact recall	2	13	0.892	-[a]	-[a]		
Verbal fluency	3	11	0.525	-[a]	-[a]		
Other language task	4	29	0.657	-[a]	-[a]		
Vocabulary	2	26	0.652	-[a]	-[a]		
Mental arithmetic	7	33	-0.014	[-0.146, 0.118]	.000		
Magnitude comparison	5	24	0.352	-[a]	-[a]		
Number line estimation	2	13	0.470	-[a]	-[a]		
Other mathematics task	5	14	0.680	-[a]	-[a]		
Time from learning phase	6	45				*ns*	.000
Learner Characteristics							
Age [years]	32	231				*ns*	.001
University students						*ns*	.016
Yes	11	63	0.229	[-0.016, 0.474]	.176		
No	7	31	0.410	[-0.099, 0.920]	.161		
Gender [%]	32	225				*ns*	.006
Study characteristics							
Randomization						-[a]	-[a]
Yes	26	163	0.391	[0.180, 0.603]	.241		
No	4	37	0.284	-[a]	-[a]		
Comparison						*ns*	.062
Pre-post gains	12	64	0.366	[0.059, 0.673]	.267		
Post-post	24	171	0.365	[0.144, 0.587]	.183		
Research group						-[a]	-[a]
Cohen Kadosh	5	15	0.727	-[a]	-[a]		
Grabner	4	27	0.217	-[a]	-[a]		
Other	26	204	0.299	[0.111, 0.487]	.203		

[a] insufficient number of data points for the analysis.

Note. ns: not significant; *$p < 0.05$, **$p < 0.01$; moderators without levels were used as continuous predictors in meta-regressions; all moderators with only one study were omitted from this table.

our hypothesis that the stimulation of learning is more effective than the simulation of test performance, the effect size was almost twice as high for studies presenting the participants with novel stimuli instead of familiar ones. The descriptive differences between task types should not be interpreted, because there were only few studies using each type of task so that task type might be confounded with other study characteristics in our analyses. For the learner and study characteristics, no significant moderator effects were found.

3.4. *Publication bias*

There was no publication bias on the study level and only a weak publication bias on the effect size level (see Fig. 2). Egger regressions for random effects (Egger et al., 1997) did not indicate asymmetry on the study level ($Z = 1.585$, $p = .113$) but did indicate asymmetry on the effect size level ($Z = 4.083$, $p < .0001$). The trim-and-fill method did not add any cases to the distribution to make it more symmetric. This indicates that the publication bias was too small to be detected with the trim-and-fill method. In line with this, the estimation of the HC intervals (Henmi & Copas, 2010) indicated only a weak publication bias and reduced the effect size slightly from $d = 0.328$, 95% CI [0.169, 0.488] to $d = 0.314$, 95% CI [0.150, 0.478] on the study level and from $d = 0.276$, 95% CI [0.194, 0.358] to $d = 0.238$, 95% CI [0.166, 0.310] on the effect size level. This shows that the positive findings cannot entirely be attributed to a publication bias.

4. Discussion

4.1. *Effects of tES on practically relevant learning tasks*

The present meta-analysis aimed to investigate the effects of brain stimulation on practically relevant learning tasks and whether the effectiveness differs due to timing of the stimulation (i.e. whether it was provided in the learning or testing phase) and characteristics of the stimulation (i.e. anodal vs. cathodal). In line with our expectations, tES had a positive overall effect on learning outcomes. Further, tES in a learning phase, where participants had to encode new information, had a much stronger effect than tES of test performance, where participants had to recall information. This may be explained by neuroplastic alterations of synaptic connections via different pathways (e.g., BDNF secretion, GABAergic activity; Castillo et al., 2011; Fritsch et al., 2011; Paulus et al., 2016; Stagg and Nitsche, 2011). Elaborating the details of these mechanisms in cognitive learning remains an important topic for future research.

