Brain Stimulation 12 (2019) 1381–1389

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Effects of beta-tACS on corticospinal excitability: A meta-analysis

Miles Wischnewski [a, *], Dennis J.L.G. Schutter [a], Michael A. Nitsche [b, c]

[a] Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands
[b] Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany
[c] University Medical Hospital Bergmannsheil, Bochum, Germany

ARTICLE INFO

Article history:
Received 18 March 2019
Received in revised form
5 July 2019
Accepted 25 July 2019
Available online 28 July 2019

Keywords:
Transcranial alternating current stimulation
Motor cortex excitability
Motor-evoked potentials
Beta frequency

ABSTRACT

Over the past decade several studies have shown that transcranial alternating current stimulation (tACS) delivered at the beta (15–25 Hz) frequency range can increase corticospinal excitability of the primary motor cortex (M1). The aim of this study was to systematically quantify the effect size of beta-tACS on corticospinal excitability in healthy volunteers, as well as to identify significant outcome predictors. A meta-analysis was performed on the results of 47 experiments reported in 21 studies. Random effects modelling of the effect sizes showed that beta-tACS significantly increases M1 excitability ($\bar{E} = 0.287$, 95% CI = 0.133–0.440). Further analysis showed that tACS intensities above 1 mA peak-to-peak yield a robust increase in M1 excitability, whereas intensities of 1 mA peak-to-peak and below do not induce a reliable change. Additionally, results showed an impact of tACS montages on these effects. No difference in effect size for online compared to offline application of tACS was found. In conclusion, these findings indicate that beta-tACS can increase cortical excitability if stimulation intensity is above 1 mA, yet more research is needed to titrate the stimulation parameters that yield optimal results.

Introduction

Two millennia after the Roman physician Scribonius Largus investigated the effects of electric currents over the human head using torpedo fish [1], the mechanisms of how transcranial electric stimulation affects brain activity are still not fully understood. Transcranial alternating current stimulation (tACS) applies weak non-invasive oscillating currents as a means of inducing neuromodulation to change neural electric excitability [2,3]. Although these currents are too small to induce neuronal firing, subtle changes in the resting membrane potential are thought to enhance rhythmicity and induce phase-locking of endogenous brain activity [4]. Neural synchronization in oscillatory patterns reflects a mechanism of communication between brain cells [5–7]. TACS may modulate such oscillations, which potentially affects task performance in an non-linear fashion. As such a linear increase in tACS parameters may have no or even opposing effects on behavior [8–10].

Neural oscillations in the beta frequency range (13–30 Hz) recorded over the medio-lateral parts of the scalp correlate to sensorimotor activation [11,12]. Beta oscillations in these areas depend on a balance between inhibitory (GABAergic) and excitatory (glutamatergic) input [13]. As such, increased GABAergic activity is related to higher resting beta power and beta desynchronization during motor-related processes [14,15]. Arguably, by manipulating the inhibitory-excitatory balance with beta tACS-induced neuromodulation, the corticospinal output to the associated muscles may be affected. Thus, these studies suggest that motor cortex oscillations relate to motor cortex excitability.

TACS studies have tested the idea that entrainment of beta oscillations affects neural excitability by measuring motor-evoked potentials (MEP) with single pulse transcranial magnetic stimulation (TMS). Whereas several studies have demonstrated increased MEP amplitudes during beta-tACS [16–20], others have found no effects [21], and in some cases even decreases in MEP amplitudes were found [22]. In addition to online effects, it has recently been suggested that tACS may induce M1 plasticity lasting up to 60 min after intervention [20,23–25]. It has been suggested that these after effects depend on spike-timing dependent plasticity (STDP), which may be induced by tACS in recurrent M1 networks. However, others have found no beta-tACS induced after effects [21,26].

* Corresponding author. Donders Institute for Brain, Cognition and Behaviour Radboud University Nijmegen, Montessorilaan 3, 6525, HR, Nijmegen, the Netherlands.
E-mail address: m.wischnewski@donders.ru.nl (M. Wischnewski).

https://doi.org/10.1016/j.brs.2019.07.023

The heterogeneity of results might partially be explained by inter- and intra-individual variability in tACS susceptibility. The variability can be traced back to individual differences, such as scalp-cortex distance, gyrification, intrinsic peak neural oscillation frequency, gender, age, genetics, current state of brain physiology, and attention. Furthermore, differences in tACS parameters, such as the montage, intensity, and whether MEPs were investigated during or after tACS contribute to the heterogeneity [27,28].

Therefore, we aimed to quantify the effect size of current research findings by performing a meta-analysis to determine whether the mean effect of beta-tACS on MEP amplitude was significantly greater than zero. Furthermore, the influence of tACS parameters (intensity, montage, online vs offline) on this mean effect was explored.

Methods

The meta-analysis was conducted following the guidelines of the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Protocols (PRISMA-P [29]).

Eligibility criteria

Studies were selected if they satisfied the following eligibility criteria: i) Peer-reviewed published studies in the English language were included; ii) studies were performed on healthy adult humans, who did not take any psychoactive medication or drugs; iii) studies received formal ethical approval; iv) the study had to include at least one baseline measurement and at least one measurement during or after tACS; v) the outcome measure had to be MEP amplitude; vi) outcome measures were obtainable from the main text, figures, tables or supplementary data; vii) tACS was administered within the beta range (15–25 Hz), with no DC offset.

Search strategy and study selection

A literature search was conducted within the scientific databases PubMed and Web of Science and the final date was set to January 31, 2019. The following search terms were included: i) "transcranial alternating current stimulation" + "beta"; ii) "tACS" + "beta"; iii) "tACS" + "X Hz", where X ranged from 15 to 25; iv) "transcranial alternating current stimulation" + "X Hz", where X ranged from 15 to 25; v) "tACS" + "MEP"; vi) "transcranial alternating current stimulation" + "MEP"; vii) "tACS" + "motor evoked potential"; viii) "transcranial alternating current stimulation" + "motor evoked potential". Furthermore, a manual search was carried out over the reference sections of the retrieved studies. The search resulted in 491 hits and after removal of 107 duplicates and 282 publications which did not cover the topic of this review, 102 articles remained. After full-text assessment 21 articles were identified as eligible for the present meta-analysis [16–23,25,26,30–40]. Since several studies had multiple measurements, the main analysis on MEP amplitude consisted of 47 data points (Fig. 1, Tables 1 and 2).

Outcome variables

For the main study, MEP amplitudes elicited by single pulse TMS were investigated as main outcome measure. The proportion change from pre-tACS baseline MEP size to the effects of tACS on MEP size was calculated. In a post-hoc analysis, the effects of tACS parameters, that included intensity, superficial current density, montage and online vs offline were investigated by the corresponding proportion change compared to baseline. Intensity was expressed in milliampere (mA) and superficial current density in mA/cm^2. Five montages were investigated: M1-Pz, M1-Oz, M1-supraorbital area (SOR), M1-shoulder, and high definition (HD) M1 stimulation. Online tACS refers to effects on MEP amplitude measured while alternating currents were applied, whereas offline tACS refers to the after-effects following a tACS intervention.

Risk of bias

Risk of bias assessment was performed using the Cochrane Collaboration's tool [41]. For each study, the authors judged the risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases. Risk of bias was categorized as low, high or uncertain. The assessment of each study and the percentage of bias are presented in Fig. 2.

