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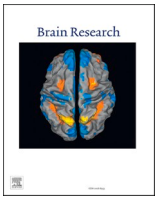

Determining the corticospinal, intracortical and motor function responses to transcranial alternating current stimulation of the motor cortex in healthy adults: A systematic review and *meta*-analysis

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A R T I C L E I N F O

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A B S T R A C T

Background: Transcranial Alternating Current Stimulation (tACS) employs low-intensity sinusoidal currents to influence cortical plasticity and motor function. Despite extensive research, inconsistent results require a comprehensive review of tACS efficacy.
Objective: This study systematically assesses tACS effects on corticospinal and intracortical excitability, and motor function over the motor cortex (M1), focusing on alpha, beta, and gamma frequencies.
Methods: Relevant studies were identified through database searches and citations were tracked until July 10, 2023. The methodological quality of the included studies (29) was evaluated by Downs and Black. Data synthesis involved *meta*-analysis (n = 25) and best evidence synthesis (n = 5).
Results: Meta-analysis revealed that alpha and beta tACS with intensities > 1 mA and tACS with individualised alpha frequency (IAF) increased corticospinal excitability (CSE). tACS over M1 improved motor function, irrespective of stimulation frequency and intensity. Sub-analysis showed that alpha and beta tACS with an intensity ≤ 1 mA led to improved motor function, while gamma tACS at 2 mA enhanced motor function. Additionally, beta tACS at a fixed frequency of 20 Hz, as well as both low gamma (30–55) and high gamma (55–80) tACS, resulted in improved motor function. A stimulation duration of 20 min led to improvements in both CSE and motor function, and tACS with electrode sizes smaller than 35 cm^2 and an electrode montage over M1-supraorbital region (SOR) were found to enhance motor function. Notably, both online and offline tACS improved motor function, regardless of stimulation factors.
Conclusion: tACS modulates CSE and improves motor function, with outcomes dependent on stimulation parameters and timing.

1. Introduction

Non-Invasive Brain Stimulation (NIBS) techniques encompass the use of electric or magnetic fields to modulate brain function and behaviour without creating an incision or damage to the skull or scalp (Barker et al., 1985; Paulus, 2011). Transcranial Electrical Stimulation (tES) involves the application of electrical currents to the scalp to modulate cortical activity and has gained considerable attention in neuroscience research and clinical applications (Paulus, 2011). A widely used NIBS technique that encompasses various modalities, tES includes transcranial Alternating Current Stimulation (tACS), transcranial Direct Current Stimulation (tDCS), transcranial Pulsed Current Stimulation (tPCS), and transcranial Random Noise Stimulation (tRNS) (Paulus, 2011; Fitzgerald, 2014). Among the different types of tES techniques, tACS is a notable approach as it entails the application of a low-intensity sinusoidal oscillatory current through two or more electrodes attached

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to the scalp, enabling the modulation of the oscillatory activity in the cortical regions (Antal, 2008; Helfrich, 2014). Previous research has provided evidence supporting the ability of tACS to enhance corticospinal excitability and improve motor function in healthy individuals (Pollok et al., 2015; Santarnecchi, 2017; Schilberg, 2018; Wischnewski et al., 2019). The underlying mechanisms through which tACS exerts its effects include two main proposed hypotheses: entrainment and spike-timing-dependent plasticity [(STDP); (Vogeti et al., 2022). Entrainment involves synchronizing the endogenous oscillations with the externally induced frequency through tACS (Vogeti et al., 2022). Endogenous oscillations denote spontaneous neural activity detectable through electroencephalography (EEG) and magnetoencephalography (MEG) during cognitive tasks, behavioral activities, rest, or unconscious states (Buzsaki and Draguhn, 2004).

Cortical oscillations encompass delta (0–3.5 Hz), theta (4–7.5 Hz), alpha (8–12 Hz), beta (12.5–30 Hz), and gamma (30–100 Hz) bands (Herrmann, 2016). Studies employing EEG and MEG consistently link oscillations in the alpha, beta, and gamma bands with motor function (Davis et al., 2012; Gaetz, 2011; Muthukumaraswamy, 2010; Pollok, 2014). Recognizing this link, tACS has emerged as a tool to modulate specific frequencies in targeted cortical regions. By introducing an external driving force, tACS holds potential for inducing plastic changes in cortical networks, resulting in functional improvements (Cabral-Calderin and Wilke, 2020; Herrmann, 2013; Vosskuhl et al., 2018). Moreover, tACS's effectiveness appears tied to aligning the induced frequency with the endogenous oscillations of the targeted neural network. The proposition is that tACS is more effective when the induced frequency closely matches or harmonically relates to ongoing oscillatory activity in cortical networks (Vogeti et al., 2022).

Spike-Timing Dependent Plasticity (STDP) refers to the phenomenon of plastic changes within a targeted neural network, influenced by the timing of neuronal firing. The concept posits that synaptic strength is augmented when pre-synaptic spikes occur before post-synaptic spikes, a process termed long-term potentiation (LTP). Conversely, when post-synaptic spikes precede pre-synaptic spikes, synapses are thought to weaken, leading to long-term depression (LTD) (Caporale and Dan, 2008; Dan and Poo, 2006). The aftereffects of tACS have been suggested to depend on STDP (Wischnewski et al., 2019; Zaehle et al., 2010; Zaghi, 2010).

The brain's functionality relies on intricate communication among distributed cortical networks. Coherent oscillations between distant cortical areas are hypothesized to play a pivotal role in facilitating functional cooperation and efficient information transfer (Fries, 2015; Siegel et al., 2012; Violante, 2017). By concurrently applying tACS over distant cortical regions, it becomes possible to synchronize neural oscillations and enhance functional connectivity (Cabral-Calderin and Wilke, 2020; Lafleur, 2020; Loffler, 2018). This synchronization is achieved through entraining cortical oscillations, where external electrical stimulation induces synchronization of endogenous oscillatory activity within targeted areas (Cabral-Calderin and Wilke, 2020; Herrmann, 2013; Vosskuhl et al., 2018).

The premotor cortex, M1, supplementary motor area, and cerebellar cortex have been identified as potential tACS targets since they are engaged in performing motor skills (Hardwick, 2013; Hikosaka, 2002). Whether stimulating a single region or multiple regions concurrently can enhance motor function. tACS has emerged as a promising technique for modulating corticospinal excitability and improving cortical and motor function (Berntsen, 2019; Fresnoza, 2018; Heise, 2016; Naro, 2017).

Transcranial magnetic stimulation (TMS) has been employed in tACS studies to assess corticospinal excitability, intracortical inhibition, and facilitation (Wischnewski et al., 2019; Fresnoza, 2018; Moliadze et al., 2010; Nowak, 2017). This involves measuring motor-evoked potentials (MEPs) and evaluating parameters like short-interval intracortical inhibition (SICI), long-interval intracortical inhibition (LICI), and intracortical facilitation (ICF) using both single-pulse and paired-pulse techniques. Several studies have demonstrated tACS's efficacy in modulating corticospinal excitability, leading to MEP amplitude changes and alterations in intracortical excitability (Lafleur, 2020; Fresnoza, 2018; Naro, 2017; Nowak, 2017; Naro, 2016). However, conflicting findings also exist, with some suggesting tACS reduces corticospinal excitability (Cappon, 2016; Giustiniani, 2019), while others indicate null effects (Moliadze et al., 2010; Bologna, 2019; Giustiniani, 2021; Kudo, 2022; Pozdniakov, 2021; Spampinato, 2021; Splittgerber, 2020).

Examining the effects of tACS on motor function has been pursued (Takeuchi and Izumi, 2021). With some studies highlighting improved motor function with tACS (Pollok et al., 2015; Santarnecchi, 2017; Naro, 2017; Naro, 2016; Harada, 2020), suggesting its potential for enhancing motor function. However, conflicting evidence also exists, with some studies failing to find significant effects on motor function (Zaghi, 2010; Giustiniani, 2021; Schoenfeld, 2021; Wessel, 2020).

Considering the emerging but equivocal body of evidence regarding the effects of tACS on corticospinal excitability/inhibition and motor function, examining which factors may contribute to these inconsistent findings is warranted. Important factors such as tACS frequency, electrode arrangement, electrode size, stimulation intensity, stimulation duration, differentiation between online and offline effects, and stimulation site are likely contributing to the heterogeneity of results. Thus, a systematic review with *meta*-analysis and best evidence synthesis will help clarify the corticospinal and motor function responses to different tACS frequencies. Therefore, the primary aim of this study was to systematically assess the effect of tACS on modulating corticospinal and intracortical excitability via various frequencies and stimulation intensities. The secondary aim was to determine the effect of tACS on improving motor function while comparing online and offline tACS effects. In addition, a comprehensive sub-group analysis focussing on tACS parameters in the alpha, beta, and gamma frequency ranges, was also performed to add clarity to the literature about the efficacy of tACS outcomes, offering further insights for future research and clinical use.

2. Methods

2.1. Search strategy

A standardized search strategy was employed to search multiple electronic databases, including Ovid MEDLINE, APA PsycInfo, CINAHL Plus, Cochrane Library, PubMed, Embase, ScienceDirect, Web of Science, SPORTDiscus, and Scopus. The search strategy adhered to the latest Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page, 2021). The databases were searched from their inception until 10th July 2023. The following keywords and phrases were included in the search strategy: "transcranial magnetic stimulation," "TMS," "TMS measurement," "motor evoked potential," "MEP," "cortical silent period," "cortical excitability," "intracortical inhibition," "intracortical facilitation," "short-latency afferent inhibition," "cortical plasticity," "corticospinal excitability," "corticomotor excitability," "neuronal plasticity," "neural inhibition," "dexterity," "manual dexterity," "dexter*," "fine," "gross," "finger tapping task," "coordination task," "bimanual task," "serial reaction time task," "balance," "postural control," "postural stability," "static balance," "postural balance," "gait," "walking," "walking speed," "lower limb*," "lower extremit*," "motor skill*," "motor learning," "motor skill learning," "motor skill acquisition," "motor performance," "motor activity," "motor behavior," "motor sequence learning," "sequence learning," "visuo-motor task," "visuomotor task," "sensorimotor task," "motor control," "function," "muscle strength," "muscle strengthening," "strength," "hand strength," "physical performance," "physical functional performance," "motor function," "functional performance," "maximum voluntary contraction," "functional outcome measure," and "reaction time," "transcranial alternating current stimulation," "transcranial Alternating Current Stimulation." Additionally, relevant articles

were sought from the references of the retrieved published literature. Fig. 1 illustrates the flow of the search strategy for the studies included in the *meta*-analysis.

2.2. Study selection

All search results obtained from the databases were imported into Covidence, a systematic review management software (https://www.covidence.org). Duplicate publications were identified and subsequently removed. Following this, all titles and abstracts were screened for eligibility according to predefined inclusion and exclusion criteria. Publications deemed irrelevant to the scope of this *meta*-analysis were excluded. The initial screening and review of included articles were conducted by two independent reviewers (MR and DJK). In cases where disagreements arose between the two reviewers, a third reviewer (US) was consulted to make the final decision on study selection, thereby resolving any discrepancies.

2.3. Eligibility Criteria-Exclusion and inclusion

The studies included in the review were required to meet the following criteria:

Full-text articles available in English.
Articles that involved healthy adults aged 18–59 years.

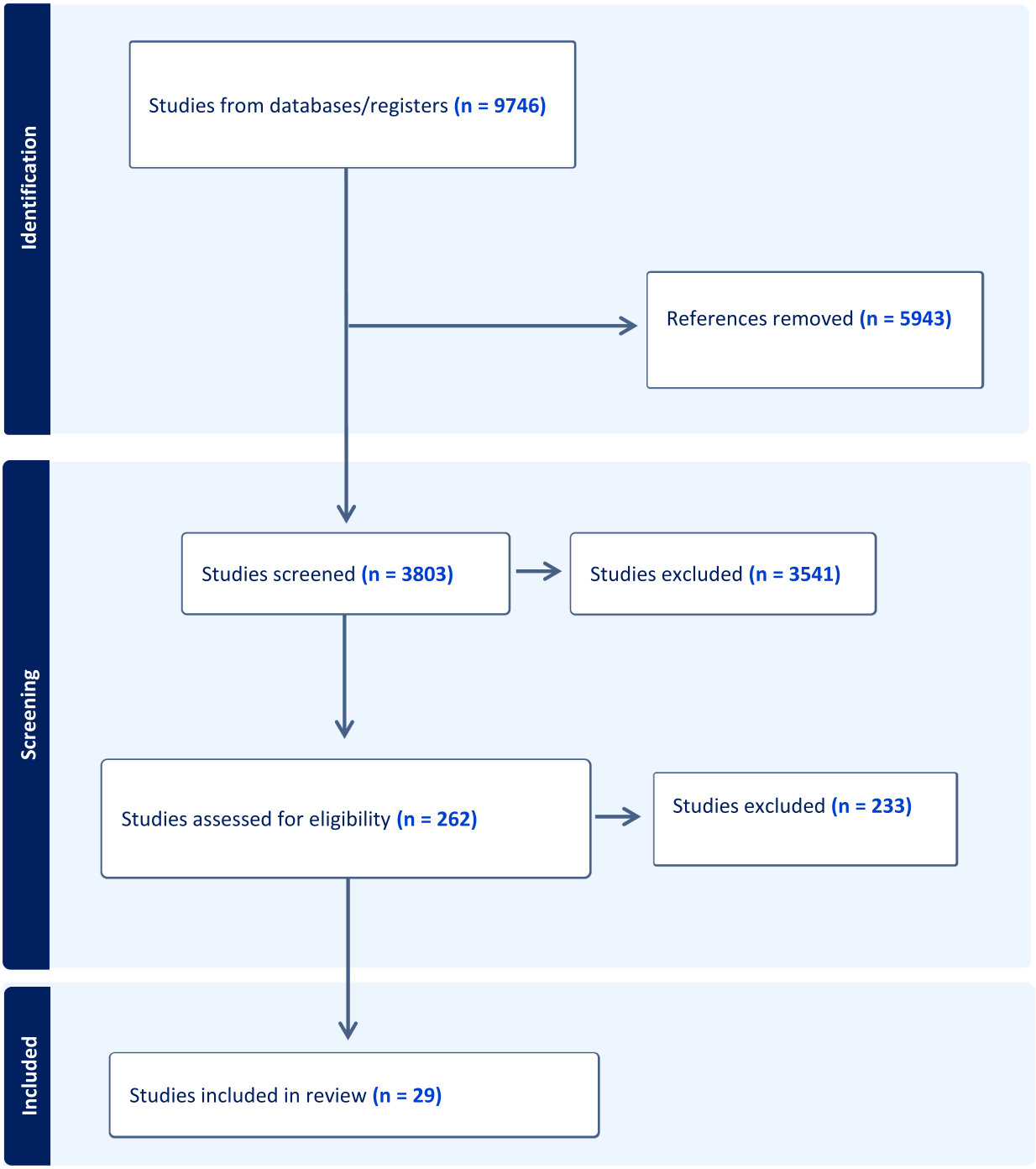

Fig. 1. PRISMA flow chart of the present *meta*-analysis.

Articles that employed tACS as an intervention over M1, with frequencies ranging from 10 to 80 Hz prior to (offline) or during (online) motor training.
Studies that included a sham condition as a control.
Studies that conducted measurements both before and after the intervention.
Included studies needed to measure changes in the motor cortex, including alterations in MEP amplitude, SICI, ICF and LICI.
Included studies were required to measure changes in the following aspects of motor function: upper limb function, strength, motor learning, lower limb function, balance, gait, and functional performance.

Exclusion criteria:

Studies conducted on populations with specific diseases or medical conditions.
Non-English publications.
Non-peer-reviewed publications and theses.
Limited peer-reviewed conference abstracts.
Studies involving other forms of transcranial electrical stimulation that were not alternating, including tDCS, tPCS, and tRNS.

2.4. Quality assessment and risk of bias

The quality of the included studies was evaluated using a modified version of the Downs and Black checklist (Downs and Black, 1998). Two authors (MR and DJK) independently assessed the studies based on 19 relevant items (1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 14, 15, 18, 20, 22, 23, 24, 27) out of a total of 27 items. These specific items were chosen to evaluate internal validity confounders, external validity, internal validity, and reporting bias. The selection was informed by prior studies (Alibazi, 2021; Siddique, 2022). In instances of disagreement between assessors on individual items, a third assessor (US) was consulted to achieve consensus. Based on the Downs and Black checklist score, studies were classified as either high quality (with a score of over 70 %) or low quality (with a score below 70 %). The methodological quality assessment of all included studies was carried out using the Cochrane Collaboration's risk of bias tool (Higgins, 2011). This tool assessed six key domains, encompassing sequence allocation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. A judgment of "high" or "low" risk of bias was assigned based on the fulfilment of criteria. In cases where information was insufficient, an "unclear" risk of bias was assigned. Possible publication bias was assessed using funnel plots (Sterne et al., 2001). Any disparities in the risk of bias assessment among assessors were addressed through discussion.