Brain stimulation was effective for anodal but not for cathodal stimulation. The findings are in line with previous meta-analytic results, indicating effectiveness of anodal but not cathodal stimulation (Jacobson et al., 2012). Research investigating the mechanisms of brain stimulation found evidence that anodal stimulation increases cortical excitability (Boros et al., 2008; Nitsche et al., 2003) and cathodal stimulation decreases cortical excitability (Ardolino et al., 2005) through modulation of membrane potentials. Following, firing threshold of neurons decrease during anodal stimulation and increase during cathodal stimulation, so that neurons in the stimulated area require less input to fire or become inhibited and require more input, respectively. These mechanisms are also relevant for learning, which likely explains

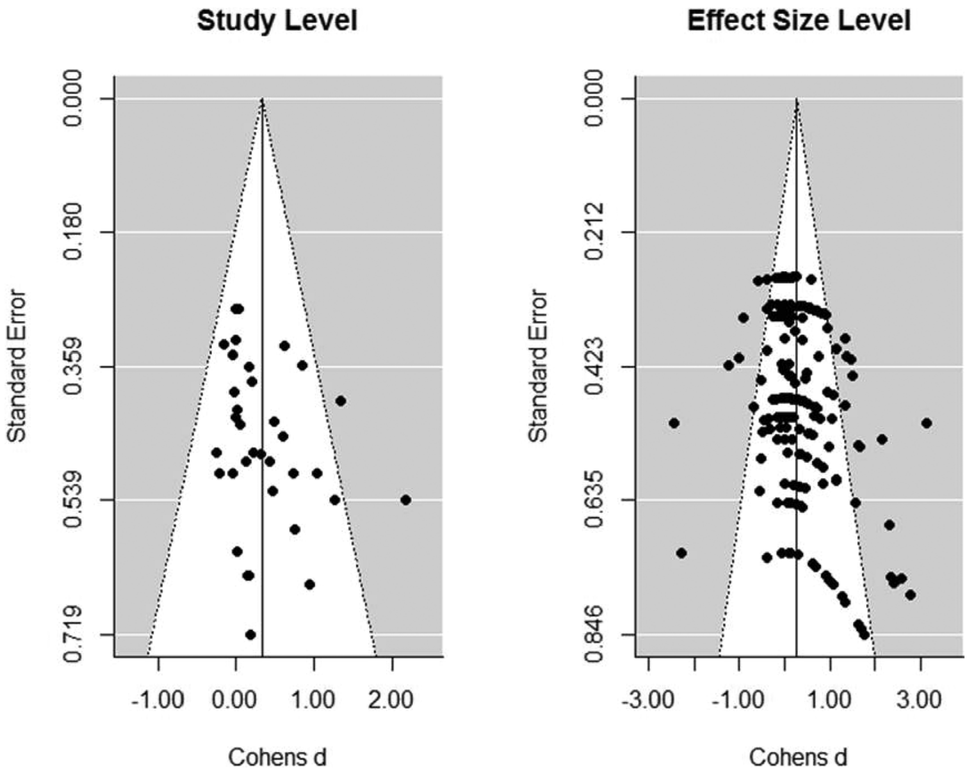

Fig. 2. Funnel plots for average effect size per study (left) and all effect sizes (right).

the present results. By averaging over (effective) anodal and (ineffective) cathodal stimulation in our meta-analysis, we obtained lower effect sizes than we would have obtained by focusing on anodal stimulation only. We still think that including anodal and cathodal stimulation in the current analyses is warranted, because the differential effects of anodal and cathodal stimulation are not well understood yet.

The effect of tES was dosage-specific. The effectiveness of tES increased with the number of stimulation sessions and was associated with the amperage and current density of the stimulation. tES was most effective for a current of 1 mA and a current density between 0.04 and 0.08 mA/cm^2. The findings therefore demonstrate that characteristics of the application of tES are essential for the effectiveness of the method.

The finding that anodal tES enhances learning mathematics and language is in line with studies suggesting that anodal tES might also have positive effects on motor learning (Ammann et al., 2016; R.Buch et al., 2017). However, we do not know of any direct comparisons of the stimulation of academic learning versus motor learning. Future stimulation studies will have to systematically investigate the commonalities and differences of academic and motor learning in terms of effective stimulation methods, stimulated brain regions, and underlying neurophysiological processes.