Data extraction and statistical analysis

If the effect size Cohen's *d* was reported, the effect sizes were extracted directly. Otherwise, the mean difference between online/offline tACS and pre-tACS values as well as the pooled standard deviation were used to calculate the Cohen's *d* effect size. Based on these values the Hedges' *g* value was calculated as a correction for biases in effect size caused by small sample sizes [42]. Subsequently, a random effects model was used to calculate the mean effect size ($\bar{E}$) and 95% confidence interval. A *Z*-statistic and *p*-value was calculated to determine whether $\bar{E}$ was significantly different from zero.

The main analysis on MEP amplitude consisted of 47 extracted effect sizes, which represent the difference between tACS-induced changes of MEP size compared to a pre-tACS baseline measurement. Positive Hedges' *g* values indicate an increase in MEP size, whereas negative values indicate a decrease in MEP size. In post-hoc analyses, tACS intensity, montage and online vs offline were investigated. For tACS intensity effect sizes were divided into two groups; studies applying 1 mA tACS or less ($n = 30$) and studies applying more than 1 mA ($n = 17$). Additionally, a Spearman rank correlation was calculated between current density values and effect size. For tACS montage, effect sizes were divided into five groups; studies using a M1-Pz ($n = 17$), M1-Oz ($n = 16$), M1-rSOR ($n = 6$), M1-shoulder ($n = 3$), or HD-M1 montage ($n = 3$). For the final post-hoc analysis effect sizes were divided into online ($n = 33$) and offline tACS ($n = 14$) designs. For all three post-hoc analyses a GLM between-subjects ANOVA was performed to get an indication of whether effect sizes differ between categories.

For all analyses, the sample distribution was checked for normality using a Kolgomorov-Smirnov (KS) test. Furthermore, total heterogeneity (Qtotal) was tested against a χ^2 distribution ($df = n\text{-}1$) to determine whether the variance of effect sizes was greater than to be expected from sampling error [42]. To investigate potential publication bias within the main MEP analysis, first the fail-safe number based on the Rosenthal method ($\alpha < 0.05$) was calculated. This value represents the amount of null findings needed to render the mean effect non-significant [43]. Second, a non-parametric rank-order correlation between effect size estimates and sample size was calculated, where non-significant results indicate low risk of bias [44]. Data were analyzed using MetaWin 2.1 [45] and IBM SPSS 25.0. All statistical tests were tested against a significance level of $\alpha \leq 0.05$ (two-tailed).

Results

Risk of bias

Risk of bias as judged by the authors is represented in Fig. 2. Generally, the risk of bias was very low, with no indications for performance, attrition or detection bias. The absence of reporting

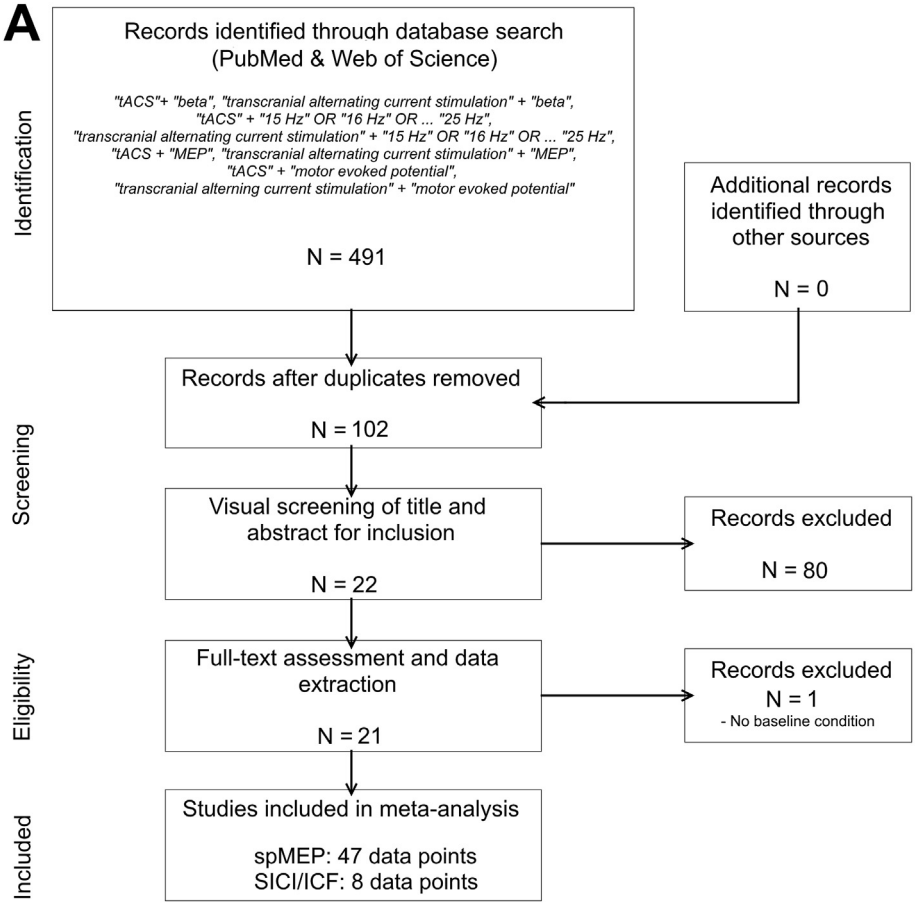

Fig. 1. PRISMA flow chart of the present meta-analysis.

MEP amplitudes in Wach et al. [31] may indicate a reporting bias. The data of this study were provided by the authors, gathered by personal communication. Two studies used a single-blind design [23,34], yielding a potential for detection bias as the experimenter was not blind to the tACS condition. In five studies blinding of the experimenter was not reported and these were categorized as uncertain for detection bias. Participants in all studies were divided into groups in a randomized manner yielding a low potential for selection bias. However, since tACS may cause a tingling or itching sensation on the skin it is important to check the adequacy of blinding after the experiment. Such post-tACS check for blinding was not explicitly reported by four studies and hence these were categorized as uncertain for selection bias. No other biases were observed.

MEP amplitude

The effect of beta-tACS on MEP amplitude over all studies ($N = 47$; Table 3) revealed a significant mean effect size of $\bar{E} = 0.287$, 95% CI = 0.133–0.440 ($Z = 3.67$, $p < .001$; Fig. 3A). Rosenthal's fail-safe method showed that 304 null-results are necessary to yield this effect size non-significant ($p > 0.05$). Total heterogeneity of effect sizes (g) was not significant, $Q_{total} = 49.43$, $p = .338$ (Fig. 3B). Inspection of the normal quantile plot, representing the standardized effect size (y-axis) compared to the standard normal distribution (x-axis), indicated that the effect size estimates (g) were normally distributed [46]. Publication bias was estimated by performing a non-parametric rank-order correlation between the effect size estimates and sample size [44]. The result indicated low risk for publication bias, $\rho = 0.08$, $p = .589$.

Next, differences in intensity, montage and online vs offline stimulation were explored. It was found that tACS intensity used in different studies significantly affects the mean effect size ($F(1,45) = 4.09$, $p = .049$; Fig. 3C). Studies using a stimulation intensity of larger than 1 mA had a mean effect size of $\bar{E} = 0.520$, CI = 0.295–0.746 ($Z = 4.53$, $p < .001$), whereas studies using a tACS intensity of 1 mA or below had a mean effect size of $\bar{E} = 0.161$, CI = −0.052 - 0.373, ($Z = 1.48$, $p = .139$). However, with regards to superficial current density, a Spearman correlation revealed no significant relationship to MEP amplitude ($\rho = 0.19$, $p = 0.193$).