2.5. Data extraction

Data extraction from all included studies was independently conducted by two authors (MR and US) using a customized approach. The extracted data underwent assessment by both authors to ensure accuracy. The following information was gathered from the studies included in the *meta*-analysis: study characteristics (year, authors, sample size, and sample design), participant demographics (age, sex), and tACS parameters (frequency, intensity, duration, electrode size and placement). Moreover, outcome measures including MEP amplitude, SICI, ICF (expressed in μV, mV, ratio, percentage changes, and normalized to M_{MAX}), as well as any available behavioural data like reaction time, velocity, grip strength, frequency, and grating orientation task (measured in msec, m/sec^2, kg, Hz, pixels, and mm) were extracted from the text of the included studies. When only figures were provided, plot digitizer software was utilized to extract the data (Rohatgi, 2014). In instances where mean ± SD or SE values for post-intervention measures were not reported, raw data (means and SD) were either derived or calculated from SE, 95 % confidence intervals (CI), *P*-values, t-values, or F-values. All extracted data were meticulously recorded within an Excel spreadsheet.

2.6. Statistical analysis

Post-intervention data from both active tACS and sham tACS were utilized for the following outcome measures: MEP, SICI, and ICF, for corticospinal responses; and reaction time, time to complete, velocity, tactile spatial discrimination, hand grip strength, visuo-motor coordination, and fast finger tapping for motor responses. Data from the included studies were combined using RevMan 5.4.1 software (Higgins, 2019). A random-effects model was employed to accommodate systematic influences and random errors between study effect sizes in the *meta*-analysis. It must be noted that *P*-values only indicate the presence of effects, and emerging evidence suggests that the size of intervention effects is more reliable than *P*-values alone (Herbert, 2019). Therefore, the standardized mean difference (SMD) with 95 % confidence intervals (CI) was used to measure the intervention effect, given the varied presentation of outcome measures in the included studies. SMD values of $0.20 \leq 0.49$, $0.50 \leq 0.79$, and ≥ 0.80 represented small, medium, and large effect sizes, respectively (Cohen, 1988). Results were presented as SMD values followed by the corresponding 95 % CI and *P*-value. To compare post-intervention outcomes to sham stimulation, SMD was used. Heterogeneity among studies was evaluated using the Chi-squared test and I^2 analysis. The I^2 statistic indicated the percentage of variance between studies, with < 25 %, 25–75 %, and > 75 % considered as low, moderate, and high heterogeneity, respectively (Siddique, 2022; Higgins, 2003). If heterogeneity exceeded this threshold, a leave-one-out sensitivity analysis was performed to examine the influence of individual studies (Siddique, 2022; Manca, 2017).

Sub-analyses were conducted based on tACS frequency (alpha, beta, gamma, fixed frequency vs. individualised frequency, and low vs. high gamma), stimulation intensity (intensity of 1 mA and lower vs. intensities above 1 mA), stimulation duration (less than 10 min, 10 min, 15 min and 20 min), electrode size (smaller than 35 cm^2 vs. 35 cm^2) and electrode montage (M1-Supraorbital Region (SOR), and M1-Pz). Distinctions between online (concurrent tACS during task or outcome assessment) and offline (tACS prior to task or outcome measurement) effects were also considered.

In cases where studies lacked a comparison group or data extraction was not possible and consequently could not be included in the *meta*-analysis, a best evidence synthesis was performed following the approach outlined by Slavin (1995) (Slavin, 1995). The level of evidence for these studies was ranked using predefined criteria that had been utilized in prior literature (Alibazi, 2021; Siddique, 2022):

- No evidence: no supportive findings in the literature
- Conflicting evidence: inconsistent findings (<75 % of studies showing consistent results)
- Limited evidence: one low-quality study
- Moderate evidence: one high-quality study and/or two or more low-quality studies with generally consistent findings (≥75 % of studies showing consistent results)
- Strong evidence: two or more high-quality studies with generally consistent findings (≥75 % of studies showing consistent results)

Studies were categorized as high quality (≥70 %) or low quality (<70 %) based on their risk-of-bias assessment scores, following the criteria established in previous studies (Alibazi, 2021; Siddique, 2022). To visualize the effect sizes and their corresponding 95 % CIs, forest plots were generated using Prism 9 for Windows (GraphPad Software Inc, La Jolla, CA, USA). It is important to note that these plots were created solely for visualization purposes. Cohen's d effect sizes of 0.2 were classified as small, 0.5 as medium, and 0.8 as large comparative effects (Cohen, 1988).

3. Results

3.1. Study selection

The PRISMA flowchart (Fig. 1) illustrates the process of identifying, screening and evaluating the eligibility of studies included in this systematic review. An initial search across various databases yielded a total of 9,746 results. Upon removing duplicates, 3,803 studies remained for title and abstract screening. Among these, 3,541 studies were found to be irrelevant and were subsequently excluded for not meeting the eligibility criteria. A total of 262 full-text articles underwent eligibility assessment, and following a thorough evaluation, 233 studies were excluded for various reasons. Ultimately, 29 studies were included in the review. Out of which, 25 studies were included in *meta*-analysis, while five studies (one of which was included in both the *meta*-analysis and best evidence synthesis) were used for the best evidence synthesis. The characteristics of the included studies are detailed in Tables 1 and 2.

3.2. Quality and risk of bias assessment

The quality of the included studies underwent assessment using a modified version of the Downs and Black checklist, and the results are outlined in Table 3. Among the 29 included studies, 19 were categorized as high quality (>70 % score), while 10 were classified as low quality (<70 % score). The mean score across all studies averaged 14.24 ± 2.85 out of 20 (68.10 %).

The Cochrane Collaboration Risk of Bias Tool was employed to examine the risk of bias for each study. The majority of the studies exhibited a low risk of bias across key domains including sequence generation, allocation concealment, participant and personnel blinding, selective reporting, and attrition bias. However, there remained some uncertainty surrounding the blinding of outcomes, leading to its classification as unclear risk (Fig. 2).

To evaluate the potential publication bias within the main corticospinal excitability and motor function analyses, we initially computed the fail-safe number using the Rosenthal method (with $\alpha < 0.05$). This number signifies the amount of non-significant findings required to negate the overall mean effect (Rosenthal, 1979). In the examination of corticospinal excitability, the observed value was 0 ($P = 0.119$), signifying an absence of publication bias. Conversely, in the context of motor function analysis, the computed value stood at 319 ($P < 0.001$), indicating a discernible publication bias within this particular domain

Subsequently, we performed both Egger's Regression and Begg and Mazumdar Rank Correlation tests. The absence of statistical significance in the outcomes of these tests suggested a minimal risk of bias (Begg and Mazumdar, 1994; Egger, 1997). For the corticospinal excitability analysis, both Egger's Regression ($P = 0.095$) and Begg and Mazumdar Rank Correlation ($P = 0.197$) indicated no publication bias. Conversely, in the motor function analysis, Begg and Mazumdar Rank Correlation ($P = 0.079$) and Egger's Regression tests ($P < 0.001$) raised concerns about potential publication bias, particularly favouring positive results (Begg and Mazumdar, 1994; Egger, 1997). For visualization purposes, we explored the relationship between effect sizes and variance by creating plots (Fig. 3). A plot that exhibits symmetry around the mean effect size, resembling an inverted funnel, suggests the absence of publication bias (Egger, 1997).

Given the complexities inherent in the included studies, we conducted sub-group analyses as depicted in the flow diagram (Fig. 4). These analyses were undertaken to investigate the effects of tACS on corticospinal excitability, intracortical inhibition and facilitation, and motor function while considering diverse factors such as frequencies, online versus offline effects, stimulation intensities, electrode montage, electrode size and stimulation duration. To address the inherent heterogeneity among the studies, we employed a further sub-group analysis to explore the effects of tACS on both corticospinal and intracortical excitability, considering various aspects such as the employed frequency (ranges alpha, beta, and gamma), electrode montage, electrode size and duration of stimulation (refer to sections 3.3.3 to 3.3.13).

Sub-group analyses were also performed to examine the effects of tACS on motor function, considering stimulation frequencies (within the alpha, beta, and gamma ranges), electrode montage, electrode size and duration of stimulation (refer to sections 3.4.2 to 3.4.7 and 3.4.9-3.4.11) and the application of tACS before (offline) or during motor tasks (online) (refer to section 3.4.8). In addition, we conducted subgroup analyses based on studies that utilized tACS with intensities of 1 mA and below, as well as studies that used intensities above 1 mA. These analyses aimed to elucidate potential variations in the effects of tACS over the motor cortex (M1) concerning corticospinal and intracortical excitability and motor function. All figures for each subset are provided in the supplementary file, including standardised mean difference, inverse variance, random effect model, confidence interval, degree of freedom, inconsistency statistic, and P-value.

3.3. Effects of tACS on corticospinal and intracortical excitability

3.3.1. The effects of alpha, beta, and gamma tACS over motor cortex on corticospinal excitability

A total of twelve studies (Antal, 2008; Schilberg, 2018; Fresnoza, 2018; Moliadze et al., 2010; Nowak, 2017; Cappon, 2016; Giustiniani, 2019; Pozdniakov, 2021; Splittgerber, 2020; Rjosk, 2016; Wang, 2021; Therrien-Blanchet, 2023) investigated the influence of tACS ($n = 228$ participants) on MEP amplitude compared to sham stimulation ($n = 230$ participants) over M1. Among these studies, six employed alpha tACS (Antal, 2008; Schilberg, 2018; Fresnoza, 2018; Cappon, 2016; Pozdniakov, 2021; Wang, 2021), nine utilized beta tACS (Antal, 2008; Schilberg, 2018; Nowak, 2017; Cappon, 2016; Pozdniakov, 2021; Splittgerber, 2020; Rjosk, 2016; Wang, 2021; Therrien-Blanchet, 2023), and four studies implemented gamma tACS (Antal, 2008; Moliadze et al., 2010; Nowak, 2017; Giustiniani, 2019).

The pooled data outcomes indicated that, regardless of the frequency, tACS applied over M1 did not exhibit a significant effect on corticospinal excitability (SMD −0.14, 95 % CI −0.48 to 0.20, $n = 230P = 0.43$, Fig. 5). The level of heterogeneity among the studies was moderate ($Tau^2 = 0.24$; $Chi^2 = 34.00$, $df = 11$, $P = 0.004$; $I^2 = 68$ %).

Among the twelve studies, eight (Antal, 2008; Moliadze et al., 2010; Nowak, 2017; Cappon, 2016; Pozdniakov, 2021; Splittgerber, 2020; Rjosk, 2016; Wang, 2021) utilized tACS with an intensity of 1 mA or lower. The findings indicated that tACS with this intensity over M1 did not significantly affect corticospinal excitability (SMD −0.35, 95 % CI −0.78 to 0.07, $n = 136$, $P = 0.11$, Fig. 5). The level of heterogeneity among the studies was moderate ($Tau^2 = 0.25$; $Chi^2 = 20.79$, $df = 7$, $P = 0.004$; $I^2 = 66$ %).

Conversely, four studies (Schilberg, 2018; Fresnoza, 2018; Giustiniani, 2019; Therrien-Blanchet, 2023) applied tACS with intensities exceeding 1 mA over M1. The results revealed no significant effect (SMD 0.28, 95 % CI −0.08 to 0.65, $n = 92$, $P = 0.13$, Fig. 5), and there was a moderate level of heterogeneity among the studies ($Tau^2 = 0.04$; $Chi^2 = 4.15.$, $df = 3$, $P = 0.25$; $I^2 = 28$ %).

3.3.2. The effects of alpha, beta, and gamma tACS over motor cortex on intracortical inhibition and facilitation

Three studies (Zaghi, 2010; Fresnoza, 2018; Nowak, 2017) investigated the effect of tACS over M1 on intracortical inhibition and facilitation. The combined results showed that tACS had no significant modulatory effect on SICI (SMD −0.11, 95 % CI −0.96 to 0.74, $n = 44$, $P = 0.80$, Fig. 6), and the level of heterogeneity was moderate ($Tau^2 = 0.041$; $Chi^2 = 7.45$, $df = 2$, $P = 0.02$; $I^2 = 73$ %). Similarly, across the same three studies (Zaghi, 2010; Fresnoza, 2018; Nowak, 2017), the results indicated no effect of tACS over M1 on ICF (SMD −0.52, 95 % CI −1.86 to 0.82, $n = 44$, $P = 0.45$, Fig. 6), with a high level of heterogeneity ($Tau^2 = 1.22$; $Chi^2 = 16.55$, $df = 2$, $P = 0.003$; $I^2 = 88$ %). Out of the three studies, two (Zaghi, 2010; Nowak, 2017) applied tACS with an

Table 1
Study and experiment characteristics of studies investigating corticospinal and intracortical excitability.

Author	Study Design	Participant's characteristics	tACS parameter	Electrode position and size	Online/ Offline	Measure	tACS effect	D & B Score (Out of 20)	Meta-Analysis	Best Evidence Synthesis
Antal et al 2008 (Antal, 2008)	Crossover	$n = 10$ healthy subjects (7 females, mean age = 26.4 ± 8.0)	10 Hz, 15 Hz, 45 Hz, sham (0.4 mA, about 7 min)	Active: left M1 (4 × 4 cm) Reference: right SOR (5 × 10 cm)	Offline	MEPs (mV)	No effect of tACS at any frequency	16	✓	
Bologna et al 2019 (Bologna, 2019)	Crossover	$n = 13$ healthy subjects (4 females, mean age: 27.5 ± 5.1)	20 Hz, 70 Hz (1 mA, about 15 min)	Active: left M1 (5 × 5 cm) Reference: Pz (5 × 5 cm)	Online	MEPs (mV) FDI	No effect for beta and gamma tACS during and after stimulation	14		✓
Cappon et al 2016 (Cappon, 2016)	Randomly assigned	$n = 15$ healthy subjects (8 females, mean age: 29)	10 Hz, 20 Hz, sham (1 mA, 10 min)	Active: left M1 (5 × 7 cm), Reference: SMA (5 ×7 cm)	Offline	MEPs (Percent variation) FDI	Beta tACS reduced CSE and there was no effect for alpha tACS	10	✓	
Fresnoza et al 2018 (Fresnoza, 2018)	Randomly assigned	$n = 12$ healthy subjects, (mean age: 24.16)	IAF, sham (1.5 mA, 10 min)	Active: left M1 (35 cm^2) Reference: right SOR (100 cm^2)	Offline	MEPs SICI ICF (μV) FDI	Alpha tACS increased CSE for both young and older adults. Alpha tACS improved SICI only in young adults Alpha tACS had no effect on ICF	15	✓	
Giustiniani et al 2019 (Giustiniani, 2019)	Crossover	$n = 17$ healthy subjects (mean age 24.5 ± 3.5)	40 Hz, sham (2 mA, about 5 min)	Active: left M1 (5 × 5 cm) Reference: right SOR (5 × 5 cm)	Offline	MEPs (μV) FDI	Gamma tACS reduced CSE	13	✓	
Heise et al 2016 (Heise, 2016)	Crossover	$n = 10$ healthy subjects (5 female, mean age: 22.81 ± 2.76)	20 Hz, sham (400 μA, 10 min)	Active: left M1 (3.4 cm diameter, 9 cm^2) Reference: right SOR	Online and offline	MEPs (in %, normalized to baseline) FDI	Beta tACS had no effect on CSE	12		✓
Kudo et al. 2022 (Kudo, 2022)	Crossover	$n = 19$ healthy subjects (8 females, mean age: 25 ± 3)	IBF, sham (2 mA, 10 min)	Active: right Leg motor cortex (41.0 cm^2) Reference: right SOR (35 cm^2)	Offline	MEPs (normalized by baseline) TA	Beta tACS had no effect on CSE	10		✓
Moliadze et al 2010 (Moliadze et al., 2010)	Randomly assigned	$n = 21$ healthy subjects (mean age: 25.9 ± 2.35)	80 Hz, sham (1 mA, 10 min)	Active: M1 (4 × 4 cm), Reference: Forehead (14 × 6 cm)	Online and Offline	MEPs, SICI ICF (mV) FDI	Gamma tACS had no effect on CSE, SICI, ICF	16	✓	
Nowak et al 2017 (Nowak, 2017)	Crossover	$n = 20$ healthy subjects (11 females, mean age: 24.9)	IBF, 75 Hz, sham (Beta frequency: 0.69 ± 0.11 mA Gamma frequency: 1.3 ± 0.36 mA 20 min)	Active: left M1 (5 × 7 cm) Reference: right SOR (5 × 7 cm)	Online and offline	MEPs, SICI, ICF (% change) FDI	Gamma tACS improved SICIBeta tACS had no effect on CSE, SICI and ICF	12	✓	
Pozdniakov et al 2021 (Pozdniakov, 2021)	Crossover	$n = 19$ healthy subjects (10 females, mean age: 21.1 ± 2.7)	10, 20 Hz, sham (1 mA, 15 min)	Active: M1 (5 × 7 cm)Reference: ipsilateral shoulder (5 × 7 cm)	offline	MEPs (% logaritmized MEPs) FDI	Alpha and beta tACS had no effect on CSE	14	✓	
Rjosk et al 2016 (Rjosk, 2016)	Crossover	$n = 19$ healthy subjects (10 females, mean age: 27.84 ± 0.82)	20 Hz, sham (1 mA, 10 min)	Active: left M1 (4.5 × 4.5 cm) Reference: Pz (5 × 7 cm)	Offline	IHI MEP size (mV) FDI	Beta tACS had no effect on CSE or IHI	17	✓	
Schilberg et al 2018 (	Crossover	$n = 15$ healthy subjects (10	IAF, IBF (1.5 mA, 36.5 min)	Active: left M1 (3 × 3 cm)	Online and Offline	MEPs (mV) FDI	Beta tACS increased CSEAlpha	10	✓	