4.2. *Generalizability of the findings*

In sum, the results of the present study support the view that tES affects performance and learning across a variety of competence measures and activated brain regions. Since most included studies were randomized trials involving a SHAM control condition, the findings can be interpreted in terms of a causal effect. Several findings demonstrate the validity and systematicity of the meta-analytic results. Direct checks indicated only a very weak publication bias, the effects of tES were dosage-specific, and were consistently found for mathematics and language learning, with accuracy and speed measures. We were also able to replicate the previous meta-analytic finding that, in direct current stimulation, anodal but not cathodal stimulation has positive causal effects. Despite the high statistical power that comes with 246 effect sizes, there was no evidence that our results would be specific to only mathematics learning or language learning, to only accuracy measures or speed measures, to only women or men, or to only university students or other participants. This demonstrates the consistency and generalizability of the findings.

Our literature search and inclusion criteria were designed to also include adequate studies on tES effects on mathematical and language learning in samples with dyslexia, dyscalculia, or math anxiety. As there was only one study matching the inclusion criteria and using a clinical sample, we excluded the study from the meta-analysis. The generalizability of our results is thus limited to healthy participants only.

4.3. *Implications for research and practice*

Overall, the results of the present study imply that previous meta-analyses might have dramatically underestimated beneficial effects of tES on cognition and performance, because they did not differentiate between the stimulation of learning and the stimulation of test performance. Most empirical studies so far investigated the latter, but as we show here, the effect sizes are more than three times higher in the former case. This is a highly relevant finding for the research field of educational neuroscience, in which tES has been intensively discussed as potential future means to support knowledge acquisition in individuals with learning difficulties, especially in language and mathematics (Iuculano and Cohen Kadosh, 2014; Krause and Cohen Kadosh, 2013). The results give evidence that despite the heterogeneity in competence measures and activated brain regions which is accompanied by significant noise, the signal was strong enough to show significant results through this noise.

These highly encouraging findings do not imply that tES should be used in practical educational contexts right away. This would be a grave mistake, both from a scientific and practical perspective. From a scientific point of view, there is reason for concern because of the low reproducibility of empirical studies in psychology and related fields

(Open Science Collaboration, 2015). These are partly because of questionable research practices, for example, using several learning outcome measures in an intervention study but reporting only the ones that showed a significant effect. So far, this problem has not been explicitly discussed in research on tES. If present in several studies, the problem could have biased the results of our meta-analysis. Therefore, the primary implication of the current findings is not that tES demonstrated effectivity, but rather that the first phase of tES research with its small sample sizes and explorative approaches should come to an end and be followed by a second phase characterized by replication attempts, preregistered trials, larger sample sizes, open data, a full documentation of rigorous research practices, and further meta-analytic integration.

From a practical perspective, there is reason for caution because the present results had exclusively been obtained in laboratory studies with healthy adults. The generalizability of the findings to learning in classroom settings and to children and adolescents, especially those suffering from learning difficulties, is unclear, as only few studies exist (e.g., Costanzo et al., 2016; Looi et al., 2017). In addition, almost nothing is currently known about the cognitive side effects of stimulation, that is, whether improving one brain function can unintentionally impair other brain functions (e.g., Iuculano and Cohen Kadosh, 2013; Sarkar et al., 2014). When tES is used, safety issues have to be carefully considered (Davis, 2014). Self-built stimulation devices are not recommended due to safety concerns and the potential for unintentional impairment of brain functions (Wurzman et al., 2016). The cost–benefit relationship needs to be considered because there is an abundance of instructional methods with lower financial costs and stronger effects on learning than tES (e.g., Hattie, 2009). Finally, there is the need for an ethical debate about cognitive self-enhancement and questions such as accepting or challenging the limits of human nature, freedom of choice for learners, informed consent in children, and the fair distribution of technological learning resources worldwide (Cohen Kadosh et al., 2012).

5. Conclusion

The meta-analytic results demonstrate that studies in which brain stimulation was administered in a learning phase found, on average, higher effect sizes than studies in which brain stimulation was administered in a test performance phase. This is in line with studies showing effects of tES on neurotransmitters and synaptic mechanisms associated with learning, that is, the encoding of new information, rather than recall or recognition. The meta-analytic results were also highly consistent in that the overall effect was stimulation-dosage specific and significant only for anodal stimulation, as had been found in a previous meta-analysis. Yet, in spite of the highly encouraging results, it is too early to use tES in practical educational settings, because there is still a lack of pre-registered independent replications, field experiments in schools, and studies with children.

Appendix A. Included studies

Included studies

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