With regards to tACS montage, the results indicated that different montages do not affect MEP amplitudes equally ($F(4,40) = 5.38$, $p = .001$; Fig. 3C), although this result should be interpreted with care given the low number of samples for some montages. A posterior reference electrode, positioned over Oz or Pz, yielded a mean effect size significantly larger than zero; M1-Oz: $\bar{E} = 0.316$, 95% CI = 0.046–0.586 ($Z = 2.30$, $p = .022$); M1-Pz: $\bar{E} = 0.284$, 95% CI = 0.086–0.483 ($Z = 2.81$, $p = .005$). In addition, the HD-tACS montage was significantly larger than zero ($Z = 2.06$, $p = .039$), with a large mean effect size of $\bar{E} = 1.478$, CI = 0.074–2.882.

Finally, no significant differences were observed for studies investigating the effect of beta-tACS on MEP amplitude online vs offline ($F(1,45) = 0.43$, $p = .517$; Fig. 3C).

Discussion

Research has provided evidence for effects of tACS on cortical physiology in the motor, visual and cognitive domain, using a variety of stimulation frequencies [3,4,47]. In the motor domain beta-

Table 1
Study and experiment characteristics of studies investigating MEPs.

#	Study	N	MEP	Stimulation	Montage (size in cm^2)	Intensity (mA)	CD (mA/cm^2)	Hedges g	Comment
1	Antal et al., 2008	10	FDI	offline	Left M1 – right SOR (16–50)	0.4	0.025	0.04	
2	Zaghi et al., 2010	11	FDI	offline	Left M1 – C4 (12.6–12.6)	1	0.080	−0.78	
3	Feurra et al., 2011	15	FDI	online	Left M1 – Pz (35–35)	1	0.029	1.18	
4	Feurra et al., 2013	18	FDI	online	Left M1 – Pz (35–35)	1	0.029	0.69	During rest
5								−0.15	During motor imagery
6	Tecchio et al., 2013	5	OP	online	Left M1 – Oz (35–35)	1	0.029	−2.06	
7	Wach et al., 2013	14	FDI	offline	Left M1 – right SOR (35–35)	1	0.029	0.00	
8	Cancelli et al., 2015a[a]	8	OP	online	Left M1 – Oz	0.85	0.024	−0.36	
9						0.875	0.025	−0.18	
10						0.9	0.026	−0.06	
11						2.175	0.062	0.26	
12						2.2	0.063	0.33	
13						2.225	0.064	0.17	
14	Cancelli et al., 2015b[a]	12	OP	Online	Left M1 – Oz (35–52)	2.2	0.063	0.85	Personalized tACS
15					Right M1 – Oz (35–52)	2.2	0.063	0.72	Personalized tACS
16			TA	Online	Left M1 – Oz (35–52)	2.2	0.063	0.70	Personalized tACS
17					Right M1 – Oz (35–52)	2.2	0.063	0.41	Personalized tACS
18			OP	Online	Left M1 – Oz (35–52)	2.2	0.063	0.33	Non-personalized tACS
19					Right M1 – Oz (35–52)	2.2	0.063	−0.29	Non-personalized tACS
20			TA	Online	Left M1 – Oz (35–52)	2.2	0.063	0.52	Non-personalized tACS
21					Right M1 – Oz (35–52)	2.2	0.063	0.82	Non-personalized tACS
22	Cappon et al., 2016	15	FDI	Offline	Left M1 – SMA (35–35)	1	0.029	−0.55	
23	Guerra et al., 2016	15	APB	Online	Left M1 – Pz (35–35)	1	0.029	0.37	
24	Heise et al., 2016	10	FDI	Offline	Left M1 – right SOR (9–35)	0.4	0.044	0.55	
25				Online		0.4	0.044	−0.67	
26				Offline	Left M1 – ring (9–35)	0.4	0.044	1.87	
27				Online		0.4	0.044	1.85	
28	Nakazono et al., 2016[b]	16	FDI	Offline	Left M1 – Pz (35–35)	1	0.029	0.42	
29				Online				0.27	
30	Rjosk et al., 2016	19	FDI	Offline	Left M1 – Pz (20.25–35)	1	0.049	0.08	
31	Braun et al., 2017	8	FDI	Online	Left M1 – Pz (10.75–35)	0.7	0.065	−0.61	
32	Nowak et al., 2017	19	FDI	Offline	Left M1 – right SOR (35–35)	0.69	0.020	−0.02	
33				Online				−0.16	
34	Raco et al., 2017	13	ECR	Online	Left M1 – Pz (14.72–30)	1	0.068	0.20	TMS at 90% of rMT
35								0.37	TMS at 100% of rMT
36								0.23	TMS at 110% of rMT
37								0.37	TMS at 120% of rMT
38								0.10	TMS at 130% of rMT
39								0.26	TMS at 140% of rMT
40	Cottone et al., 2018	13	OP	Online	Left M1 – Oz (35–35)	1	0.029	0.61	
41	Galasch et al., 2018	14	FDI	Offline	Left M1 – shoulder (35–100)	1.5	0.043	1.06	TMS at 110% of rMT
42								0.57	TMS at 130% of rMT
43								0.42	TMS at 150% of rMT
44	Guerra et al., 2018	18	FDI	Online	Left M1 – Pz (25–25)	0.61	0.024	−0.08	
45	Schilberg et al., 2018	15	FDI	Offline	Left M1 – Pz (9–9)	1.5	0.167	0.46	
46				Online		1.5	0.167	0.47	
47	Wischnewski et al., 2018	11	ADM	Offline	Left M1 – T7, F3, Cz, P3 (3.14 all)	2	0.637	0.93	

Abbreviations: ADM: Abductor digiti minimi muscle; APB: Abductor pollicis brevis muscle; ECR: Extensor carpi radialis muscle; FDI: Flexor digitorum indices muscle; OP: Opponens pollicis muscle; rMT: Resting motor threshold; SMA: Supplementary motor area; SOR: Supraorbital region; TA: Tibialis anterior muscle.

[a] Customized electrodes were used which followed the central sulcus.

[b] For calculation of effect size the different phases at which TMS was applied were pooled.

tACS has been of particular interest, since evidence from EEG studies suggests beta oscillations to be the default rhythm of the sensorimotor system [8,9]. Consequently, several studies have aimed to alter motor cortex excitability by applying tACS in the beta range over the motor cortex. In the present meta-analysis we show that beta-tACS is able to increase corticospinal excitability, with a small-to-moderate effect size in healthy volunteers ($\bar{E} = 0.29$).