(*continued on next page*)

Table 1 (*continued*)

Author	Study Design	Participant's characteristics	tACS parameter	Electrode position and size	Online/ Offline	Measure	tACS effect	D & B Score (Out of 20)	Meta-Analysis	Best Evidence Synthesis
Schilberg, 2018)		females, mean age: 24.4 ± 3.7)		Reference: Pz (3 × 3 cm)			tACS had no effect on CSE			
Schutter et al 2011 (Schutter and Hortensius, 2011)	Randomly assigned	*n* = 6 healthy subjects (3 females, mean age: 23.33 ± 2.94)	10 Hz (1 mA,10 min)	Active: left M1 (5 × 7 cm) Reference: right M1 (5 × 7 cm)	Offline	MEPs (mV) APB	Alpha tACS had no effect on CSE	10		✓
Splittgerber et al 2020 (Splittgerber, 2020)	Crossover	*n* = 28 healthy subjects (9 females, mean age: 24.4 ± 2.5)	20 Hz, sham (1 mA, 10 min)	Active: right M1 (5 × 7 cm) Reference: contralateral SOR (5 × 7 cm)	Offline	MEPs, SICI, ICF (mV) FDI	Beta tACS had no effect on CSE, SICI and ICF	17	✓	
Therrien-Blanchet 2023 et al (Therrien-Blanchet, 2023)	Cross over	*n* = 48 healthy subjects (mean age: 23.10 ± 3.64)	20 Hz, sham (2 mA, 20 min)	Active: left M1 (35 cm^2) Reference: SOR (35 cm^2)	Offline	MEPs amplitude (mV) APB	Beta tACS had no effect on CSE		✓	
Wang et al 2021 (Wang, 2021)	Randomly assigned	*n* = 28 healthy subjects (10 females, mean age: 24.29 ± 3.30)	10, 20 Hz, sham (1 mA, 10 min)	Active: left M1 (5 × 5 cm) Reference: over the contralateral SOR (5 × 5 cm)	Offline	MEPs (mV) FDI	Beta tACS reduced CSE	12	✓	
Wischnewski et al 2019 (Wischnewski, 2019)	Randomly assigned	*n* = 11 healthy subjects (9 females, mean age: 23.1 ± 3.4)	20 Hz (2 mA, 15 min)	Active: M1 Reference: T7, F3, Cz, and P3 (Round electrode, surface area: 3.14 cm^2)	Offline	MEPs ADM	Beta tACS increased CSE	11		✓
Zaghi et al 2010 (Zaghi, 2010)	Crossover	*n* = 11 healthy adults (6 females, mean age: 27.8 ± 8.9)	15 Hz, sham (1 mA, 20 min)	Active: C3 (left M1)Reference: C4 (right M1) (12.56 cm^2)	Offline	SICI ICF (mV) FDI	Beta tACS reduced CSE and decreased ICF	**15**	✓	

Abbreviations: ADM: Abductor digiti minimi muscle; APB: Abductor pollicis brevis muscle; CSE: Corticospinal Excitability; Cz: Midline central; D & B score: Downs and Black checklist score; F3: Left dorsolateral prefrontal cortex; FDI: Flexor digitorum indices muscle; IAF: Individualised Alpha Frequency; IBF: Individualised Beta Frequency; ICF: Intracortical Facilitation: IHI: Interhemispheric Inhibition; M1: Motor cortex; P3: Left Parietal; Pz: Midline parietal; SICI: Short interval Intracortical Inhibition; SMA: Supplementary Motor Area; SOR: Supraorbital Region; T7: Left posterior temporal; TA: Tibialis anterior muscle; tACS: transcranial Alternating Current Stimulation.

intensity of 1 mA. These studies revealed that tACS with an intensity of 1 mA had no effect on either SICI (SMD −0.35, 95 % CI −1.70 to 1, n = 32, P = 0.61) or ICF (SMD −0.82, 95 % CI −3.24 to 1.61, n = 32, P = 0.51). The level of heterogeneity between studies for both SICI (Tau^2 = 0.80; Chi^2 = 6.42, df = 1, P = 0.01; I^2 = 84 %) and ICF (Tau^2 = 2.88; Chi^2 = 16.24, df = 1, P < 0.001; I^2 = 94 %) was high.

3.3.3. *The effects of alpha tACS over motor cortex on corticospinal excitability*

A total of six studies (Antal, 2008; Schilberg, 2018; Fresnoza, 2018; Cappon, 2016; Pozdniakov, 2021; Wang, 2021) investigated the effects of alpha tACS over M1 on MEP amplitude. The combined results indicated that alpha tACS over M1 had no significant effect on corticospinal excitability (SMD 0.21, 95 % CI −0.20 to 0.61, n = 87, P = 0.32, Fig. 5), and the level of heterogeneity among the studies was moderate (Tau^2 = 0.11; Chi^2 = 8.93, df = 5, P = 0.11; I^2 = 44 %).

Among the four studies (Antal, 2008; Cappon, 2016; Pozdniakov, 2021; Wang, 2021) that applied alpha tACS with an intensity of 1 mA or lower, the combined results revealed no significant effect (SMD −0.06, 95 % CI −0.42 to 0.30, n = 87, P = 0.30, Fig. 5), and there was no observed heterogeneity (Tau^2 = 0.00; Chi^2 = 1.85, df = 3, P = 0.60; I^2 = 0 %).

Two studies (Schilberg, 2018; Fresnoza, 2018) applied alpha tACS with an intensity of 1.5 mA. The findings indicated an increase in corticospinal excitability following alpha tACS with the intensity of 1.5 mA (SMD 0.84, 95 % CI 0.28, to1.40, n = 27, P = 0.003, Fig. 5), and there was no observed heterogeneity (Tau^2 = 0.00; Chi^2 = 0.05, df = 1, P = 0.83; I^2 = 0 %).

3.3.4. *The effects of 10 Hz tACS versus individualised alpha frequency on corticospinal excitability*

Four studies (Antal, 2008; Cappon, 2016; Pozdniakov, 2021; Wang, 2021) specifically examined the effect of 10 Hz tACS over M1 on MEP amplitude. The combined results showed that 10 Hz tACS did not have a significant modulatory effect on corticospinal excitability (SMD −0.06, 95 % CI −0.42 to 0.30, n = 60, P = 0.73, Fig. 5), and there was no observed heterogeneity (Tau^2 = 0.00; Chi^2 = 1.85, df = 3, P = 0.60; I^2 = 0 %).

Two studies (Schilberg, 2018; Fresnoza, 2018) applied tACS over M1 with individualised alpha frequency. The findings indicated an increase in corticospinal excitability following tACS with IAF (SMD 0.84, 95 % CI 0.28, to1.40, n = 27, P = 0.003, Fig. 5), and there was no observed heterogeneity (Tau^2 = 0.00; Chi^2 = 0.05, df = 1, P = 0.83; I^2 = 0 %).

3.3.5. *The effects of beta tACS over motor cortex on corticospinal excitability*

Nine studies (Antal, 2008; Schilberg, 2018; Nowak, 2017; Cappon, 2016; Pozdniakov, 2021; Splittgerber, 2020; Rjosk, 2016; Wang, 2021; Therrien-Blanchet, 2023) were included in the assessment of the effect of beta tACS over M1 on corticospinal excitability. The results indicated

Table 2
Study and experiment characteristics of studies investigating motor function.

Author	Study Design	Participant's characteristics	tACS parameter	Electrode position and size	Online/ Offline	Measure or task	tACS effect	D & B Score (Out of 20)	Meta-Analysis	Best Evidence Synthesis
Antal et al 2008 (Antal, 2008)	Crossover	$n = 8$ healthy subjects (5 females, mean age: 26.4 ± 8.0)	10 Hz, sham (0.4 mA, about 7 min)	Active: left M1 (4 × 4 cm) Reference: right SOR (5 × 10 cm)	Online	SRTT(ms)	Alpha tACS facilitated motor acquisition during stimulation	16	✓	
Berntsen et al 2019 (Berntsen, 2019)	Randomly assigned	$n = 60$ healthy subjects (32 females, mean age: 24.15 ± 4.38)	IAF, sham (1 mA, 20 min)	Active: left M1 (3 × 3 cm) Reference: right SOR (3 × 3 cm)	Offline	Bilateral hand motor sequenceMotor sequence reproduction, (correct sequence reproduced) (% change)	Alpha-tACS had no effect on motor acquisition	12	✓	
Bologna et al 2019 (Bologna, 2019)	Crossover	$n = 16$ healthy subjects (4 females, mean age: 27.4 ± 3.9)	20 Hz, 70 Hz, sham (1 mA, about 15 min)	Active: left M1 (5 × 5 cm) Reference: Pz (5 × 5 cm)	Online	Rapid abduction of index finger task (Acceleration ratio m/sec^2)	Beta tACS had a detrimental effect on motor acquisition during stimulation Beta tACS had no effect on motor retention after stimulation Gamma tACS improved motor acquisition during stimulation, but it had a detrimental effect on motor retention	14	✓	
Cappon et al 2016 (Cappon, 2016)	Randomly assigned	$n = 16$ healthy subjects (4 females, mean age: 27.4 ± 3.9) $n = 15$ healthy subjects (8 females, mean age 29)	10 Hz, 20 Hz, sham (1 mA, 10 min)	Active: left M1 (5 × 7 cm), Reference: SMA (3 cm anterior to Cz) (5 × 7 cm)	Online and offline	Visou-motor task(ms)	Beta tACS reduced reaction time, Alpha tACS had no effect	**10**	✓	
Fresnoza et al 2020 (Fresnoza, 2020)	Crossover	$n = 20$ healthy subjects (mean age: 23.8 ± 3.90)	IAF, IAF + 2 Hz, sham (1.5 mA, 15 min)	Active: left M1 (5 × 7 cm) Reference: right SOR (5 × 7 cm)	Offline	SRTT(ms)	Alpha tACS and alpha + 2 Hz-tACS improved consolidation of general motor and sequence-specific skills during post-tACS training sessions in the old group. Alpha-tACS impaired the consolidation of sequence-specific skills and the alpha + 2 Hz-tACS was detrimental to the consolidation of both skills in the young group	**16**	✓	
Giustiniani et al 2019 (Giustiniani, 2019)	Crossover	$n = 17$ healthy subjects (mean age 24.5 ± 3.5)	40 Hz, sham (2 mA, about 5 min)	Active: left M1 (5 × 5 cm) Reference: right SOR (5 × 5 cm)	Online	SRTT(ms)	Gamma tACS inhibited motor acquisition	**13**	✓	
Giustiniani et al 2021a (Giustiniani, 2021)	Randomly assigned	$n = 17$ healthy subjects (10 female, mean age: 27.29 ± 10.65)	50 Hz, sham (1.5 mA, 10 min)	Active: left M1 (5 × 5 cm) Reference: right M1 (5 × 5 cm)	Offline	Handgrip Test (kg)	Gamma tACS could not improve grip strength	**15**	✓	
Harada et al 2020 (Harada, 2020)	Randomly assigned	$n = 33$ healthy subjects	10 Hz, 20 Hz, sham	Active: left M1 (5 × 7 cm) Reference:	Offline	Visuomotor adaptation task	Alpha tACS facilitated the initial	**14**	✓	

(*continued on next page*)

Table 2 (*continued*)

Author	Study Design	Participant's characteristics	tACS parameter	Electrode position and size	Online/ Offline	Measure or task	tACS effect	D & B Score (Out of 20)	Meta-Analysis	Best Evidence Synthesis
		(mean age: 21.82 ± 5.73)	(1 mA, 10 min)	right SOR (5 × 7 cm)		(Peak velocity, m/sec^2)	motor acquisition Beta tACS had no effect			
Krause et al 2016 (Krause, 2016)	Randomly assigned	$n = 36$ healthy subjects 10 Hz tACS (7 males, 5 females, mean age: 26.17 ± 1.18) 20 Hz tACS (8 males, 4 females; mean age: 26.42 ± 1.18) sham group (7 males, 5 females; mean age: 25.33 ± 0.94)	10 Hz, 20 Hz, sham (1 mA, 10 min)	Active: left M1 (5 × 7 cm) Reference: right SOR (5 × 7 cm)	Offline	SRTT (ms)	Beta tACS facilitated retrieval of motor sequence Alpha tACS had no effect	16	✓	
Moliadze et al 2010 (Moliadze et al., 2010)	Randomly assigned	$n = 21$ healthy subjects (mean age: 25.9 ± 2.35 years)	80 Hz, sham (1 mA, 10 min)	Active: M1 (4 × 4 cm) Reference: Forehead (14 × 6 cm)	Online and Offline	SRTT (ms)	Gamma tACS had no effect on motor learning	16	✓	
Pollok et al 2015 (Pollok et al., 2015)	Crossover	$n = 13$ healthy subjects (7 females, mean age: 22.08 ± 0.71)	10 Hz, 20 Hz, 35 Hz, sham (1 mA, about 12 min)	Active: left M1 (5 × 7 cm) Reference: right SOR (5 × 7 cm)	Online	SRTT(ms)	Both alpha and beta tACS facilitated motor acquisition during stimulationGamma tACS had no effect	17	✓	
Santarnecchi et al 2017 (Santarnecchi, 2017)	Randomly assigned	$n = 14$ healthy subjects (7 females, mean age: 25 ± 4, 7 males, mean age: 28 ± 3)	20 Hz, 60 Hz, 80 Hz, sham (1 mA, 7 min)	Active: left M1 (5 × 5 cm), Reference:Cz (5 × 5 cm)	Online	fine visuomotor coordination skills (pixel)	Gamma tACS enhanced motor performance	13	✓	
Schoenfeld et al 2021 (Schoenfeld, 2021)	Randomly assigned	$n = 54$ healthy subjects (28 females, mean age: 24.05 ± 4.76)	IBF, sham (2 mA, 20 min)	Active: bilateral M1 (5 × 7 cm) Reference: bilateral shoulders (5 × 7 cm)	Online	Bimanual motor learning task (Sec)	Beta tACS did not improve motor learning	15	✓	
Spooner et al 2023 (Spooner and Wilson, 2023)	Cross over	$n = 25$ healthy subjects (12 female, mean age: 25.34)	IGF ± 10 Hz, sham (2 mA, 20 min)	Active: left M1Reference: C1, C5, FC3, CP3	Online	Sequential movement task (ms)	Gamma tACS improved motor performance		✓	
Sugata et al 2018 (Sugata, 2018)	Randomly assigned	$n = 52$ healthy subjects (mean age: 32.7 ± 6.8)	10 Hz, 20 Hz, 70 Hz, sham (2 mA, about 5 min)	Active: left M1 (5 × 7 cm) Reference: right SOR (5 × 7 cm)	Online	SRTT(ms)	Gamma tACS improved motor learning	12	✓	
Wach et al 2013 (Wach, 2013)	Crossover	$n = 15$ healthy subjects (7 females, mean age: 30.7 ± 2.4)	10 Hz, 20 Hz, sham (1 mA, 10 min)	Active: left M1 (5 × 7 cm) Reference: contralateral SOR (5 × 7 cm)	Offline	Fast finger tapping (Frequency-Hz)	Alpha tACS increased behavioural variability, while Beta tACS yielded movement slowing	**15**	✓	

Abbreviations: C1: Left anterior central region; C5: Right posterior central region; CP3: Left posterior central region; Cz: Midline central; D & B score: Downs and Black checklist score; FC3: left frontal central region; IAF: Individualised Alpha Frequency; IBF: Individualised Beta Frequency; IGF: Individualised Gamma Frequency; M1: Motor cortex; Pz: Midline parietal; SMA: Supplementary Motor Area; SOR: Supraorbital Region; SRTT: Serial reaction time task; TA: Tibialis anterior muscle; tACS: transcranial Alternating Current Stimulation.

that beta tACS over M1 had no effect on MEP amplitude (SMD −0.37, 95 % CI −0.88 to 0.15, $n = 190$, $P = 0.16$, Fig. 5), with a high level of heterogeneity ($Tau^2 = 0.49$; $Chi^2 = 45.11$, df = 8, $P < 0.001$; $I^2 = 82$ %).

Seven studies (Antal, 2008; Nowak, 2017; Cappon, 2016; Pozdniakov, 2021; Splittgerber, 2020; Rjosk, 2016; Wang, 2021) out of nine applied beta tACS with an intensity of 1 mA or lower. The results indicated that beta tACS with an intensity of 1 mA or lower had no effect on corticospinal excitability (SMD −0.58, 95 % CI −1.20 to 0.05, $n =$

Table 3
Itemised scoring of quality assessment using a modified Downs and Black checklist.

Study	1	2	3	4	5	6	7	8	10	11	12	14	15	18	20	22	23	24	27	Total	%	Quality
Antal et al 2008 (Antal, 2008)	1	1	0	2	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	16	80	High
Berntsen et al 2019 (Berntsen, 2019)	1	1	0	2	1	1	1	0	1	0	0	1	0	1	1	0	1	0	0	12	60	Low
Bologna et al 2019 (Bologna, 2019)	1	1	0	2	0	1	1	1	1	0	0	1	1	1	1	0	1	1	0	14	70	High
Cappon et al 2016 (Cappon, 2016)	1	1	0	2	0	1	1	0	1	0	0	0	0	1	1	0	1	0	0	10	50	Low
Fresnoza et al 2018 (Fresnoza, 2018)	1	1	1	2	1	1	1	1	1	0	0	1	0	1	1	1	1	0	1	15	75	High
Fresnoza et al 2020 (Fresnoza, 2020)	1	1	1	2	0	1	1	1	1	0	0	1	0	1	1	1	1	0	1	16	80	High
Giustiniani et al 2019 (Giustiniani, 2019)	1	1	1	2	0	1	1	1	1	0	0	1	0	1	1	0	1	0	0	13	65	Low
Giustiniani et al 2021a (Giustiniani, 2021)	1	1	1	2	0	1	1	0	1	0	0	1	1	1	1	0	1	1	0	15	75	High
Harada et al 2020 (Harada, 2020)	1	1	1	2	1	1	1	1	1	0	0	1	0	1	1	0	1	0	0	14	70	High
Heise et al 2016 (Heise, 2016)	1	1	0	0	0	1	1	1	0	0	0	1	1	1	1	0	1	1	1	12	60	Low
Krause et al 2016 (Krause, 2016)	1	1	1	2	1	1	1	0	1	0	0	1	1	1	1	0	1	1	1	16	80	High
Kudo et al 2022 (Kudo, 2022)	1	1	0	2	0	1	1	0	1	0	0	0	0	1	1	0	1	0	0	10	50	Low
Moliadze et al 2010 (Moliadze et al., 2010)	1	1	1	2	1	1	1	1	1	0	0	1	0	1	1	1	1	0	1	16	80	High
Nowak et al 2017 (Nowak, 2017)	1	1	0	2	1	1	1	0	1	0	0	1	0	1	1	0	1	0	0	12	60	Low
Pollok et al 2015 (Pollok et al., 2015)	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	0	1	1	1	17	85	High
Pozdniakov et al 2021 (Pozdniakov, 2021)	1	1	0	2	1	1	1	1	1	0	0	1	0	1	1	0	1	0	1	14	70	High
Rjosk et al 2016 (Rjosk, 2016)	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	17	85	High
Santarnecchi et al 2017 (Santarnecchi, 2017)	1	1	1	2	0	1	1	1	1	0	0	1	0	1	1	0	1	0	0	13	65	Low
Schilberg et al 2018 (Schilberg, 2018)	1	1	0	2	0	1	1	0	1	0	0	0	0	1	1	0	1	0	0	10	50	Low
Schoenfeld et al 2021 (Schoenfeld, 2021)	1	1	0	2	1	1	1	0	1	0	0	1	1	1	1	1	1	1	0	15	75	High
Schutter et al 2011 (Schutter and Hortensius, 2011)	1	1	0	0	0	1	1	0	1	0	0	1	0	1	1	1	1	0	0	10	50	Low
Splittgerber et al 2020 (Splittgerber, 2020)	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	17	85	High
Spooner et al 2023 (Spooner and Wilson, 2023)	1	1	1	2	0	1	1	0	1	0	0	1	1	1	1	0	1	0	1	13	65	Low
Therrien-Blanchet 2023 (Therrien-Blanchet, 2023)	1	1	1	2	1	1	1	1	1	0	0	1	0	1	1	1	1	0	1	16	80	High
Sugata et al 2018 (Sugata, 2018)	1	1	0	2	1	1	1	0	1	0	0	1	0	1	1	0	1	0	0	12	60	Low
Wach et al 2013 (Wach, 2013)	1	1	1	2	0	1	1	1	1	0	0	1	1	1	1	0	1	1	0	15	75	High
Wang et al 2021 (Wang, 2021)	1	1	1	2	0	1	1	0	1	0	0	1	0	1	1	0	1	0	0	12	60	Low
Wischnewski et al 2019 (Wischnewski, 2019)	1	1	1	0	0	1	1	0	1	0	0	1	1	1	1	0	0	1	0	11	55	Low
Zaghi et al 2010 (Zaghi, 2010)	1	1	1	2	0	1	1	1	1	0	0	1	1	1	1	0	1	1	0	15	75	High

Low-quality studies were defined as having a risk-of-bias assessment score of < 70 %, whereas high-quality studies had a score of ≥ 70 %.

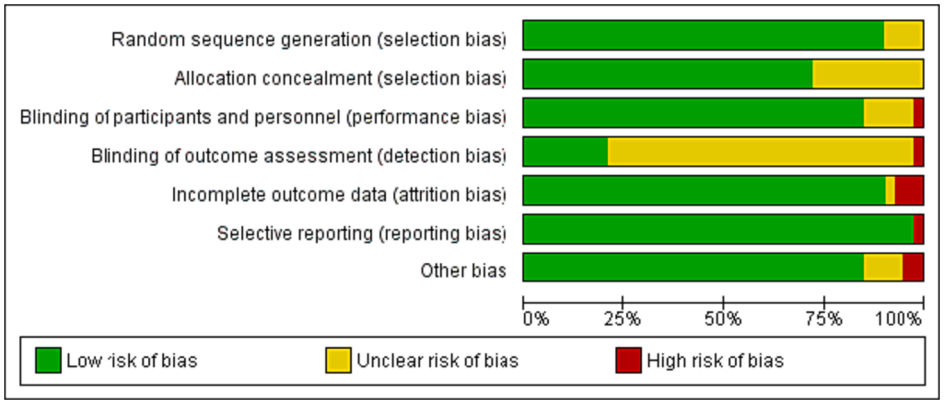

Fig. 2. Risk of bias graph: Review authors' judgements about each risk of bias item presented as percentages across all included studies.

127, $P = 0.07$, Fig. 4), with high heterogeneity observed among studies ($Tau^2 = 0.58$; $Chi^2 = 33.6$, df = 6, $P < 0.001$; $I^2 = 82$ %).

While two studies (Schilberg, 2018; Therrien-Blanchet, 2023) applied beta tACS with intensities above 1 mA, the results showed that beta tACS with intensities above 1 mA had borderline effect on increasing corticospinal excitability (SMD 0.36, 95 % CI 0.01 to 0.71, $n = 63$, $P = 0.05$, Fig. 4), with no heterogeneity between studies ($Tau^2 = 0.00$; $Chi^2 = 0.98$, df = 1, $P = 0.32$; $I^2 = 0$ %).

3.3.6. *The effects of beta tACS over motor cortex on intracortical inhibition and facilitation*

In relation to the effects of beta tACS on intracortical inhibition and facilitation, two studies (Zaghi, 2010; Nowak, 2017) were included. These studies applied tACS with an intensity of 1 mA. The results indicated that beta tACS did not exhibit a modulatory effect on SICI (SMD −0.29, 95 % CI −1.76 to 1.19, $n = 32$, $P = 0.70$, Fig. 6) or ICF (SMD −0.81, 95 % CI −3.26 to 1.65, $n = 32$, $P = 0.52$, Fig. 6). High levels of heterogeneity were observed for both SICI ($Tau^2 = 0.99$; $Chi^2 = 7.61$, df

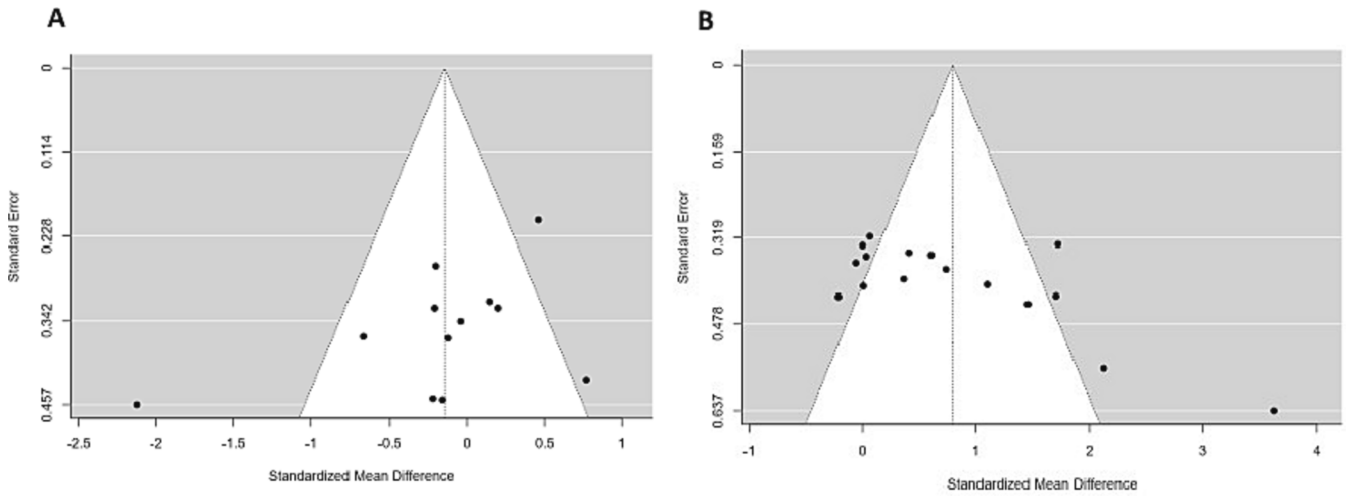

Fig. 3. Funnel plots for A) corticospinal analysis, B) motor function

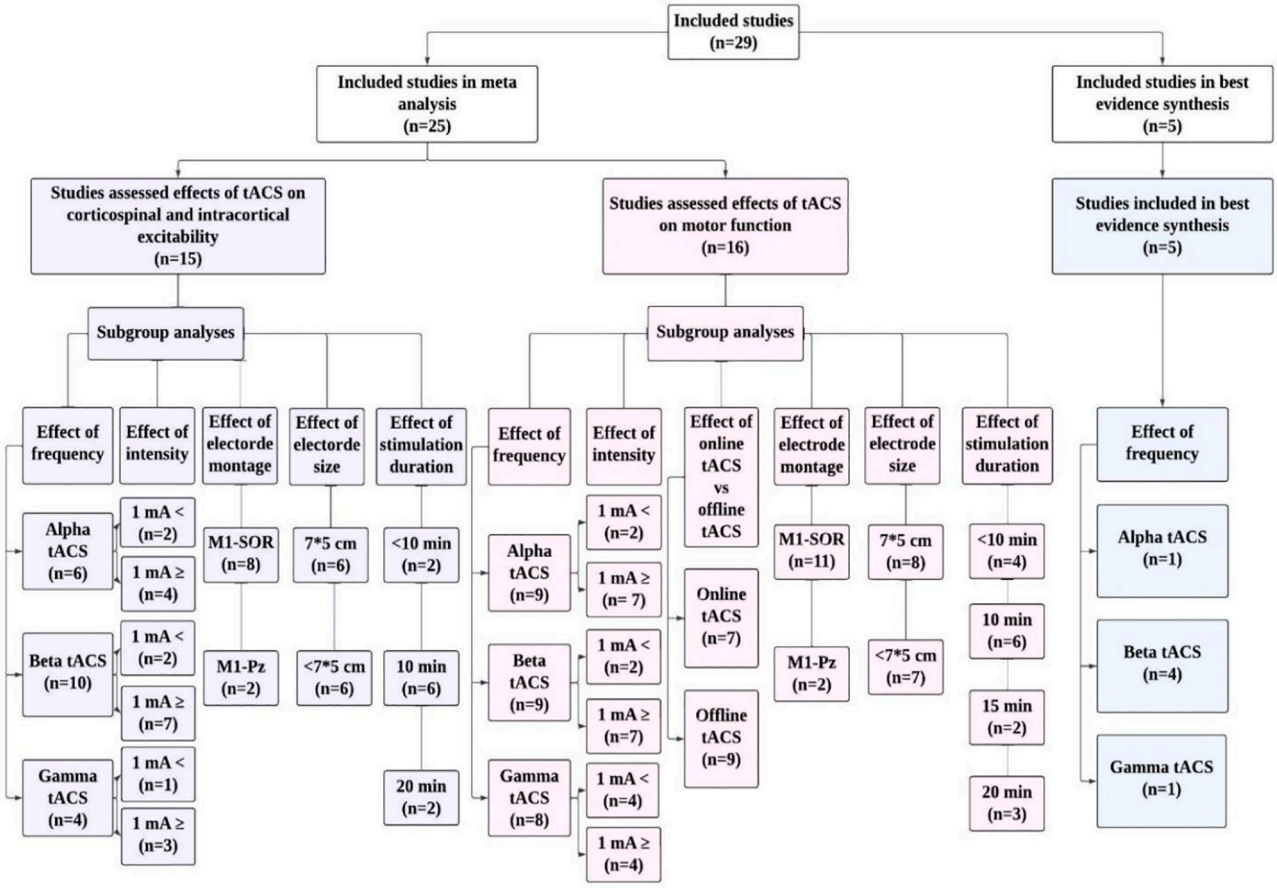

Fig. 4. Flow diagram of subgroup analyses. SOR: Supraorbital Region, tACS: transcranial Alternating Current Stimulation; tACS ≤ 1 mA: tACS with the intensity of 1 mA or lower; tACS > 1 mA: tACS with intensities greater than 1 mA.

= 1, $P = 0.006$; $I^2 = 87$ %) and ICF ($Tau^2 = 2.95$; $Chi^2 = 16.58$, df = 1, P < 0.001; $I^2 = 94$ %).

3.3.7. *The effects of 20 Hz tACS versus individualised beta frequency on corticospinal excitability*

Six studies (Cappon, 2016; Pozdniakov, 2021; Splittgerber, 2020; Rjosk, 2016; Wang, 2021; Therrien-Blanchet, 2023) applied 20 Hz tACS over M1. The results indicated that 20 Hz tACS had no effect on corticospinal excitability (SMD −0.59, 95 % CI −1.35 to 0.17, n = 145, P = 0.13, Fig. 5), with high heterogeneity observed among studies ($Tau^2 = 0.77$; $Chi^2 = 44.40$, df = 5, P < 0.001; $I^2 = 89$ %).

Two studies (Schilberg, 2018; Nowak, 2017) applied tACS over M1 with individualised beta frequency. The findings indicated no increase in corticospinal excitability following tACS with IBF (SMD 0.07, 95 % CI −0.40, to 0.53, n = 35, P = 0.78, Fig. 5), and there was no observed heterogeneity ($Tau^2 = 0.00$; $Chi^2 = 0.01$, df = 1, P = 0.94; $I^2 = 0$ %).

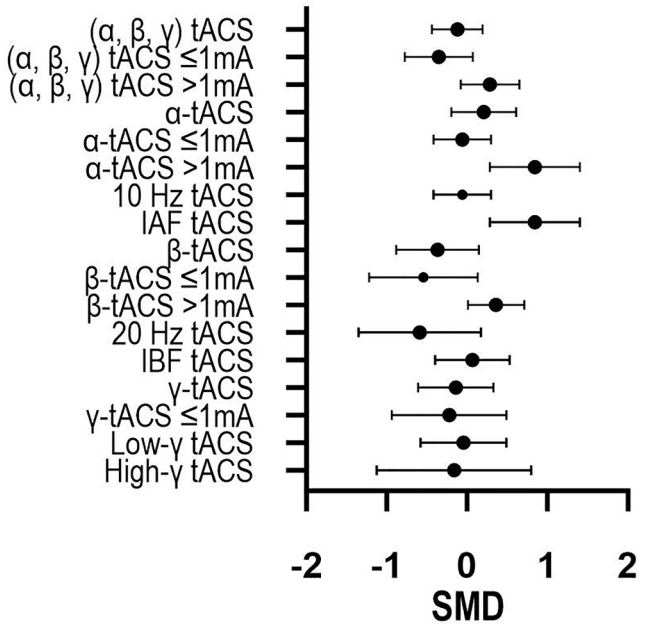

Fig. 5. Forest plot showing the effect of tACS on Corticospinal Excitability (CSE). SMD: standardised mean difference; tACS: transcranial Alternating Current Stimulation; α-tACS: Alpha tACS; IAF: Individualised Alpha Frequency; β-tACS: Beta tACS; IBF: Individualised Beta Frequency; γ-tACS: Gamma tACS; Low-γ: 30–55 Hz; High-γ: 55–80; tACS ≤ 1 mA: tACS with the intensity of 1 mA or lower; tACS > 1 mA: tACS with intensities greater than 1 mA.

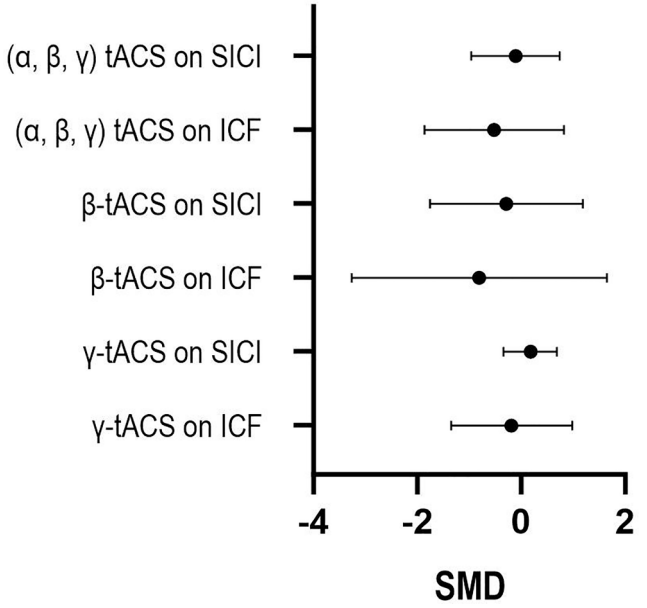

Fig. 6. Forest plot showing the effect of tACS on short interval intracortical inhibition (SICI) and intracortical facilitation (ICF). SMD: standardised mean difference; tACS: transcranial Alternating Current Stimulation; β-tACS: Beta tACS; γ-tACS: Gamma tACS.