Examination of tACS parameters revealed a significant effect of stimulation intensity. Whereas tACS studies applying currents of 1 mA peak-to-peak or less did not significantly affect MEP amplitudes ($\bar{E} = 0.16$), studies using more than 1 mA did increase MEP size with a medium effect size ($\bar{E} = 0.52$). Indeed, Cancelli and colleagues [16] specifically investigated the effects of tACS intensity and found that stimulation around 2.2 mA increased cortical excitability, whereas stimulation around 0.875 mA decreased cortical excitability. This finding contrasts with the results from a recent transcranial direct current stimulation (tDCS) study, indicating that for tDCS there is no superior effect of stimulation intensities above 1 mA [48]. However, our present results concur with a previous meta-analysis on the effects of tACS on cognitive performance [47]. In this previous study a significantly larger effect of tACS with an intensity of >1 mA ($\bar{E} = 0.90$) compared to effects of ≤1 mA intensities ($\bar{E} = -0.08$) was found for anterior-to-posterior montages. Evidence from both that and the present meta-analysis suggest that higher intensities may be required for tACS compared to tDCS, at least for some montages. It is important to note that tACS intensities reflect peak-to-peak amplitudes, whereas tDCS intensities relate to a constant current. That is, an intensity of 1 mA peak-to-peak implies that the maximum current applied on the head is 0.5 mA oscillating around a mean of 0. Furthermore, due to the oscillating nature of tACS, the intensity is only maximal at the peaks and submaximal at any other point of the cycle, meaning that less current passes through the skull with a given stimulation duration. Thus, tACS studies using an intensity of 1 mA (peak-to-

Table 2
Demographic and sensation data from each study.

	N	Age ±SD	Age range	Female/male	Right/left handed	Skin sensation	Phosphenes	Other sensation
Antal et al., 2008	10	26.4 ± 8.0	22–43	7/3	10/0	2	None reported	Headache by 6
Zaghi et al., 2010	11	27.8 ± 8.9		6/5	11/0	6	None reported	Headache by 1
Feurra et al., 2011	15	33.3 ± 8.8		7/8	15/0	0	4	None reported
Feurra et al., 2013	18	32.2 ± 7.0		8/10	18/0	0	0	None reported
Tecchio et al., 2013	5		25–56	4/1	5/0	None reported	None reported	None reported
Wach et al. 2013[a]	14	30.7 ± 9.3	20–58	7/7	14/0	7	Externally masked	Skin irritation after tACS by 1
Cancellli et al., 2015a	8		25–47	5/3	8/0	0	None reported	None reported
Cancellli et al., 2015b	12		25–47	9/3	12/0	None reported	None reported	None reported
Cappon et al., 2016	15	29	26–33	8/7		None reported	None reported	None reported
Guerra et al., 2016	15	25	20–33	8/7	15/0	0	0	None reported
Heise et al., 2016	10	22.8 ± 2.8	20–30	5/5	10/0	None reported	None reported	0
Nakazono et al., 2016	16	26.1 ± 5.5		6/10	16/0	2	3	None reported
Rjosk et al., 2016	19	27.8 ± 3.6	22–35	10/9	19/0	9	None reported	0
Braun et al., 2017	8	29.4 ± 4.9		0/8	8/0	None reported	None reported	None reported
Nowak et al. 2017[b]	19	24.9	21–30	10/9	19/0	0	0	0
Raco et al., 2017	13	25	20–28	7/6	13/0	0	0	0
Cottone et al., 2018	13	30.1 ± 8.9	19–51		13/0	6	None reported	None reported
Galasch et al., 2018	14	27.1 ± 3.1		4/10	14/0	None reported	3	None reported
Guerra et al. 2018[b]	18	26.4 ± 3.5		7/11	18/0	0	0	0
Schilberg et al., 2018	15	24.4 ± 3.7		10/5	15/0	None reported	None reported	None reported
Wischnewski et al., 2018	11	23.1 ± 3.4	19–28	9/2	11/0	5	0	0
Total	279			137/129	264/0	18.5%	7.2%	

"None reported" was used if skin sensations or phosphene perception was not explicitly reported by the authors. This may mean that indeed no sensations were observed, or that participants were not specifically asked about this.
Out of the studies that explicitly documented skin sensations (n = 14), 7 studies reported no skin sensation at all. In total, 18.5% of participants reported on feeling the stimulation.
Out of the studies that explicitly documented phosphenes, (n = 9), 6 studies reported no perception of phosphenes at all. In total, 7.2% of participants reported perceiving visual sensation.
[a] Wach et al. (2013) used a flickering computer screen to override any perception of tACS-induced retinal phosphenes.
[b] Nowak et al. (2017) and Guerra et al. (2018) used the phospene and sensation threshold as a marker for stimulation intensity.

peak) apply, in total, smaller currents than tDCS studies using an intensity of 1 mA. Since the current intensity that eventually reaches the cortical tissue is just a fraction of the intensity applied on the scalp, it is possible that alternating currents are ineffective if the intensity is too small. Our data suggest that tACS intensities larger than 1 mA may be desirable.

However, the exact relationship between induced currents and MEP amplitude needs to be further addressed in future studies, particularly because no significant correlation was found between superficial current density and effect size. This is surprising, since current density is a reflection of intensity controlled for electrode size and given the findings on tACS intensity, a positive relationship was expected. It should however be noted that low current density montages (<0.1 mA/cm^2) with large electrodes have been used by the majority of studies investigated here. More studies using HD electrode montages and parametrical manipulation of both stimulation intensities and electrode size are required to provide a definitive conclusion on this matter.

Furthermore, a significant effect of the tACS montage on MEP size was found. Montages that have been used most frequently are M1-Oz and M1-Pz. This is a noticeable difference compared to studies applying anodal tDCS, in which the 'traditional' montage is M1-SOR, yet for tACS this montage has only been used by four studies. This is remarkable since online anodal tDCS is ineffective in altering M1 excitability using posterior montages, at least when applied for brief stimulation periods of 4 s [49]. However, posterior montages were preferred by several studies to minimize the chance of participants perceiving phosphenes, which is more likely for, but not exclusive to, anterior montages [50,51]. Interestingly, our meta-analytic data showed that both posterior montages M1-Pz and M1-Oz, significantly increased MEP amplitudes. Even more surprisingly, the conventional M1-SOR montage did not significantly increase MEP amplitudes. These results may suggest that montages, and possibly other parameters, cannot simply be extrapolated from tDCS to tACS. However, results of the analysis on montages should be interpreted with caution, since the sample size was small and more research is needed to establish the optimal tACS montage for affecting MEP amplitude.

Furthermore, the comparison between online and offline tACS showed no significant difference on MEP amplitude. Despite comparable effect sizes, the mechanisms behind online and offline tACS effects are not necessarily the same. Typically, entrainment of cortical oscillations inducing neural synchronization is described as one of the main mechanism of tACS, which inherently relates to online effects. However, more recently STDP has been proposed to explain offline tACS effects [4,52–55]. According to this explanation, the effects of tACS dependent on the intrinsic natural frequency of recurrent networks in a particular brain region. Synaptic strength will increase when pre-synaptic potentials precede post-synaptic potentials, as is the natural order of synaptic transmission [56,57]. Consequently, tACS effects are predicted to be excitatory if the exogenous current frequency is similar or slightly below the endogenous recurrent network frequency [53,55]. Indeed, Vossen et al. [53] showed maximal offline tACS effects on oscillations slightly above the stimulated frequency (+0.5 Hz). Conversely, when post-synaptic precedes pre-synaptic activity, which may occur when exogenous current frequency is above the endogenous recurrent network frequency, an inhibitory effect may be observed [54]. Wischnewski et al. [25] suggested that 2 mA beta-tACS for 15 min can have after effects on MEP amplitudes for at least 60 min. This finding concurs with findings of Kasten et al. [24] who showed after-effect of tACS on hemodynamic cortical activity that lasted approximately 70 min.

The interaction between stimulation and recurrent network frequency, and thus the specific peak oscillating frequency, emphasizes that the effects of tACS are brain state-dependent [27,58].

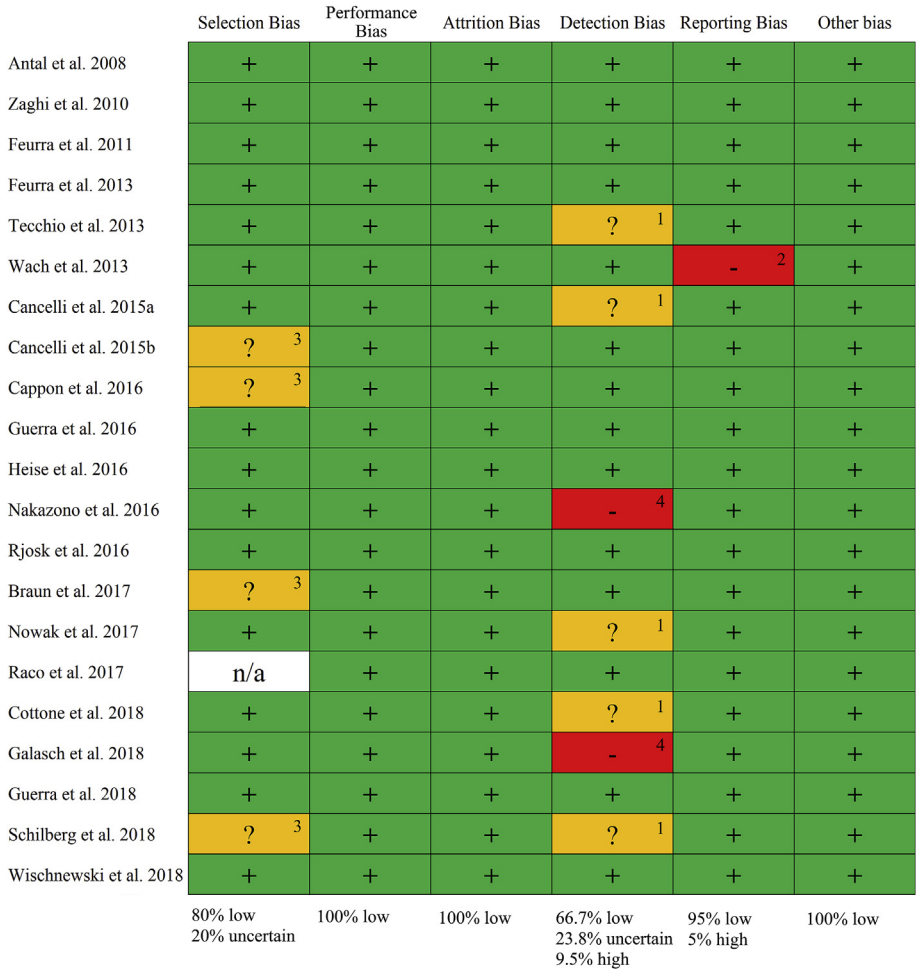

Fig. 2. Risk of bias assessment. [1] Unknown whether experimenter was blinded. [2] MEP amplitude data not reported. Data was retrieved via personal communication. [3] No report on participant blinding. [4] Experimenter was not blinded.

Table 3
Summary of statistical analysis on beta tACS parameters.

		N	KS test	Qtotal	$\bar{E}$	Statistic
Overall		47	KS = 0.10, p > .20	Qt = 49.43, p = .34	**0.287**	
Intensity	≤1 mA	30	KS = 0.15, p = .10	Qt = 33.60, p = .25	0.161	F(1,45) = 4.09, p = .049
	>1 mA	17	KS = 0.11, p > .20	Qt = 8.51, p = .93	**0.520**	
Montage	M1-Oz	16	KS = 0.19, p = .13	Qt = 15.47, p = .42	**0.316**	F(4,40) = 5.38, p = .001
	M1-Pz	17	KS = 0.18, p = .13	Qt = 12.89, p = .68	**0.284**	
	M1-SOR	6	KS = 0.25, p > .20	Qt = 3.37, p = .64	−0.05	
	M1-Shoulder	3	[a]	[a]	0.672	
	HD M1	3	[a]	[a]	**1.478**	
Online vs offline	Online	33	KS = 0.14, p = .13	Qt = 33.76, p = .38	**0.279**	F(1,45) = 0.43, p = .517
	Offline	14	KS = 0.16, p > .20	Qt = 14.51, p = .34	0.317	

[a] Sample size too small.

As is proposed for other non-invasive brain stimulation techniques, tACS cortical effects most likely follow homeostatic properties [10,59]. Given that the brain has limited amount of energetic resources [60], neural populations that are asynchronous may be susceptible tACS neuromodulation, whereas neural populations that are highly synchronous may be less susceptible to tACS [58]. Furthermore, recent studies have demonstrated that the phase-relation between the TMS pulse and tACS oscillation can affect the MEP size [33,34,36,40]. However, the results have not yet been consistent. For example, whereas Schilberg et al. [40] found the largest amplitudes when MEPs were tested on the rising flank of the oscillation, Guerra et al. [33] observed the largest MEP amplitudes at the trough of the oscillation. The divergent results may be explained by differences in other parameters between Guerra et al. [33] and Schilberg et al. [40], such as tACS intensity (1 mA vs. 1.5 mA, respectively) and electrode size (35 cm^2 vs. 9 cm^2, respectively). Yet, more studies are needed to elucidate phase-related influences of tACS on MEP amplitude.

When administering tACS it is important to consider the influence of transcutaneous and retinal stimulation [50,51,61]. For instance, Schutter & Hortensius [50] found that participants perceived phosphenes during 20 Hz tACS at an intensity of 1 mA for