3.3.8. The effects of gamma tACS over motor cortex on corticospinal excitability

Four studies (Antal, 2008; Moliadze et al., 2010; Nowak, 2017; Giustiniani, 2019) were included in assessing the effect of gamma tACS over M1 on corticospinal excitability. The results demonstrated no significant effect of gamma tACS on modulating MEP amplitude (SMD −0.14, 95 % CI −0.61 to 0.33, $n = 56$, $P = 0.57$, Fig. 5). Additionally, the level of heterogeneity among the studies was low ($Tau^2 = 0.08$; $Chi^2 = 4.54$, df = 3, $P = 0.21$; $I^2 = 34$ %).

Three studies (Antal, 2008; Moliadze et al., 2010; Nowak, 2017) applied gamma tACS with the intensity of 1 mA or lower, and the results showed no effect (SMD −0.22, 95 % CI −0.94 to 0.49, $n = 39$, $P = 0.54$, Fig. 5) with moderate heterogeneity among studies ($Tau^2 = 0.22$; $Chi^2 = 4.50$, df = 2, $P = 0.11$; $I^2 = 56$ %).

3.3.9. The effects of gamma tACS over motor cortex on intracortical inhibition and facilitation

Two studies (Moliadze et al., 2010; Nowak, 2017) examined the effect of gamma tACS ($n = 28$ participants) with the intensity of 1 mA over M1 on intracortical inhibition and facilitation in comparison to sham tACS ($n = 32$ participants). The results indicated that gamma tACS did not have a significant modulatory effect on SICI (SMD 0.18, 95 % CI −0.34 to 0.69, $n = 32$, $P = 0.50$, Fig. 6) and ICF (SMD −0.19, 95 % CI −1.35 to 0.98, $n = 32$, $P = 0.75$, Fig. 6). There was no observed heterogeneity for SICI ($Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1, $P = 0.97$; $I^2 = 0$ %), but for ICF, the level of heterogeneity was relatively high ($Tau^2 = 0.55$; $Chi^2 = 4.31$, df = 1, $P = 0.04$; $I^2 = 77$ %).

3.3.10. The effects of low gamma versus high gamma tACS on corticospinal excitability

Two studies (Antal, 2008; Giustiniani, 2019) applied low gamma tACS over M1, and the results showed no effect on corticospinal excitability (SMD −0.05, 95 % CI −0.58 to 0.49, n = 27, P = 0.86, Fig. 5) with no observed heterogeneity among studies ($Tau^2 = 0.00$; $Chi^2 = 0.0$, df = 1, P = 0.98; $I^2 = 0$ %).

Two studies (Moliadze et al., 2010; Nowak, 2017) examined the effect of high gamma tACS over M1 on MEP amplitude. The results indicated that high gamma tACS did not have a significant modulatory effect on corticospinal excitability (SMD −0.36, 95 % CI −1.61 to 0.88, n = 29, P = 0.57, Fig. 5) and the level of heterogeneity was relatively high ($Tau^2 = 0.63$; $Chi^2 = 4.47$, df = 1, P = 0.03; $I^2 = 78$ %).

3.3.11. The effects of electrode montage on corticospinal excitability, intracortical inhibition and facilitation

In most of the included studies, there was a common trend in electrode placement. Specifically, among the 13 studies that examined the effects of tACS on corticospinal and intracortical excitability, the majority (Antal, 2008; Fresnoza, 2018; Moliadze et al., 2010; Nowak, 2017; Giustiniani, 2019; Splittgerber, 2020; Wang, 2021; Therrien-Blanchet, 2023) (8 out of 13) positioned the electrodes over the M1 and the contralateral supraorbital region. Additionally, 2 studies (Fresnoza, 2018; Nowak, 2017) utilized tACS over M1 and Pz. There was only one study that placed electrodes bilaterally over M1 (Zaghi, 2010), while another study (Pozdniakov, 2021) positioned them over M1 and the shoulder. Similarly, one study (Cappon, 2016) targeted M1 and the supplementary motor area (SMA).

Given this distribution of electrode montages across the studies, subgroup analysis was conducted for only two specific montages: A) M1-SOR, as well as B) M1-Pz.

A) M1 and supraorbital region

Eight studies (Antal, 2008; Fresnoza, 2018; Moliadze et al., 2010; Nowak, 2017; Giustiniani, 2019; Splittgerber, 2020; Wang, 2021; Therrien-Blanchet, 2023) positioned the electrodes over the primary motor cortex (M1) and the contralateral supraorbital region. The results indicated that tACS with this montage did not have any significant modulatory effect on corticospinal excitability (SMD 0.04, 95 % CI −0.27 to 0.34, $n = 162$, $P = 0.82$, Fig. 7) and the level of heterogeneity among studies remained moderate ($Tau^2 = 0.08$; $Chi^2 = 12.24$, df = 7, $P = 0.09$; $I^2 = 43$ %).

Two studies (Fresnoza, 2018; Nowak, 2017) examined the effect of tACS over M1 and contralateral supraorbital region on intracortical inhibition and facilitation. The results indicated that tACS with this montage did not have a significant modulatory effect on SICI (SMD 0.32, 95 % CI −0.18 to 0.81, $n = 32$, $P = 0.21$, Fig. 7) and ICF (SMD 0.23, 95 %

CI −0.26 to 0.73, $n = 32$, $P = 0.35$, Fig. 7). There was no observed heterogeneity for SICI ($Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1, $P = 0.97$; $I^2 = 0$ %), and ICF ($Tau^2 = 0.00$; $Chi^2 = 0.58$, df = 1, $P = 0.45$; $I^2 = 0$ %).

B) M1-Pz

Two studies (Schilberg, 2018; Rjosk, 2016) positioned the electrodes over the primary motor cortex (M1) and the Pz. The results indicated that tACS with this montage did not have any significant modulatory effect on corticospinal excitability (SMD −0.17, 95 % CI −0.65 to 0.30, $n = 34$, $P = 0.48$, Fig. 7) with no observed heterogeneity among studies ($Tau^2 = 0.00$; $Chi^2 = 0.03$, df = 1, $P = 0.86$; $I^2 = 0$ %).

3.3.12. The effects of electrode size on corticospinal excitability, intracortical inhibition and facilitation

While the majority of the included studies utilized active electrodes with a size of 5x7 cm or 35 cm^2, it is noteworthy that there was considerable variability in electrode sizes among the studies varied from 3 to 35 cm^2. In light of this variability, a sub-analysis was performed by categorizing the studies into two main groups: A) studies employing electrodes sized 7x5 cm, and B) studies utilizing smaller electrodes, with sizes such as 3x3, 4x4, and 5x5 cm.

A) Studies employing electrodes sized 7x5 cm

Six studies (Fresnoza, 2018; Nowak, 2017; Cappon, 2016; Pozdniakov, 2021; Splittgerber, 2020; Therrien-Blanchet, 2023) applied tACS with an electrode size of 35 cm^2. The findings showed no effect for tACS with an active electrode size of 35 cm2 (SMD −0.08, 95 % CI −0.69 to 0.54, $n = 142$, $P = 0.81$, Fig. 8) with a high level of heterogeneity among studies ($Tau^2 = 0.47$; $Chi^2 = 29.38$, df = 5, $P < 0.001$; $I^2 = 83$ %).

Two studies (Fresnoza, 2018; Nowak, 2017) applied tACS with an electrode size of 35 cm^2. The results indicated that tACS with this size of electrode did not have a significant modulatory effect on SICI (SMD 0.32, 95 % CI −0.18 to 0.81, $n = 32$, $P = 0.21$, Fig. 8) and ICF (SMD 0.23, 95 % CI −0.26 to 0.73, $n = 32$, $P = 0.35$, Fig. 8). There was no observed heterogeneity for SICI ($Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1, $P = 0.97$; $I^2 = 0$ %), and ICF ($Tau^2 = 0.00$; $Chi^2 = 0.58$, df = 1, $P = 0.45$; $I^2 = 0$ %).

B) Studies employing electrodes sized smaller than 5 × 7

Six studies (Antal, 2008; Schilberg, 2018; Moliadze et al., 2010; Giustiniani, 2019; Rjosk, 2016; Wang, 2021) in total applied tACS over M1 with electrode sizes smaller than 35 cm^2. The combined results showed that tACS had no significant modulatory effect on corticospinal excitability (SMD −0.24, 95 % CI −0.54 to 0.06, $n = 88$, $P = 0.12$, Fig. 8) with no observed heterogeneity among studies ($Tau^2 = 0.00$; $Chi^2 = 1.86$, df = 5, $P = 0.87$; $I^2 = 0$ %).

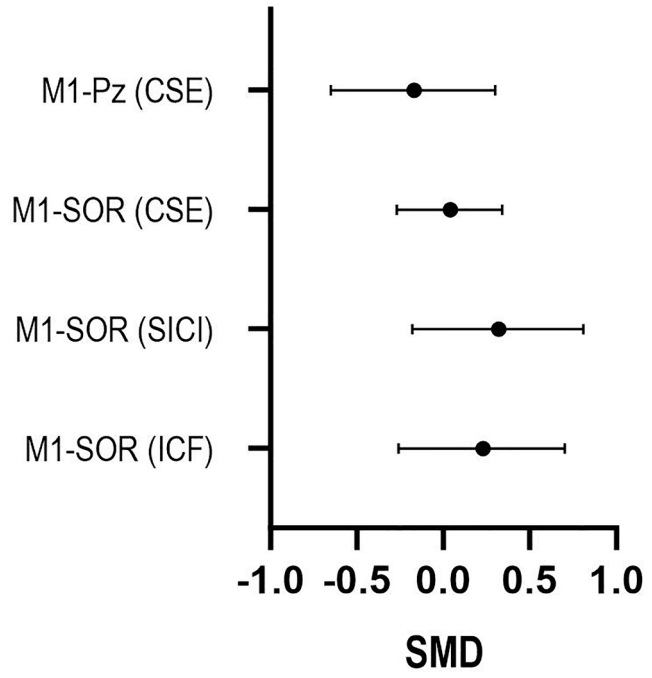

Fig. 7. Forest plot showing the effect of electrode montage on Corticospinal Excitability (CSE), short interval intracortical inhibition (SICI) and intracortical facilitation (ICF). M1: Motor cortex; P3; Pz: Midline parietal; SMD: standardised mean difference; SOR: Supraorbital region

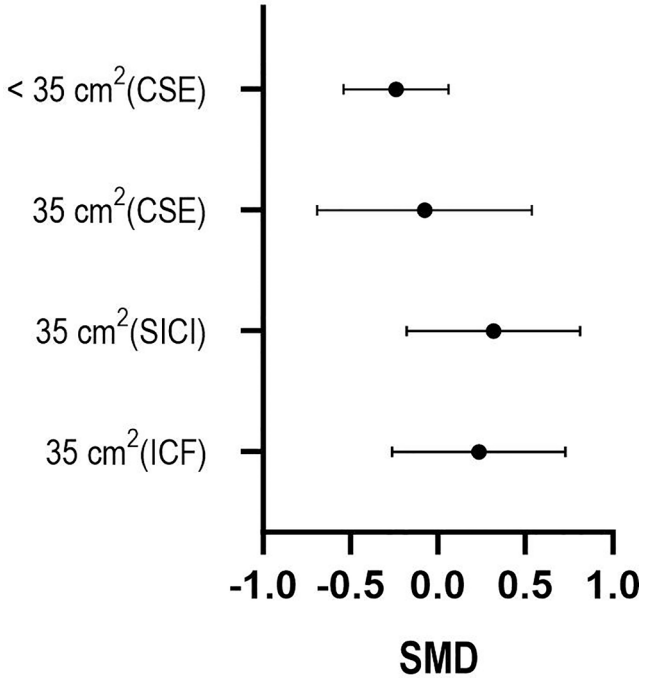

Fig. 8. Forest plot showing the effect of electrode size on Corticospinal Excitability (CSE), short interval intracortical inhibition (SICI) and intracortical facilitation (ICF). < 35^2: Electrodes with the sizes smaller than 35 cm^2; 35 cm^2: Electrode with the size of 35 cm^2; SMD: standardised mean difference;

3.3.13. The effects of stimulation duration on corticospinal excitability, intracortical inhibition and facilitation

The duration of stimulation varied significantly among studies. The stimulation duration of included studies ranged between 5- and 36.5-min. Studies were divided into three distinct sub-groups: A) studies that applied tACS for less than 10 min, B) studies where tACS was administered for a duration of 10 min, and C) studies that extended the tACS duration to 20 min.

A) Studies that applied tACS for less than 10 min

Two studies (Antal, 2008; Giustiniani, 2019) investigated the effects of tACS over M1 with the duration of less than 1o minutes. The results showed no effect for tACS with the duration of less than 10 min on corticospinal excitability (SMD −0.11, 95 % CI −0.64 to 0.43, $n = 27$, $P = 0.69$, Fig. 9) with no observed heterogeneity among studies ($Tau^2 = 0.00$; $Chi^2 = 0.10$, df = 1, $P = 0.75$; $I^2 = 0$ %).

B) Studies that applied tACS for 10 min

Six studies (Fresnoza, 2018; Moliadze et al., 2010; Cappon, 2016; Splittgerber, 2020; Rjosk, 2016; Wang, 2021) applied tACS over M1 for 10 min. The findings indicated that applying tACS for 10 min did not have a significant modulatory effect on corticospinal excitability (SMD −0.41, 95 % CI −1.04 to 0.22, $n = 101$, $P = 0.20$, Fig. 9) with relatively high observed heterogeneity among studies ($Tau^2 = 0.48$; $Chi^2 = 22.64$, df = 5, $P = 0.0045$; $I^2 = 78$ %).

C) Studies that applied tACS for 20 min

Two studies (Nowak, 2017; Therrien-Blanchet, 2023) examined the effects of tACS for the duration of 20 min on corticospinal excitability. The results indicated that 20 min of tACS over M1 significantly improved corticospinal excitability (SMD 0.37, 95 % CI 0.03 to 0.71, n

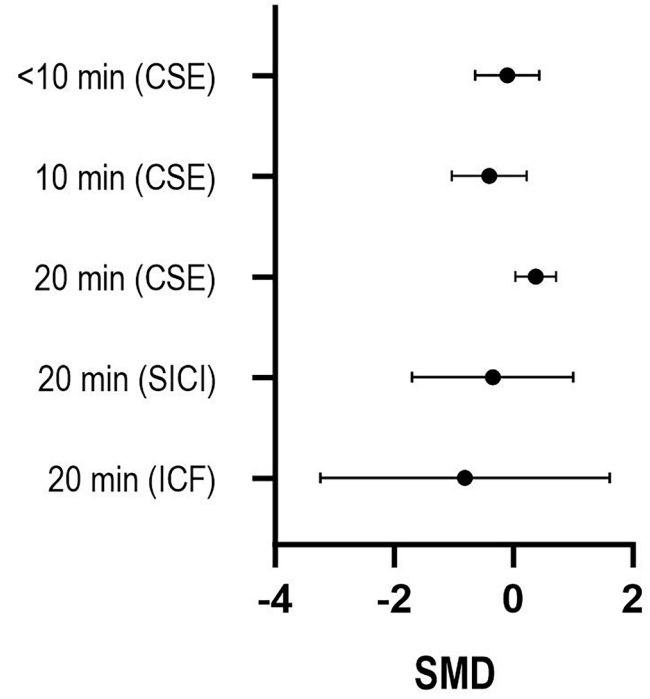

Fig. 9. Forest plot showing the effect of stimulation duration on Corticospinal Excitability (CSE), short interval intracortical inhibition (SICI) and intracortical facilitation (ICF). SMD: standardised mean difference.

= 68, $P = 0.03$, Fig. 9) with no observed heterogeneity among studies ($Tau^2 = 0.00$; $Chi^2 = 0.70$, df = 1, $P = 0.40$; $I^2 = 0$ %).

Two studies (Zaghi, 2010; Nowak, 2017) investigated the effects of 20 min tACS on SICI and ICF. The results indicated that 20 min tACS did not have a significant modulatory effect on SICI (SMD −0.35, 95 % CI −1.70 to 1, $n = 32$, $P = 0.61$, Fig. 9) and ICF (SMD −0.82, 95 % CI −3.24 to 1.61, n = 32, P = 0.51, Fig. 9). The level of observed heterogeneity between studies for both SICI ($Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1, $P = 0.97$; $I^2 = 0$ %), and ICF ($Tau^2 = 0.00$; $Chi^2 = 0.58$, df = 1, $P = 0.45$; $I^2 = 0$ %) was high.