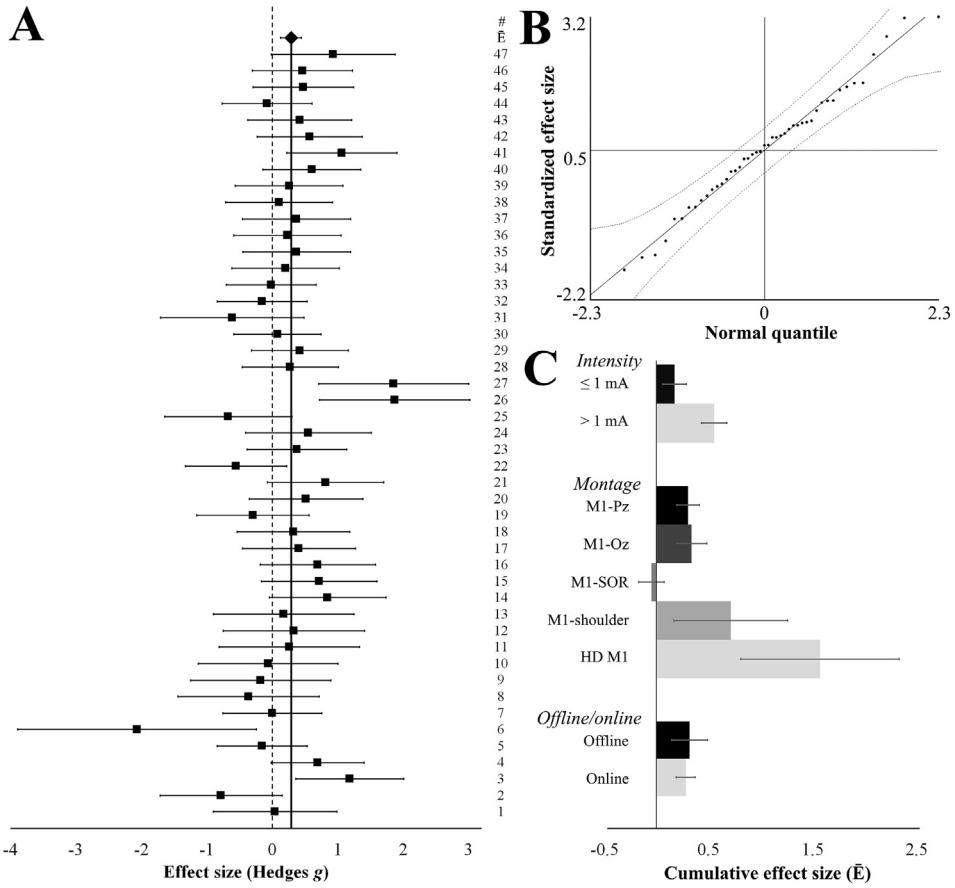

Fig. 3. A) Forest plot depicting all effect size estimates (Hedges' *d*) and 95% confidence interval. The number labels refer to the experiments listed in Table 1. B) Normal quantile plot The quantiles of the distribution of the effect size estimations are plotted against the quantiles of the standard normal distribution with a mean of 0 and standard deviation of 1. Data points are close to the line X = Y and within the 95% confidence bands indicating that the data set does not deviate from normality. C) Mean ± SEM effect size of intensity, montage and online/offline comparison.

an occipital-vertex montage and even at 0.25 mA for an frontopolar-vertex montage. Both montages induced voltage potentials that were measureable near the eyes and elicited phosphenes. Concerning transcutaneous effects, Asamoah et al. [61] demonstrated that peripheral nerve stimulation in rats and humans can induce entrainment of oscillations in the motor cortex. Therefore, controlling for these confounding effects is crucial in tACS experiments. Out of the studies investigated n the present meta-analysis that reported on these effects, 18.5% of participants reported having skin sensations and 7.2% of participants reported perceiving phosphenes (Table 2). It can therefore not be ruled out completely that such confounds may in part contribute to the present tACS findings. Therefore, attention should be directed to reducing skin sensations and phosphene perception if possible, by choosing optimal parameters and keeping electrode resistance as low as possible.

For the interpretation of the present meta-analysis it is relevant to acknowledge several limitations. First, due to the variability in parameters, the sample sizes were not sufficiently large for investigating detailed tACS setting specifics. As such analysis of montage and intensity do not take into account variables such as stimulation duration or scalp-cortex distance. Furthermore, superficial current density values were distributed unevenly. That is, a large amount of studies used conventional electrode setups with low current densities, whereas only a few used HD-montages with higher current densities. Therefore, interpretation of the present results on superficial current density remain tentative. Second, the effect sizes represented here reflect the difference between online/offline tACS and a pre-stimulation baseline, without an additional control condition, such as sham tACS. Since a number of valuable studies did not contain a sham condition [18–20,25,34,37], no comparative effect sizes were calculated. Third, the majority of studies in the meta-analysis investigated the left M1, which corresponds typically to the dominant hand. Also, hemispheric asymmetries in cortical excitability and beta power in resting state EEG have been reported [62]. Therefore, the results cannot simply be extrapolated to the right M1. Finally, relatively young individuals around the age of 25–30 were investigated by most studies. Since the effects and mechanisms of non-invasive brain stimulation are suggested to vary with age [28,63], the present results can therefore not be generalized to individuals of older age.

Some studies have investigated whether a beta-tACS-induced change in M1 excitability translates to a behavioral outcome variable such as motor learning. Pollok et al. [64] showed that acquisition in a serial reaction time task was enhanced after 20 Hz, compared to tACS at a control frequency. Furthermore, Krause et al. [65] showed that the retrieval of previously learned motor sequences was facilitated after beta-tACS. These findings may hint at future applications of tACS in clinical populations for aiding recovery of motor-related diseases, following in the footsteps of tDCS [66,67].

In conclusion, the results suggest that beta-tACS enhances the excitability of the corticospinal tract by a small-to-moderate effect size in healthy volunteers. This effect is particularly pronounced

when stimulation intensity was above 1 mA. Furthermore, montage significantly affected effect size, suggesting that posterior-occipital references are more effective than orbito-frontal ones when using beta-tACS. Altogether these findings may spark a venture into behavioral modulation using this technique. However, more research is needed to titrate the stimulation parameters and montages to further reduce variability and increase efficacy.

Conflicts of interest

M.A. Nitsche is a member of the Scientific Advisory Board of Neuroelectrics. All other authors declare no conflicts of interest.

References

[1] Priori A. Brain polarization in humans: a reappraisal of an old tool for prolonged non-invasive modulation of brain excitability. Clin Neurophysiol 2003;121:589–95. https://doi.org/10.1016/S1388-2457(02)00437-6.

[2] Kuo MF, Nitsche MA. Effects of transcranial electrical stimulation on cognition. Clin EEG Neurosci 2013;43(3):192–9. https://doi.org/10.1177/1550059412444975.

[3] Schutter DJLG. Syncing your brain: electric currents to enhance cognition. Trends Cogn Sci 2014;18(7):331–3. https://doi.org/10.1016/j.tics.2014.02.011.

[4] Herrmann CS, Rach S, Neuling T, Strüber D. Transcranial alternating current stimulation: a review of the underlying mechanisms and modulation of cognitive processes. Front Hum Neurosci 2013;7:279. https://doi.org/10.3389/fnhum.2013.00279.

[5] Fries P. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends Cogn Sci 2005;9(10):474–80. https://doi.org/10.1016/j.tics.2005.08.011.

[6] Fries P. Rhythms for cognition: communication through coherence. Neuron 2015;88(1):220–35. https://doi.org/10.1016/j.neuron.2015.09.034.

[7] Schutter DJLG, Knyazev GG. Cross-frequency coupling of brain oscillations in studying motivation and emotion. Motiv Emot 2012;36(1):46–54. https://doi.org/10.1007/s11031-011-9237-6.

[8] Benwell CSY, Learmonth G, Miniussi C, Harvey M, Thut G. Non-linear effects of transcranial direct current stimulation as a function of individual baseline performance: evidence from biparietal tDCS influence on lateralized attention bias. Cortex 2015;69:152–65. https://doi.org/10.1016/j.cortex.2015.05.007.

[9] Miniussi C, Harris JA, Ruzzoli M. Modelling non-invasive brain stimulation in cognitive neuroscience. Neurosci Behav Rev 2013;37(8):1702–12. https://doi.org/10.1016/j.neubiorev.2013.06.014.

[10] Ziemann U, Siebner HR. Modifying motor learning through gating and homeostatic metaplasticity. Brain Stimul 2008;1(1):60–6. https://doi.org/10.1016/j.brs.2007.08.003.

[11] Pfurtscheller G. Central beta rhythm during sensorimotor activities in man. Electroencephalogr Clin Neurophysiol 1981;51(3):253–64. https://doi.org/10.1016/0013-4694(81)90139-5.

[12] Pfurtscheller G, Lopes da Silva FH. Event-related EEG/MEG synchronization and desynchronization: basic principles. Clin Neurophysiol 1999;110(11):1842–57. https://doi.org/10.1016/S1388-2457(99)00141-8.

[13] Rossiter HE, Davis EM, Clark EV, Boudrias MH, Ward NS. Beta oscillations reflect changes in motor cortex inhibition in healthy ageing. Neuroimage 2014;91:360–5. https://doi.org/10.1016/j.neuroimage.2014.01.012.

[14] Hall SD, Barnes GR, Furlong PL, Seri S, Hillebrand A. Neuronal network pharmacodynamics of GABAergic modulation in the human cortex determined using pharmaco-magnetoencephalography. Hum Brain Mapp 2010;31:581–94. https://dx.doi.org/10.1002/hbm.20889.

[15] Muthukumaraswamy SD, Myers JFM, Wilson SJ, Nutt DJ, Lingford-Hughes A, Singh KD, Hamandi K. The effects of elevated endogenous GABA levels on movement-related network oscillations. Neuroimage 2012;66:36–41. https://doi.org/10.1016/j.neuroimage.2012.10.054.

[16] Cancelli A, Cottone C, Zito G, Di Giorgio M, Pasqualetti P, Tecchio F. Cortical inhibition and excitation by bilateral transcranial alternating current stimulation. Restor Neurol Neurosci 2015a;33:105–14. https://doi.org/10.3233/RNN-140411.

[17] Cancelli A, Cottone C, Di Giorgio M, Carducci F, Tecchio F. Personalizing the electrode to neuromodulate an extended cortical region. Brain Stimul 2015b;8:555–60. https://dx.doi.org/10.1016/j.brs.2015.01.398.

[18] Feurra M, Bianco G, Santarnecchi E, Del Testa M, Rossi A, Rossi S. Frequency-dependent tuning of the human motor system induced by transcranial oscillatory potentials. J Neurosci 2011;31(34):12165–70. https://doi.org/10.1523/JNEUROSCI.0978-11.2011.

[19] Feurra M, Pasqualetti P, Bianco G, Santarnecchi E, Rossi A, Rossi S. State-dependent effects of transcranial oscillatory currents on the motor system: what you think matters. J Neurosci 2013;33(44):17483–9. https://doi.org/10.1523/JNEUROSCI.1414-13.2013.

[20] Heise KF, Kortzorg N, Saturnino BC, Fijuyama H, Cuypers K, Thielscher A, Swinnen SP. Evaluation of a modified high-definition electrode montage for transcranial alternating current stimulation (tACS) of pre-central areas. Brain Stimul 2016;9:700–4. https://dx.doi.org/10.1016/j.brs.2016.04.009.

[21] Nowak M, Hinson E, van Ede F, Pogosyan A, Guerra A, Quinn A, et al. Driving human motor cortical oscillations leads to behaviorally relevant changes in local GABAA inhibition: a tACS study. J Neurosci 2017;37(17):4481–92. https://dx.doi.org/10.1523/JNEUROSCI.0098-17.2017.

[22] Tecchio F, Cancelli A, Cottone C, Tomasevic L, Devigus B, Zito G, et al. Regional personalized electrodes to select transcranial current stimulation target. Front Hum Neurosci 2013;7:131. https://doi.org/10.3389/fnhum.2013.00131.

[23] Gallasch E, Rafolt D, Postruznik M, Fresnoza S, Christova M. Decrease of motor cortex excitability following exposure to a 20 Hz magnetic field as generated by a rotating permanent magnet. Clin Neurophysiol 2018;129:1397–402. https://doi.org/10.1016/j.clinph.2018.03.045.

[24] Kasten FH, Dowsett J, Herrmann CS. Sustained aftereffect of α-tACS up to 70 min after stimulation. Front Hum Neurosci 2016;10:245. https://doi.org/10.3389/fnhum.2016.00245.

[25] Wischnewski M, Engelhardt M, Salehinejad MA, Schutter DJLG, Kuo MF, Nitsche MA. NMDA receptor-mediated motor cortex plasticity after 20 Hz transcranial alternating current stimulation. Cerebr Cortex 2018:bhy160. https://dx.doi.org/10.1093/cercor/bhy160.

[26] Zaghi S, de Freitas Rezende L, de Oliveira LM, El-Nazer R, Menning S, Tadini L, Fregni F. Inhibition of motor cortex excitability with 15Hz transcranial alternating current stimulation (tACS). Neurosci Lett 2010;479(3):211–4. https://doi.org/10.1016/j.neulet.2010.05.060.

[27] Fuscà M, Ruhnau P, Neuling T, Weisz N. Local network-level integration mediates effects of transcranial alternating current stimulation. Brain Connect 2018;8(4):212–9. https://doi.org/10.1089/brain.2017.0564.

[28] Ridding MC, Ziemann U. Determinants of the induction of cortical plasticity by non-invasive brain stimulation in healthy subjects. J Physiol 2010;588(13):2291–304. https://doi.org/10.1113/jphysiol.2010.190314.

[29] Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4(1):1. https://dx.doi.org/10.1186/2046-4053-4-1.

[30] Antal A, Boros K, Poreisz C, Chaieb L, Terney D, Paulus W. Comparatively weak after-effects of transcranial alternating current stimulation (tACS) on cortical excitability in humans. Brain Stimul 2008;1:97–105. https://doi.org/10.1016/j.brs.2007.10.001.

[31] Wach C, Krause V, Moliadze V, Paulus W, Schnitzler A, Pollok B. Effects of 10 Hz and 20 Hz transcranial alternating current stimulation (tACS) on motor functions and motor cortical excitability. Behav Brain Res 2013;241:1–6. https://dx.doi.org/10.1016/j.bbr.2012.11.038.

[32] Cappon D, D'Ostilio K, Garraux G, Rothwell J, Bisiacchi P. Effects of 10 Hz and 20 Hz transcranial alternating current stimulation on automatic motor control. Brain Stimul 2016;9:518–24. https://dx.doi.org/10.1016/j.brs.2016.01.001.

[33] Guerra A, Pogosyan A, Nowak M, Tan H, Ferreri F, Di Lazzaro V, Brown P. Phase dependency of the human primary motor cortex and cholinergic inhibition cancelation during beta tACS. Cerebr Cortex 2016;26:3977–90. https://doi.org/10.1093/cercor/bhw245.

[34] Nakazono H, Ogata K, Kuroda T, Tobimatsu S. Phase and frequency-dependent effects of transcranial alternating current stimulation on motor cortical excitability. PLoS One 2016;11(9):e0162521. https://dx.doi.org/10.1371/journal.pone.0162521.

[35] Rjosk V, Kaminski E, Hoff M, Gundlach C, Villringer A, Sehm B, Ragert P. Transcranial alternating current stimulation at beta frequency: lack of immediate effects on excitation and interhemispheric inhibition of the human motor cortex. Front Hum Neurosci 2016;10:560. https://doi.org/10.3389/fnhum.2016.00560.

[36] Braun V, Sokoliuk R, Hanslmayr S. On the effectiveness of event-related beta tACS on episodic memory formation and motor cortex excitability. Brain Stimul 2017;10:910–8. https://dx.doi.org/10.1016/j.brs.2017.04.129.

[37] Raco V, Bauer R, Norim S, Gharabaghi A. Cumulative effects of single TMS pulses during beta-tACS are stimulation intensity-dependent. Brain Stimul 2017;10:1055–60. https://dx.doi.org/10.1016/j.brs.2017.07.009.