3.4. Effects of tACS on motor function

3.4.1. The effects of alpha, beta and gamma tACS over motor cortex on motor function

Overall, a total of 16 studies (Antal, 2008; Pollok et al., 2015; Santarnecchi, 2017; Berntsen, 2019; Moliadze et al., 2010; Cappon, 2016; Giustiniani, 2019; Bologna, 2019; Giustiniani, 2021; Harada, 2020; Schoenfeld, 2021; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013; Spooner and Wilson, 2023) investigated the effects of tACS at different frequencies (such as alpha, beta, and gamma) over M1 on motor function compared to sham stimulation. Nine studies (Antal, 2008; Pollok et al., 2015; Berntsen, 2019; Cappon, 2016; Harada, 2020; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) applied alpha tACS, nine studies (Pollok et al., 2015; Santarnecchi, 2017; Cappon, 2016; Bologna, 2019; Harada, 2020; Schoenfeld, 2021; Krause, 2016; Sugata, 2018; Wach, 2013) used beta tACS and eight studies (Pollok et al., 2015; Santarnecchi, 2017; Moliadze et al., 2010; Giustiniani, 2019; Bologna, 2019; Giustiniani, 2021; Sugata, 2018; Spooner and Wilson, 2023) utilised gamma tACS. The collective findings indicated a significant increase in motor function following tACS regardless of stimulation frequency (SMD 0.77, 95 % CI 0.36 to 1.18, $n = 244$, $P = 0.002$, Fig. 10). However, it is important to note that these studies exhibited a relatively high level of heterogeneity ($Tau^2 = 0.54$; $Chi^2 = 68.23$, df = 15, $P < 0.001$; $I^2 = 78$ %).

Ten studies (Antal, 2008; Pollok et al., 2015; Santarnecchi, 2017; Berntsen, 2019; Moliadze et al., 2010; Cappon, 2016; Bologna, 2019; Harada, 2020; Krause, 2016; Wach, 2013) applied tACS with the intensity of 1 mA or lower. The results indicated significant improvement following tACS with the intensity of 1 mA or lower (SMD 0.67, 95 % CI 0.20 to 1.15, $n = 134$, $P = 0.005$, Fig. 10) and the level of heterogeneity was relatively high ($Tau^2 = 0.40$; $Chi^2 = 30.46$, df = 9, $P = 0.0004$; $I^2 = 70$ %).

Six studies (Giustiniani, 2019; Giustiniani, 2021; Schoenfeld, 2021; Fresnoza, 2020; Sugata, 2018; Spooner and Wilson, 2023) applied tACS with intensities above 1 mA. The results showed significant improvement following tACS with intensities above 1 mA (SMD 0.96, 95 % CI 0.17 to 1.76, $n = 110$, $P = 0.02$, Fig. 10) and the level of heterogeneity among studies was high ($Tau^2 = 0.83$; $Chi^2 = 36.62$, df = 5, $P < 0.001$; $I^2 = 86$ %).

Considering the level of heterogeneity among studies, subgroup analysis was conducted to investigate the effects of tACS on motor function based on different factors such as the frequency employed (See section 3.4.2 to 3.4.4), and whether tACS was applied before (offline) or concurrently (online) with motor function (See section 3.4.5). This analysis aimed to explore potential variations in the effects of tACS over M1 on motor function.

3.4.2. The effects of alpha tACS over motor cortex on motor function

Nine studies (Antal, 2008; Pollok et al., 2015; Berntsen, 2019; Cappon, 2016; Harada, 2020; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) investigated the effects of alpha tACS over M1 on motor function. The results revealed that alpha tACS has a significant positive effect on motor function (SMD 0.99, 95 % CI 0.28 to 1.69$n = 124$, $P = 0.006$, Fig. 10). However, it is important to note that there was a high level of heterogeneity among the studies ($Tau^2 = 0.95$; $Chi^2 = 50.27$, df = 8, $P < 0.001$; $I^2 = 84$ %).

Seven studies (Antal, 2008; Pollok et al., 2015; Berntsen, 2019; Cappon, 2016; Harada, 2020; Krause, 2016; Wach, 2013) applied alpha tACS with the intensity of 1 mA or lower. The results showed that alpha tACS over M1 with the intensity of 1 mA or lower improved motor

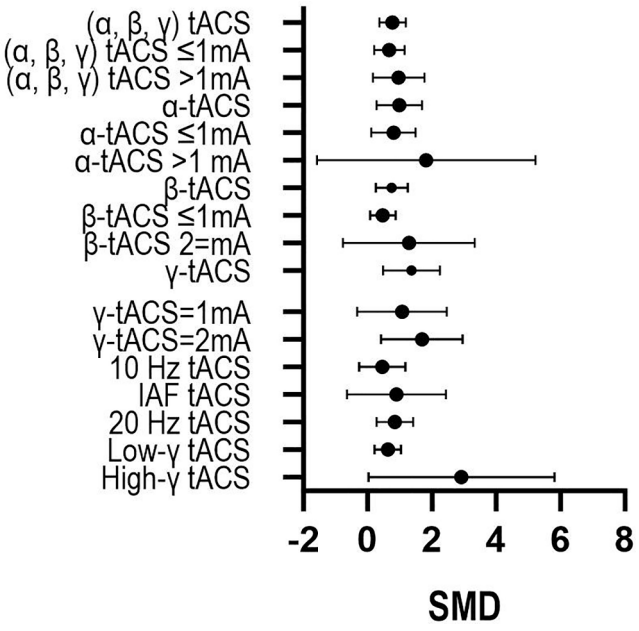

Fig. 10. Forest plot showing the effect of tACS on motor function. SMD: standardised mean difference; tACS: transcranial Alternating Current Stimulation; α-tACS: Alpha tACS; IAF: Individualised Alpha Frequency; β-tACS: Beta tACS; IBF: Individualised Beta Frequency; γ-tACS: Gamma tACS; Low-γ: 30–55 Hz; High-γ: 55–80; tACS = 1 mA: tACS with the intensity of 1 mA; tACS = 2 mA: tACS with the intensity of 2 mA; tACS ≤ 1 mA: tACS with the intensity of 1 mA or lower; tACS > 1 mA: tACS with intensities greater than 1 mA.

function (SMD 0.80, 95 % CI 0.11 to 1.49, $n = 91$, $P = 0.02$, Fig. 10). The level of heterogeneity among studies was high ($Tau^2 = 0.68$; $Chi^2 = 28.33$, df = 6, $P < 0.001$; $I^2 = 79$ %).

Two studies (Fresnoza, 2020; Sugata, 2018) applied alpha tACS with intensities above 1 mA. Results indicated that alpha tACS with intensities above 1 mA had no effect on motor function (SMD 1.82, 95 % CI −1.58 to 5.22, $n = 33$, $P = 0.29$, Fig. 10) and the level of heterogeneity between studies was very high ($Tau^2 = 5.75$; $Chi^2 = 21.96$, df = 1, $P < 0.001$; $I^2 = 95$ %).

3.4.3. The effects of alpha versus individualised alpha frequency on motor function

Seven studies (Antal, 2008; Pollok et al., 2015; Cappon, 2016; Harada, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) specifically examined the effect of 10 Hz tACS over M1 on motor function. After sensitivity analysis, two studies (Pollok et al., 2015; Sugata, 2018) were removed. The combined results showed that 10 Hz tACS did not have an effect on motor function (SMD 0.45, 95 % CI −0.27 to 1.17, $n = 89$, $P = 0.22$, Fig. 10), and the level of heterogeneity among studies was relatively high ($Tau^2 = 0.49$; $Chi^2 = 15.00$, df = 4, $P = 0.005$; $I^2 = 73$ %).

Two studies (Berntsen, 2019; Fresnoza, 2020) applied tACS over M1 with individualised alpha frequency. The findings indicated no improvement in motor function following tACS with IAF (SMD 0.89, 95 % CI −0.65, to 2.43, $n = 35$, $P = 0.26$, Fig. 10), and the level of heterogeneity among studies was high ($Tau^2 = 1.09$; $Chi^2 = 8.52$, df = 1, $P = 0.004$; $I^2 = 88$ %).

3.4.4. The effects of beta tACS over motor cortex on motor function

Nine studies (Pollok et al., 2015; Santarnecchi, 2017; Cappon, 2016; Bologna, 2019; Harada, 2020; Schoenfeld, 2021; Krause, 2016; Sugata, 2018; Wach, 2013) examined the effects of beta tACS over M1 on motor function, after sensitivity analysis two studies (Santarnecchi, 2017; Harada, 2020) were removed. The results of the pooled data indicated significant effects for beta tACS over M1 on improving motor function (SMD 0.75, 95 % CI 0.25 to 1.24, $n = 102$, $P = 0.003$, Fig. 10). The level of heterogeneity among these studies was moderate ($Tau^2 = 0.28$; $Chi^2 = 16.89$, df = 6, $P = 0.010$; $I^2 = 64$ %).

Seven studies (Pollok et al., 2015; Santarnecchi, 2017; Cappon, 2016; Bologna, 2019; Harada, 2020; Krause, 2016; Wach, 2013) applied beta tACS with the intensity of 1 mA or lower, after sensitivity analysis one study was removed (Santarnecchi, 2017). The results of the pooled data showed a significant effect of beta tACS with the intensity of 1 mA or lower on improving motor function (SMD 0.47, 95 % CI 0.07 to 0.87, $n = 82$, $P = 0.02$, Fig. 10). The level of heterogeneity among these studies was low ($Tau^2 = 0.09$; $Chi^2 = 7.90$, df = 5, $P = 0.16$; $I^2 = 37$ %).

Two studies (Schoenfeld, 2021; Sugata, 2018) applied 2 mA beta tACS, and the results indicated that 2 mA tACS had no effect on motor function (SMD 1.28, 95 % CI −0.77 to 3.33, $n = 31$, $P = 0.22$, Fig. 10). The level of heterogeneity among these studies was high ($Tau^2 = 2$; $Chi^2 = 11.16$, df = 1, $P = 0.0008$; $I^2 = 91$ %).

3.4.5. The effects of 20 Hz tACS over M1 on motor function

Six studies (Pollok et al., 2015; Cappon, 2016; Bologna, 2019; Krause, 2016; Sugata, 2018; Wach, 2013) examined the effects of 20 Hz tACS over M1 on motor function. The results of the pooled data indicated significant effects for beta tACS over M1 on improving motor function (SMD 0.84, 95 % CI 0.27 to 1.41, $n = 84$, $P = 0.004$, Fig. 10). The level of heterogeneity among these studies was moderate ($Tau^2 = 0.34$; $Chi^2 = 15.24$, df = 5, $P = 0.009$; $I^2 = 67$ %).

3.4.6. The effects of gamma tACS over motor cortex on motor function

Eight studies (Pollok et al., 2015; Santarnecchi, 2017; Moliadze et al., 2010; Giustiniani, 2019; Bologna, 2019; Giustiniani, 2021; Sugata, 2018; Spooner and Wilson, 2023) investigated the effects of gamma tACS over M1 on motor function compared to sham tACS. The results demonstrated that gamma tACS improves motor function (SMD 1.36, 95 % CI 0.48 to 2.24, $n = 128$, $P = 0.002$, Fig. 10). However, there was a high level of heterogeneity observed among the studies ($Tau^2 = 1.40$; $Chi^2 = 65.44$, df = 7, $P < 0.001$; $I^2 = 89$ %).

Four studies (Pollok et al., 2015; Santarnecchi, 2017; Moliadze et al., 2010; Bologna, 2019) applied 1 mA gamma tACS. The results showed that 1 mA gamma tACS had no effect on motor function (SMD 1.07, 95 % CI −0.33 to 2.46, $n = 56$, $P = 0.13$, Fig. 10) and the level of heterogeneity among studies was high ($Tau^2 = 1.81$; $Chi^2 = 31.89$, df = 3, $P < 0.001$; $I^2 = 91$ %).

Also, four studies (Giustiniani, 2019; Giustiniani, 2021; Sugata, 2018; Spooner and Wilson, 2023) applied 2 mA gamma tACS. The result indicated significant improvement following 2 mA gamma tACS (SMD 1.68, 95 % CI 0.42 to 2.95, $n = 72$, $P = 0.009$, Fig. 10), and the level of observed heterogeneity among studies was high ($Tau^2 = 1.43$; $Chi^2 = 29.78$, df = 3, $P < 0.001$; $I^2 = 90$ %).

3.4.7. The effects of low gamma versus high gamma tACS on motor function

Three studies (Pollok et al., 2015; Giustiniani, 2019; Giustiniani, 2021) examined the effects of low gamma tACS over M1 on motor function. The results of the pooled data indicated significant effects for low gamma tACS over M1 on improving motor function (SMD 0.62, 95 % CI 0.21 to 1.04, $n = 47$, $P = 0.003$, Fig. 10) and no heterogeneity was observed among studies ($Tau^2 = 0.00$; $Chi^2 = 1.03$, df = 2, $P = 0.60$; $I^2 = 0$ %).

Four studies (Santarnecchi, 2017; Moliadze et al., 2010; Bologna, 2019; Sugata, 2018) applied high gamma tACS over M1, after sensitivity analysis one study (Bologna, 2019) was removed. The results showed that high gamma tACS had borderline effect on improving motor function (SMD 2.91, 95 % CI 0.02 to 5.81, $n = 40$, $P = 0.05$, Fig. 10), and the level of heterogeneity between studies was high ($Tau^2 = 6.13$; $Chi^2 = 35.21$, df = 2, $P < 0.001$; $I^2 = 94$ %).

3.4.8. The effects of online tACS vs. Offline tACS over motor cortex on motor function

Subgroup analysis was conducted to examine the effects of tACS over M1 on motor function considering applying tACS prior to or concurrent with the motor task. Nine studies (Berntsen, 2019; Moliadze et al., 2010; Giustiniani, 2021; Harada, 2020; Schoenfeld, 2021; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) investigated the effects of tACS over M1 prior to motor function. Six studies (Berntsen, 2019; Harada, 2020; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) utilised alpha tACS, five studies (Harada, 2020; Schoenfeld, 2021; Krause, 2016; Sugata, 2018; Wach, 2013) applied beta tACS and three studies (Moliadze et al., 2010; Giustiniani, 2021; Sugata, 2018) used gamma tACS. The results indicated a significant improvement in motor function following offline tACS regardless of stimulation frequency (SMD 0.65, 95 % CI 0.08 to 1.21, $n = 134$, $P = 0.02$, Fig. 11). The level of heterogeneity among these studies was relatively high ($Tau^2 = 0.57$; $Chi^2 = 37.84$, df = 8, $P < 0.001$; $I^2 = 79$ %).

Five studies (Berntsen, 2019; Moliadze et al., 2010; Harada, 2020; Krause, 2016; Wach, 2013) applied 1 mA tACS prior to motor function. The results showed that 1 mA offline tACS has no effect on motor function (SMD 0.52, 95 % CI −0.11 to 1.15, $n = 66$, $P = 0.11$, Fig. 11) and the level of heterogeneity among studies was moderate ($Tau^2 = 0.35$; $Chi^2 = 12.40$, df = 4, $P = 0.01$; $I^2 = 68$ %).

Four studies (Fresnoza, 2018; Giustiniani, 2021; Schoenfeld, 2021; Sugata, 2018) applied tACS with intensities above 1 mA prior to motor function, with the results indicating no significant improvement following offline tACS with intensities above 1 mA (SMD 0.89, 95 % CI −0.20 to 1.99, $n = 68$, $P = 0.11$, Fig. 11) and observed heterogeneity among studies was high ($Tau^2 = 1.07$; $Chi^2 = 25.34$, df = 3, $P < 0.001$; $I^2 = 88$ %).

Seven studies (Antal, 2008; Pollok et al., 2015; Santarnecchi, 2017; Cappon, 2016; Giustiniani, 2019; Bologna, 2019; Spooner and Wilson, 2023) examined the effects of tACS over M1 applied concurrently with

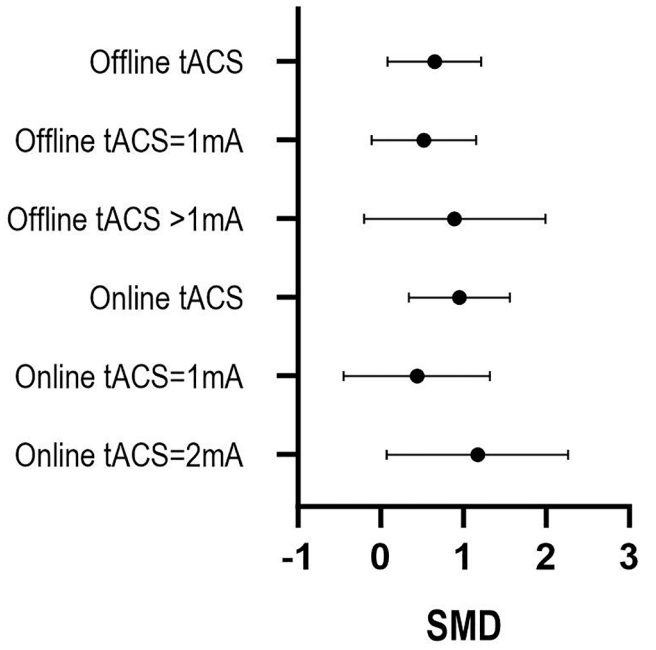

Fig. 11. Forest plot showing the effect of offline and online tACS on motor function. SMD: standardised mean difference; tACS: transcranial Alternating Current Stimulation; tACS = 1 mA: tACS with the intensity of 1 mA; tACS = 2 mA: tACS with the intensity of 2 mA; tACS > 1 mA: tACS with intensities greater than 1 mA.

the motor task. Three studies (Antal, 2008; Pollok et al., 2015; Cappon, 2016) used alpha tACS, four studies (Pollok et al., 2015; Santarnecchi, 2017; Cappon, 2016; Bologna, 2019) utilised beta tACS and five studies (Pollok et al., 2015; Santarnecchi, 2017; Giustiniani, 2019; Bologna, 2019; Spooner and Wilson, 2023) applied gamma tACS. The results demonstrated a significant improvement in motor function following online tACS regardless of stimulation frequency (SMD 0.95, 95 % CI 0.34 to 1.56, $n = 110$, $P = 0.002$, Fig. 11). The level of heterogeneity among these studies was also high ($Tau^2 = 0.51$; $Chi^2 = 25.80$, df = 6, $P = 0.0002$; $I^2 = 77$ %).

Five studies (Antal, 2008; Pollok et al., 2015; Santarnecchi, 2017; Cappon, 2016; Bologna, 2019) applied tACS with the intensity of 1 mA or lower concurrently with motor function. After performing sensitivity analysis two studies (Antal, 2008; Santarnecchi, 2017) were removed. The pooled data from the remaining studies indicated that 1 mA online tACS had no effect on motor function (SMD 0.44, 95 % CI −0.45 to 1.32, $n = 44$, $P = 0.33$, Fig. 11) and the level of heterogeneity among studies was high ($Tau^2 = 0.46$; $Chi^2 = 8.13$, df = 2, $P = 0.02$; $I^2 = 75$ %).

On the other hand, two studies (Giustiniani, 2019; Spooner and Wilson, 2023) applied 2 mA tACS concurrent with motor function. The results showed that 2 mA online tACS improved motor function (SMD 1.17, 95 % CI 0.07 to 2.26, $n = 42$, $P = 0.04$, Fig. 11) and the level of heterogeneity was high ($Tau^2 = 0.51$; $Chi^2 = 5.30$, df = 1, $P = 0.02$; $I^2 = 81$ %).

3.4.9. *The effects of electrode montage on motor function*

In the majority of the studies included, a consistent trend emerged regarding the placement of electrodes. Specifically, among the 16 studies investigating the effects of tACS on motor function, a significant number (11 out of 16) positioned the electrodes over the M1 and the contralateral supraorbital region, including studies (Antal, 2008; Pollok et al., 2015; Berntsen, 2019; Moliadze et al., 2010; Giustiniani, 2019; Giustiniani, 2021; Harada, 2020; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013). Two other studies (Santarnecchi, 2017; Bologna, 2019) employed tACS over M1 and Pz. Only one study (Giustiniani, 2021) placed electrodes bilaterally over M1, while another study (Schoenfeld, 2021) positioned electrodes over M1 and the shoulder. Similarly, one study (Cappon, 2016) targeted M1 and the SMA, and one study (Spooner and Wilson, 2023) used HD tACS. Due to this distribution of electrode montages across the studies, subgroup analysis was specifically conducted for two specific montages: A) M1-SOR, and B) M1- Pz.

A) M1-SOR

Eleven studies (Antal, 2008; Pollok et al., 2015; Berntsen, 2019; Moliadze et al., 2010; Giustiniani, 2019; Giustiniani, 2021; Harada, 2020; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) positioned the electrodes over the primary motor cortex (M1) and the contralateral supraorbital region. The results indicated that tACS with this montage has a significant effect on improving motor function (SMD 0.89, 95 % CI 0.36 to 1.41, $n = 156$, $P = 0.001$, Fig. 12) and the level of heterogeneity among studies remained relatively high ($Tau^2 = 0.60$; $Chi^2 = 46.08$, df = 10, $P < 0.001$; $I^2 = 78$ %).

B) M1-Pz

Two studies (Santarnecchi, 2017; Bologna, 2019) positioned the electrodes over the primary motor cortex (M1) and the Pz. The results indicated that tACS with this montage did not have any significant effect on improving motor function (SMD 0.54, 95 % CI −0.50 to 1.59, n = 30, P = 0.31, Fig. 12) with relatively high observed heterogeneity among studies ($Tau^2 = 0.42$; $Chi^2 = 3.87$, df = 1, $P = 0.05$; $I^2 = 74$ %).

3.4.10. *The effects of electrode size on motor function*

In most of the studies included, active electrodes with the size of 35 cm2 were predominantly used. However, it's important to highlight that there was significant diversity in electrode sizes across the studies, ranging from 3 cm2 to 35 cm2. To account for this variation, a subgroup analysis was carried out by classifying the studies into two main groups: A) one group employed 35 cm2 active electrodes, while B) the other group utilized electrode sizes smaller than 35 cm2.

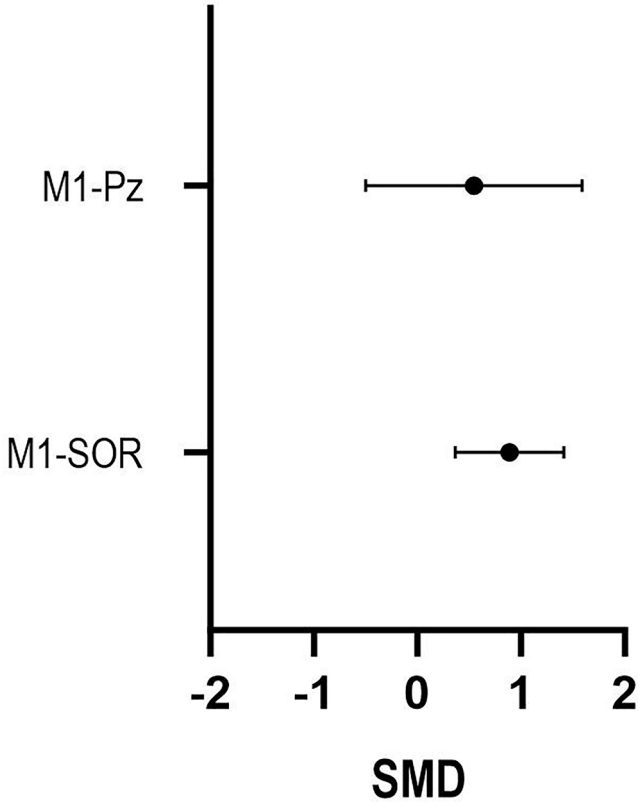

Fig. 12. Forest plot showing the effect of electrode montage on motor function. M1: Motor cortex; P3; Pz: Midline parietal; SMD: standardised mean difference; SOR: Supraorbital region

A) Studies employing electrodes sized 7x5 cm

Eight studies (Pollok et al., 2015; Cappon, 2016; Harada, 2020; Schoenfeld, 2021; Fresnoza, 2020; Krause, 2016; Sugata, 2018; Wach, 2013) applied tACS with an electrode size of 35 cm^2. The findings showed no effect for tACS with an active electrode size of 35 cm^2 on motor function (SMD 0.59, 95 % CI −0.05 to 1.22, $n = 117$, $P = 0.07$, Fig. 13) with a high level of heterogeneity among studies ($Tau^2 = 0.66$; $Chi^2 = 36.43$, df = 7, $P < 0.001$; $I^2 = 81$ %).

B) Studies employing electrodes sized smaller than 5 × 7 cm

Seven studies (Antal, 2008; Santarnecchi, 2017; Berntsen, 2019; Moliadze et al., 2010; Giustiniani, 2019; Bologna, 2019; Giustiniani, 2021) investigated the effects of tACS with the electrode sizes smaller than 35 cm^2. The results showed a significant effect for tACS with smaller electrode size on motor function (SMD 0.83, 95 % CI 0.32 to 1.33, $n = 102$, $P = 0.001$, Fig. 13) with a moderate level of heterogeneity among studies ($Tau^2 = 0.30$; $Chi^2 = 17.29$, df = 6, $P = 0.008$; $I^2 = 65$ %).

3.4.11. *The effects of stimulation duration on motor function*

Stimulation durations within the included studies ranged from 5 to 20 min. The duration of stimulation exhibited substantial variability across the studies. These studies were categorized into four distinct subgroups: A) those applying tACS for less than 10 min, B) those using a 10-minute duration, and those extending tACS to either C) 15 or D) 20 min.

A) Studies that applied tACS for less than 10 min

Four studies (Antal, 2008; Santarnecchi, 2017; Giustiniani, 2019; Sugata, 2018) applied tACS over M1 for less than 10 min. The results showed that applying tACS for less than 10 min improved motor function (SMD 1.76, 95 % CI 0.60 to 2.92, $n = 54$, $P = 0.003$, Fig. 14) and the level of heterogeneity among studies was high ($Tau^2 = 1.14$; $Chi^2 = 18.10$, df = 3, $P = 0.004$; $I^2 = 83$ %).

B) Studies that applied tACS for 10 min

Six studies (Moliadze et al., 2010; Cappon, 2016; Giustiniani, 2021; Harada, 2020; Krause, 2016; Wach, 2013) examined the effect of 10 min tACS over M1 on motor function, The findings indicated that 10 min tACS had no significant effect on improving motor function (SMD 0.23, 95 % CI −0.08 to 0.53, $n = 83$, $P = 0.15$, Fig. 14) and no heterogeneity among studies was observed ($Tau^2 = 0.00$; $Chi^2 = 4.16$, df = 5, $P = 0.53$; $I^2 = 0$ %).

C) Studies that applied tACS for 15 min

Two studies (Bologna, 2019; Fresnoza, 2020) investigated the effect of 15 min tACS over M1 on motor function. The results showed no significant effect for 15 min of tACS on motor function (SMD 0.05, 95 % CI −0.41 to 0.51, $n = 36$, $P = 0.83$, Fig. 14) with no heterogeneity between studies ($Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1, $P = 0.95$; $I^2 = 0$ %).

D) Studies that applied tACS for 20 min

Three studies (Berntsen, 2019; Schoenfeld, 2021; Spooner and Wilson, 2023) applied tACS over M1 for 20 min. After sensitivity analysis, one study (Schoenfeld, 2021) was removed and the results from remaining studies indicated that 20 min of tACS had a significant effect on improving motor function (SMD 1.72, 95 % CI 1.20 to 2.24, n = 40, $P < 0.001$, Fig. 14) with no heterogeneity between studies ($Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1, $P = 0.97$; $I^2 = 0$ %).

3.5. *Best evidence synthesis*

3.5.1. *Alpha tACS*

3.5.1.1. Pre-post changes in corticospinal excitability. Limited evidence from a single study (Schutter and Hortensius, 2011) suggests that alpha tACS over M1 with the intensity of 1 mA led to a decrease in MEP amplitude, with a large effect size (*SMD* 0.89, 95 % CI −2.08 to 0.28, Fig. 15-A).

3.5.2. *Beta tACS*

3.5.2.1. Pre-post changes in corticospinal excitability. Four studies

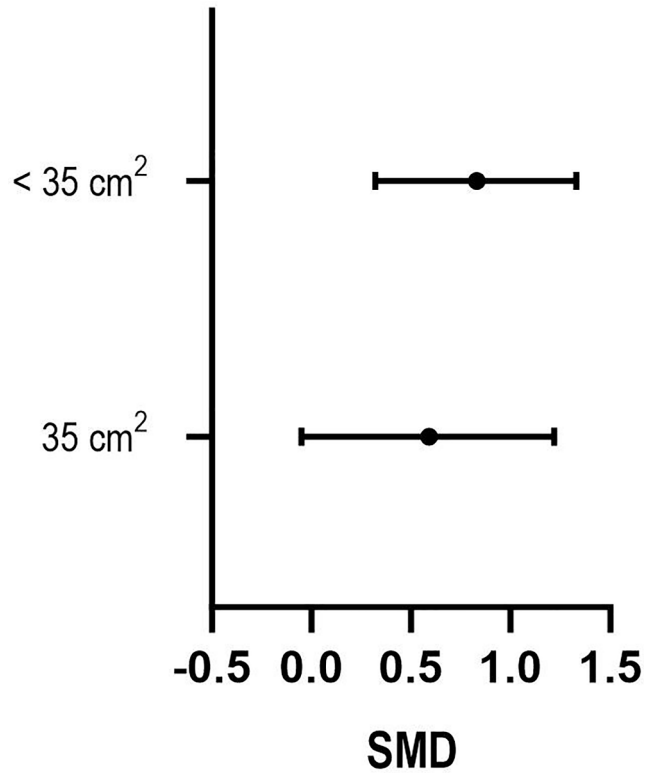

Fig. 13. Forest plot showing the effect of electrode size on motor function. < 35^2: Electrodes with the sizes smaller than 35 cm^2; 35 cm^2: Electrode with the size of 35 cm^2; SMD: standardised mean difference.

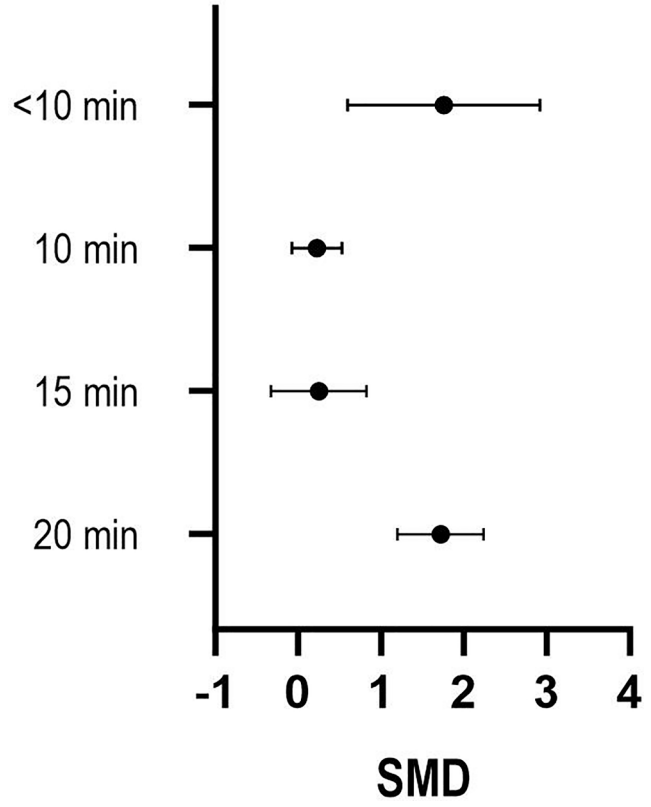

Fig. 14. Forest plot showing the effect of stimulation duration on motor function. SMD: standardised mean difference.

(Heise, 2016; Bologna, 2019; Kudo, 2022; Wischnewski, 2019) examined changes in corticospinal excitability following beta tACS over M1. The results from these studies provide limited evidence, indicating beta tACS may not have a significant effect on MEPs amplitude, as indicated by effect sizes ranging from *SMD* 0.03 to 0.61 (Fig. 15-B).

3.5.3. Gamma tACS

3.5.3.1. Pre-post changes in corticospinal excitability. One study (Bologna, 2019) investigated changes in corticospinal excitability following 1 mA gamma tACS over M1 which was included in the best evidence synthesis. The findings suggest that gamma tACS decreases MEP amplitude, with a small effect size (*SMD* 0.22, 95 % CI −0.91 to 0.48, Fig. 15-C), which provides moderate evidence.

4. Discussion

In this systematic review involving *meta*-analysis and best evidence synthesis, our aim was to identify potential effects of tACS across the alpha, beta, and gamma ranges over the M1. We examined the effects of tACS on corticospinal excitability, intracortical inhibition and facilitation, as well as motor function. Overall, the findings revealed:

- 20 minutes of tACS over M1 led to greater corticospinal excitability, regardless of stimulation frequency and intensity
- Alpha tACS, applied with intensities above 1 mA over M1, increased corticospinal excitability.
- tACS with individualised alpha frequency over M1 improved corticospinal excitability.
- Beta tACS, with intensities above 1 mA over M1, similarly increased corticospinal excitability.
- tACS over M1 led to enhanced motor function, irrespective of stimulation frequency and intensity.
- tACS with electrodes positioned over M1 and supraorbital region resulted in improved motor function.
- tACS with electrode sizes smaller than 35 cm^2 led to improved motor function.
- tACS for the duration less than 10 min, and 20 min increased motor function.
- Alpha, beta, and gamma tACS all exhibited improved motor function, regardless of stimulation intensity.
- Both alpha and beta tACS, using an intensity of 1 mA or lower, contributed to superior motor function.
- Beta tACS with the fixed frequency of 20 Hz, led to enhanced motor function.
- Gamma tACS applied over M1, with intensities above 1 mA, resulted in improved motor function.
- Both low gamma and high gamma tACS increased motor function.
- Intriguingly, both online and offline tACS over M1, with intensities exceeding 1 mA, demonstrated improved motor function, irrespective of stimulation frequency.

4.1. The effects of tACS on corticospinal and intracortical excitability

Our findings generally indicate that tACS applied over the M1 in the alpha, beta, and gamma ranges does not significantly modulate corticospinal and intracortical excitability. These results align with numerous studies reporting no effect of tACS with different frequencies on corticospinal excitability (e.g., (Antal, 2008; Heise, 2016; Moliadze et al., 2010; Kudo, 2022; Pozdniakov, 2021; Spampinato, 2021; Splittgerber, 2020; Wessel, 2020; Rjosk, 2016; Therrien-Blanchet, 2023; Schutter and Hortensius, 2011). However, previous studies have indicated that alpha, beta, and gamma tACS can indeed increase MEP amplitude, suggesting an excitatory effect (Schilberg, 2018; Fresnoza, 2018; Heise, 2016; Naro, 2017; Naro, 2016). Additionally, inhibitory effects on corticospinal excitability through MEP amplitude reduction have been reported in several studies within these frequency ranges (e.g., (Zaghi, 2010; Lafleur, 2020; Nowak, 2017; Cappon, 2016; Giustiniani, 2019; Wang, 2021).