[38] Cottone C, Cancelli A, Pasqualetti P, Porcaro C, Salustri C. A new, high-efficacy, non-invasive transcranial electric stimulation tuned to local neurodynamics. J Neurosci 2018;38(3):586–94. https://dx.doi.org/10.1523/JNEUROSCI.2521-16.2017.

[39] Guerra A, Bologna M, Paparella G, Suppa A, Colella D, Di Lazzaro V, et al. Effects of transcranial alternating current stimulation on repetitive finger movements in healthy humans. Neural Plast 2018:4593095. https://doi.org/10.1155/2018/4593095.

[40] Schilberg L, Engelen T, ten Oever S, Schuhmann T, de Gelder B, de Graaf TA, Sack AT. Phase of beta-frequency tACS over primary motor cortex modulates corticospinal excitability. Cortex 2018;103:142–52. https://doi.org/10.1016/j.cortex.2018.03.001.

[41] Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928. https://doi.org/10.1136/bmj.d5928.

[42] Hedges LV, Olkin I. Statistical methods for meta-analysis. Orlando, FL, USA: Academic Press; 1985. https://dx.doi.org/10.2307/1164953.

[43] Rosenthal R. The file drawer problem and tolerance for null results. Psychol Bull 1979;86:638–41. https://dx.doi.org/10.1037/0033-2909.86.3.638.

[44] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50(4):1088–101. https://doi.org/10.2307/2533446.
[45] Rosenberg MS, Adams DC, Gurevitch J. MetaWin: statistical software for meta-analysis: version 2.0. Sunderland, Massachusetts, USA: Sinauer Associates; 2000.
[46] Wang MC, Bushman BJ. Using the normal quantile plot to explore meta-analytic data sets. Psychol Methods 1998;3(1):46–54. https://doi.org/10.1037/1082-989X.3.1.46.
[47] Schutter DJLG, Wischnewski M. A meta-analytic study of exogenous oscillatory electric potentials in neuroenhancement. Neuropsychologia 2016;86:110–8. https://doi.org/10.1016/j.neuropsychologia.2016.04.011.
[48] Jamil A, Batsikadze G, Kuo HI, Labruna L, Hasan A, Paulus W, Nitsche MA. Systematic evaluation of the impact of stimulation intensity on neuroplastic after-effects induced by transcranial direct current stimulation. J Physiol 2017;595(4):1273–88. https://doi.org/10.1113/JP272738.
[49] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol 2000;527(3):633–9. https://dx.doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x.
[50] Schutter DJLG, Hortensius R. Retinal origin of phosphenes to transcranial alternating current stimulation. Clin Neurophysiol 2010;121(7):1080–4. https://doi.org/10.1016/j.clinph.2009.10.038.
[51] Schutter DJLG. Cutaneous retinal activation and neural entrainment in transcranial alternating current stimulation: a systematic review. Neuroimage 2016;140:83–8. https://doi.org/10.1016/j.neuroimage.2015.09.067.
[52] Veniero D, Vossen A, Gross J, Thut G. Lasting EEG/MEG aftereffects of rhythmic transcranial brain stimulation: level of control over oscillatory network activity. Front Cell Neurosci 2015;9:477. https://doi.org/10.3389/fncel.2015.00477.
[53] Vossen A, Gross J, Thut G. Alpha power increase after transcranial alternating current stimulation at alpha frequency (α-tACS) reflects plastic changes rather than entrainment. Brain Stimul 2015;8(3):499–508. https://doi.org/10.1016/j.brs.2014.12.004.
[54] Wischnewski M, Schutter DJLG. After-effects of transcranial alternating current stimulation on evoked delta and theta power. Clin Neurophysiol 2017;128(11):2227–32. https://doi.org/10.1016/j.clinph.2017.08.029.
[55] Zaehle T, Rach S, Herrmann CS. Trancranial alternating current stimulation enhances individual alpha activity in human EEG. PLoS One 2010;5(11):e13766. https://doi.org/10.1371/journal.pone.0013766.
[56] Hutcheon B, Yarom Y. Resonance, oscillation and the intrinsic frequency preferences of neurons. Trends Neurosci 2000;23:216–22. https://dx.doi.org/10.1016/S0166-2236(00)01547-2.
[57] Markram H, Lubke J, Frotscher M, Sakmann B. Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. Science 1997;275:213–5. https://dx.doi.org/10.1126/science.275.5297.213.
[58] Neuling T, Rach S, Herrmann CS. Orchestrating neuronal networks: sustained after-effects of transcranial alternating current stimulation depend upon brain states. Front Hum Neurosci 2013;7:161. https://doi.org/10.3389/fnhum.2013.00161.
[59] Karabanov A, Ziemann U, Hamada M, George MS, Quartarone A, Classen J, et al. Consensus paper: probing homeostatic plasticity of human cortex with non-invasive transcranial brain stimulation. Brain Stimul 2015;8(5):993–1006. https://doi.org/10.1016/j.brs.2015.06.017.
[60] Brem AK, Fried PJ, Horvath JC, Robertson EM, Pascual-Leone A. Is neuroenhancement by noninvasive brain stimulation a net zero-sum proposition? Neuroimage 2014;85(3):1058–68. https://doi.org/10.1016/j.neuroimage.2013.07.038.
[61] Asamoah B, Khatoun A, McLaughlin M. tACS motor system effects can be caused by transcutaneous stimulation of peripheral nerves. Nat Commun 2019;10(1):266. https://doi.org/10.1038/s41467-018-08183-w.
[62] Schutter DJLG, de Weijer AD, Meuwese JD, Morgan B, van Honk J. Interrelations between motivational stance, cortical excitability, and the frontal electroencephalogram asymmetry of emotion: a transcranial magnetic stimulation study. Hum Brain Mapp 2008;29(5):574–80. https://doi.org/10.1002/hbm.20417.
[63] Emonson MRL, Fitzgerald PB, Rogasch NC, Hoy KE. Neurobiological effects of transcranial direct current stimulation in younger adults, older adults and mild cognitive impairment. Neuropsychologia 2019;125:51–61. https://doi.org/10.1016/j.neuropsychologia.2019.01.003.
[64] Pollok B, Boysen AC, Krause V. The effect of transcranial alternating current stimulation (tACS) at alpha and beta frequency on motor learning. Behav Brain Res 2015;293:234–40. https://dx.doi.org/10.1016/j.bbr.2015.07.049.
[65] Krause V, Meier A, Dinkelbach L, Pollok B. Beta band transcranial alternating current stimulation (tACS) and direct current stimulation (tDCS) applied after initial learning facilitate retrieval of a motor sequence. Front Behav Neurosci 2016;10:4. https://doi.org/10.3389/fnbeh.2016.00004.
[66] Brunoni AR, Nitsche MA, Bolognini N, Bikson M, Wagner T, Merabet L, et al. Clinical research with transcranial direct current stimulation (tDCS): challenges and future directions. Brain Stimul 2012;5(3):175–95. https://doi.org/10.1016/j.brs.2011.03.002.
[67] Shin YI, Foerster A, Nitsche MA. Transcranial direct current stimulation (tDCS) – application in neuropsychology. Neuropsychologia 2015;69:154–75. https://doi.org/10.1016/j.neuropsychologia.2015.02.002.