Recent studies have highlighted the potential benefits of individualised frequencies in comparison to fixed frequencies for tACS aftereffects (Berntsen, 2019; Schoenfeld, 2021; Fresnoza, 2020; Spooner and Wilson, 2023). Our findings demonstrated that tACS with individualised alpha frequency increased corticospinal excitability. However, tACS with individualised beta frequency did not yield any significant changes in corticospinal excitability. It is important to note that there were no studies included that used individualised gamma frequency, and the number of studies employing individualised frequencies, in comparison to fixed frequencies, was limited.

The variation in responses to tACS on corticospinal excitability could be attributed to inter-individual differences, a common factor in human NIBS studies (Guerra, 2020). Despite large sample sizes, substantial variability persists in these studies (Guerra, 2020; Huang, 2017; Minkova, 2019). Consequently, inter-individual response variability might play a decisive role in explaining the inconsistent outcomes observed in NIBS studies (Guerra, 2020; López-Alonso, 2014; López-Alonso, 2015; Dissanayaka, 2017; Biabani, 2017), which is further supported by our current findings showing inconsistent outcomes following tACS.

Although the overall conclusion of our *meta*-analysis suggests that alpha, beta, and gamma tACS over M1 do not generally increase corticospinal excitability, a closer examination of tACS parameters highlights significant effects of stimulation intensity and duration. While studies using currents of 1 mA peak-to-peak or lower did not significantly affect MEP amplitudes, those employing currents above 1 mA reported increased MEP sizes for both alpha and beta tACS, with a large effect size for alpha and a medium one for beta.

The current findings regarding the effect of intensity on corticospinal excitability following tACS agree with two previous *meta*-analyses on the effects of tACS on corticospinal excitability and cognitive function (Wischnewski et al., 2019; Schutter and Wischnewski, 2016). Furthermore, Cancelli et al., (2015) (Cancelli, 2015) examined the effect of beta tACS intensity on corticospinal excitability and reported an increase in corticospinal excitability following tACS with an intensity of 2 mA. Conversely, stimulation at or around 0.875 mA resulted in a decrease in corticospinal excitability. Previously, the effect of intensity on corticospinal excitability has been investigated in a systematic review of studies

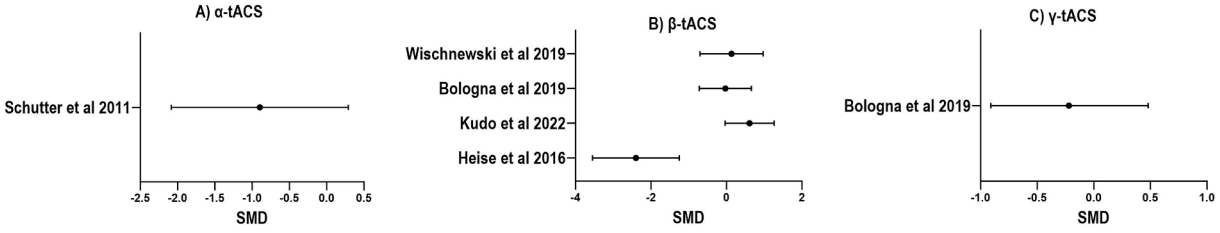

Fig. 15. Forest plot showing effect size for corticospinal excitability following A) Alpha tACS, B) beta tACS and C) gamma tACS. tACS: transcranial Alternating Current Stimulation; α-tACS: Alpha tACS; β-tACS: Beta tACS; γ-tACS: Gamma tACS.

on tDCS, suggesting that stimulation intensities above 1 mA do not exhibit a superior effect for tDCS (Jamil, 2017).

It is necessary to understand the distinction between tACS and tDCS intensities. tACS intensities represent peak-to-peak amplitudes, while tDCS intensities correspond to a constant current. Specifically, an intensity of 1 mA peak-to-peak indicates that the maximum current applied to the skull is 0.5 mA. Moreover, as tACS involves oscillating currents, the intensity is only at its maximum during the peaks and is submaximal at other points in the cycle. Consequently, tACS studies utilizing an intensity of 1 mA (peak-to-peak) apply smaller total currents than tDCS studies employing the same intensity. Given that the actual current intensity reaching the cortical tissue is only a fraction of the applied intensity on the scalp, there is a possibility that alternating currents might be ineffective if the intensity is too low (Wischnewski et al., 2019; Herman, 2011).

In the present *meta*-analysis, concerning gamma tACS, which demonstrated no effect on corticospinal excitability, three out of four reviewed studies applied 1 mA gamma tACS over M1. This observation aligns with the current findings regarding the effect of tACS intensity on corticospinal excitability. Therefore, based on our data and previous studies (Wischnewski et al., 2019; Schutter and Wischnewski, 2016), it is suggested that higher tACS intensities are more desirable to induce corticospinal plasticity.

In addition to intensity, the duration of stimulation plays a vital role in modulating corticospinal excitability. Our results align with two previous systematic reviews, highlighting the significance of longer stimulation durations for tES in improving corticospinal excitability (Dissanayaka, 2017; Bastani and Jaberzadeh, 2012). Specifically, our findings show that, irrespective of frequency, 20 min of tACS is effective in enhancing corticospinal excitability.

In light of the above, the present *meta*-analysis found no significant effect of tACS, at any frequency, on intracortical excitability, including SICI and ICF. These results are consistent with other tES studies that have shown no effect on SICI following anodal tDCS (Jamil, 2017; Nuzum, 2016) and this is expected given the significant variability observed in response to paired-pulse TMS (Boroojerdi, 2000; Farzan, 2010; Ferland, 2019; Dyke, 2018). It should be noted, however, that sub-analysis of intracortical excitability in the present study only included three studies, which represents a relatively low sample size. Further, two of these studies applied 1 mA tACS over M1, which might not be sufficient to modulate the short-latency inhibitory circuits of the M1. Therefore, the exact reason for the observed variations remains unclear, and comparisons between paired-pulse studies are challenging due to differences in experimental conditions (such as stimulation parameters, montage, etc.) and potential inter-subject variability.

4.2. The effect of tACS on motor function

In this systematic review, our findings indicate a general enhancement in motor function through the application of tACS. A more detailed sub-analysis revealed that alpha, beta, and gamma tACS all led to improved motor function, yielding effect sizes of SMD = 1.2, SMD = 0.75, and SMD = 1.36, respectively. These effect sizes indicate moderate to high levels of comparative effects. Moreover, both online and offline tACS demonstrated the capability to enhance motor function, irrespective of the frequency employed. Considering tACS parameters, regardless of the specific frequency used, across studies employing tACS intensities of both 1 mA or lower, as well as greater than 1 mA, improvements in motor function were observed. Furthermore, studies that employed tACS sessions lasting less than 10 min or extending to 20 min, along with the use of smaller electrodes (less than 35 cm^2) or the M1-SOR montage, demonstrated improvements in motor function.

Consequently, our findings strongly suggest that tACS within the alpha, beta, and gamma frequency ranges, whether administered prior to or concurrently with a motor task, can effectively enhance motor function. As per our findings, tACS with a fixed frequency of 20 Hz resulted in improved motor function and notably, both low gamma (30–55 Hz) and high gamma (55–80 Hz) frequencies demonstrated enhancement in motor function. However, it is important to note that only one study applied individualised beta frequency, making it impossible to draw a meaningful comparison between the effects of fixed and individualised frequencies in the beta range on motor function.

Overall, our findings indicate that alpha and beta tACS with intensities greater than 1 mA, as well as IAF tACS, led to increased corticospinal excitability. However, none of these approaches resulted in improved motor function. Despite this, there was still a noticeable improvement in motor function following tACS. This finding suggests that alterations in motor function might not necessarily reflect changes in corticospinal and intracortical excitability (Bologna, 2019). Furthermore, it's important to note that the studies included in our systematic review examined diverse motor tasks, potentially engaging distinct cortical networks and pathways.

While theories such as cortical oscillation entrainment and STDP have been proposed as the primary mechanisms underlying the effects of tACS, the specific relationship between these mechanisms and the modulation of motor function remains to be elucidated (Cabral-Calderin and Wilke, 2020; Takeuchi and Izumi, 2021).

In addition to frequency, it is essential to consider other tACS parameters, including intensity, montage, duration, and electrode size. As stimulation intensity has been reported to play a significant role in tACS effects (Wischnewski et al., 2019; Cancelli, 2015), a more detailed examination of the effects of intensity on alpha, beta, and gamma frequency tACS revealed that both alpha and beta tACS with an intensity of 1 mA or lower resulted in improved motor function with moderate to large effects (SMD = 0.80 and SMD = 0.47, respectively). Gamma tACS with an intensity of 2 mA showed a large effect for improving motor function (SMD = 1.68). However, in the study conducted by Cancelli et al. (2015) (Cancelli, 2015), it was reported that beta tACS with intensities below 1 mA resulted in a decrease in corticospinal excitability. Interestingly, our findings revealed that both alpha and beta tACS, with intensities of 1 mA or lower, demonstrated the ability to improve motor function, although our findings did not indicate any decrease in corticospinal excitability following tACS with intensities of 1 mA or lower.

The results of our sub-analysis concerning electrode montage revealed that the most frequently used montage (M1-SOR) was effective in improving motor function, while M1-Pz did not have a significant effect on motor function. It is worth noting that a previous systematic review reported an effect for posterior montages, such as M1-Pz, on corticospinal excitability (Wischnewski et al., 2019), but our study found no significant difference in the effect of electrode montage on corticospinal excitability. Two important points should be considered. First, only two studies applied tACS over M1-Pz for either corticospinal excitability or motor function, which represents a limited number of studies with a small sample size. Second, it is more likely that the M1-SOR montage induced phosphenes (Schutter, 2016; Schutter and Hortensius, 2010) which might challenge the participants' blindness, potentially contributing to the improvement in motor function. However, this effect did not extend to MEP amplitude, which is a neurophysiological measurement.

As it was observed for corticospinal excitability, a 20-minute session of tACS applied over M1 also demonstrated an improvement in motor function. However, it's important to note that only two studies, both for corticospinal excitability and motor function, employed a 20-minute duration, so these findings should be interpreted cautiously. Conversely, tACS sessions lasting less than 10 min were associated with improved motor function.

Electrode size exhibited significant variation across the studies. The size of the electrode and the associated current density are pivotal factors in modulating corticospinal excitability. Studies have suggested that higher current densities or the use of smaller electrodes may be more effective in influencing cortical plasticity (Dissanayaka, 2017; Bastani and Jaberzadeh, 2013). Notably, a 35 cm^2 electrode size is the most

commonly used in tES studies (Dissanayaka, 2017). In our current *meta*-analysis, studies were categorized into two primary groups: those employing active electrode sizes of 35 cm^2 and those using smaller electrode sizes. Our findings indicated that alpha and beta tACS with intensities greater than 1 mA can enhance corticospinal excitability. This led to the expectation that smaller electrode sizes might have similar effects on corticospinal excitability, which, however, was not confirmed by our current findings. Nonetheless, studies that applied tACS with electrode sizes smaller than 35 cm^2 showed improvements in motor function. However, our findings regarding the effects of intensity on motor function revealed no significant differences between intensities.

The only scenario where both corticospinal excitability and motor function improved was with 20 min of tACS, regardless of the tACS frequency used. It is important to acknowledge that this observation is based on a limited number of studies; only two studies were included in the aforementioned datasets. This limited sample size calls for caution in interpreting the results, emphasising the need for further research to draw definitive conclusions.

Given the information provided, our systematic review and best evidence synthesis concerning the effects of tACS on corticospinal excitability across various frequency ranges, including alpha, beta, and gamma tACS, yielded consistent findings with both our *meta*-analysis and previous studies (Wischnewski et al., 2019; Cancelli, 2015). This suggests an association between intensity and corticospinal excitability. In the case of alpha and gamma tACS, evidence from a single study indicated that the application of 1 mA tACS over the M1 region resulted in a decrease in corticospinal excitability. Notably, the observed effect size was substantial for alpha tACS and relatively minor for gamma tACS. Nevertheless, these effects did not achieve statistical significance. Furthermore, our analysis encompassed four studies involving beta tACS, and the outcomes presented restricted evidence suggesting that beta tACS directed over the M1 might not yield a notable effect on corticospinal excitability. Effect sizes across these studies ranged from small to moderate.

Considering the heterogeneity among studies and the inconsistencies in their findings, it is important to consider several key points. First, in the section focusing on corticospinal excitability, all sub-analyses that resulted in changes in corticospinal plasticity, including IAF tACS, alpha and beta tACS with intensities greater than 1 mA, and 20-minute tACS, were based on only two studies. It is important to recognize that this observation is derived from a very limited number of studies. The restricted sample size underscores the need for a cautious interpretation of the results and highlights the importance of further research to establish more powerful conclusions.

Secondly, in the motor function section, it is noteworthy that each dataset included a considerable number of studies with substantial sample sizes. However, it is imperative to approach the interpretation of these results with caution because a significant publication bias was apparent in studies examining the effects of tACS on motor function. To achieve a more definitive understanding, further research that encompasses both positive and negative results is warranted.

Thirdly, despite the promising potential of tACS to enhance motor function, certain sub-analyses, such as IAF, alpha and beta tACS with intensities exceeding 1 mA, stimulation durations of 15 min, and electrode montages like M1-Pz, which exhibited no potential for improving motor function, were based on a limited number of studies (only 2), with small sample sizes.

5. Limitations

It is important to identify certain limitations in this systematic review to ensure a clear understanding of our findings. Our primary focus was on examining the effects of tACS on corticospinal and intracortical excitability, along with motor function, specifically targeting the M1 region.

The scope of our analysis was restricted due to the limited number of studies that assessed intracortical excitability, or studies applying individualised frequencies, tACS for longer than 10 min, intensities greater than 1 mA and studies with electrode montages different from M1-SOR leading to a small sample size for this particular aspect of the review which might restrict comprehensive conclusions for this intensity range.

All the studies included in this research focused on healthy young adults. Given that the effects and mechanisms of NIBS are believed to vary with age (Ridding and Ziemann, 2010), it is important to note that the findings from this study may not be applicable to individuals of older age.

Considering the variability in results and the numerous influencing factors such as stimulation intensity, duration, electrode size, montage, frequency, and online vs. offline effects, there is a need for more meticulously designed randomized controlled trials (RCTs). These trials should encompass adequate sample sizes and implement appropriate blinding for both participants and researchers. Moreover, comprehensive RCTs that compare the effects of different factors within a single study are warranted. For example, such studies could compare different montages or explore variations between alpha, beta, and gamma frequencies, while also considering individualised frequencies and high or low gamma frequencies. This approach would contribute to enhancing the overall quality of research in this field.

The precise physiological mechanism through which tACS enhances motor function remains elusive. Currently, TMS is the most widely used technique for investigating corticospinal responses. In our review, we incorporated various neurophysiological measurements, including MEPs, SICI, and ICF. However, we did not establish a direct link between corticospinal responses and motor function improvements. One potential solution is to integrate EEG studies, which could establish a more direct connection between changes in brain function and resulting motor function improvements induced by tACS. To address these limitations and to gain a comprehensive understanding of tACS effects, future research should encompass a broader range of contributing factors. Additionally, the combination of tACS with neuroimaging techniques, such as simultaneous high-temporal-resolution EEG or EEG combined with functional near-infrared spectroscopy (fNIRS), holds the potential to provide valuable insights into the mechanisms underlying tACS-induced modifications in both motor function and cortical function.

6. Conclusion

Our findings highlight that tACS with individual alpha frequency (IAF), a stimulation duration of 20 min, and both alpha and beta tACS with stimulation intensity exceeding 1 mA can effectively enhance corticospinal excitability. Our observations indicate that alpha, beta, and gamma tACS applied over the M1 region results in improved motor function, regardless of whether the application is prior to or concurrent with the motor task. Notably, alpha and beta tACS at intensities of 1 mA or lower can improve motor function, implying that a direct increase in corticospinal excitability might not consistently correlate with enhanced motor function. Additionally, beta tACS with the fixed frequency of 20 Hz as well as both low and high gamma has the potential to improve motor function. tACS parameters such as electrode size, and montage seem to be determining factors in this regard. These findings clarify the potential of tACS and emphasise the role of stimulation intensity, and duration in modulating corticospinal excitability as well as electrode size, stimulation duration, and electrode montage in improving motor function. These findings carry significant implications for both future research and clinical applications.

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8. Statement

During the preparation of this work, the first author used [OpenAI. (2023). ChatGPT (August 3 Version)/ https://chat.openai.com] in order to [improve readability and grammar check]. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

CRediT authorship contribution statement

Mohamad Rostami: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft. **Annemarie Lee:** Writing – review & editing. **Ashlyn K Frazer:** Writing – original draft. **Yonas Akalu:** Conceptualization, Methodology, Data curation, Formal analysis. **Ummatul Siddique:** Conceptualization, Methodology, Data curation, Formal analysis. **Alan J. Pearce:** Writing – original draft, Writing – review & editing. **Jamie Tallent:** Writing – review & editing. **Dawson J Kidgell:** Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brainres.2023.148650.

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