Brain Stimulation 18 (2025) 1257–1265

Contents lists available at ScienceDirect

Brain Stimulation

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

Increased variability in response to transcranial direct current stimulation in healthy older compared to young adults: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Aging
Variability
Stimulation effect
Transcranial electrical stimulation (tES)
Transcranial direct current stimulation (tDCS)
Meta-analysis

ABSTRACT

Background: Healthy aging is associated with a decline in cognitive and motor functions, affecting daily activities and quality of life. Combining transcranial direct current stimulation (tDCS) with behavioral training may be a promising intervention against this decline. However, individual response variability may obscure group-level effects and mislead conclusions about tDCS efficacy. Quantifying this variability is crucial for accurately assessing stimulation effects and understanding individual response factors, like age. Yet, no study has quantitatively compared tDCS variability across age groups. This systematic review and meta-analysis examine age-related variability in cognitive and motor responses to tDCS.

Methods: Following PRISMA guidelines, we searched PubMed and Cochrane for studies directly comparing young and healthy older adults under similar experimental conditions. Across 19 studies comprising 390 older adults (mean ± SD age: 67 ± 5 years) and 384 young adults (mean ± SD age: 24 ± 3 years) receiving transcranial direct current (tDCS), we quantified behavioral variability using the log-transformed coefficient of variation ratio (lnCVR).

Results: Results revealed substantially higher response variability in healthy older compared to young adults during active tES (21 %, $\ln CVR_{active} = -0.24$ [-0.43, −0.04], $p = 0.02$), but not during sham conditions ($\ln CVR_{sham} = -0.18$ [-0.42, 0.05], $p = 0.13$).

Conclusion: These findings provide the first quantitative evidence that advanced age increases behavioral tDCS response variability, highlighting the need to develop personalized tDCS approaches to optimize their efficacy in older populations.

1. Introduction

Healthy aging is associated with declines in cognitive and motor functions, impacting everyday activities and quality of life [1–3]. Cognitive decline is evident in domains such as memory, executive functions, attention, and processing speed [1,4,5], while motor impairment manifests in reduced accuracy, slower movement, and increased risk of falling [6,7]. Transcranial direct current stimulation (tDCS) has emerged as a promising, noninvasive and cost-effective approach to counteract age-related functional decline [8,9]. This technique applies direct low-intensity current (typically 1–2 mA) via two or more scalp-attached electrodes to modulate neuronal excitability and promote synaptic plasticity by altering membrane potentials [10,11]. While tDCS does not directly induce action potentials, it can influence network-level activity and facilitate long-lasting changes in synaptic strength through plasticity-related mechanisms [12–15]. When applied during cognitive or motor tasks, tDCS has been shown to enhance performance both in young and older adults [3,6,16,17]. These findings highlight its potential as a compensatory intervention [18,19]. However, tDCS effects are inconsistent across studies, particularly in

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https://doi.org/10.1016/j.brs.2025.06.005
Received 18 March 2025; Received in revised form 21 May 2025; Accepted 6 June 2025
Available online 8 July 2025

older adults [20,21]. Several studies report only small or even a lack of stimulation effects [22–24], while others suggest that older adults experience greater performance gains than young adults [3,25,26]. This divergence may be because individuals with lower baseline performance, having more room for improvement, often gain greater benefits from tDCS interventions than those with initially higher performance levels [27–29]. However, older adults may exhibit reduced plasticity than young adults, diminishing their responsiveness to both training-based and tDCS approaches [23,30].

In addition to conflicting findings between studies, responses to tDCS vary widely between individuals [31–34]. Interindividual differences in brain anatomy and function likely influence this variability. The former affects the current flow to the target regions for tDCS, hence its functional network organization and activity [35,36]. Such response variability can obscure group-level effects, potentially leading to the incorrect assumption that tDCS lacks efficacy when, in fact, individual differences may drive mixed outcomes [31,37]. In some cases, this variability can lead to highly significant effects, driven by a subset of individuals who exhibit exceptionally strong responses, even though the majority experience minimal or no benefit [33,38]. Quantifying this response variability is a crucial step in accurately evaluating tDCS efficacy. In other therapeutic contexts, such as antipsychotic treatment for schizophrenia, this variability quantification can enable the identification of responder subgroups [39,40], potentially supporting the development of personalized or stratified treatment approaches [41]. Variability measurement provides insight into the consistency of an intervention's effects across individuals, helps to identify factors that influence differential outcomes like age and might guide the refinement of interventional strategies [39]. Notably, reduced response variability often reflects enhanced treatment effectiveness [39,42].

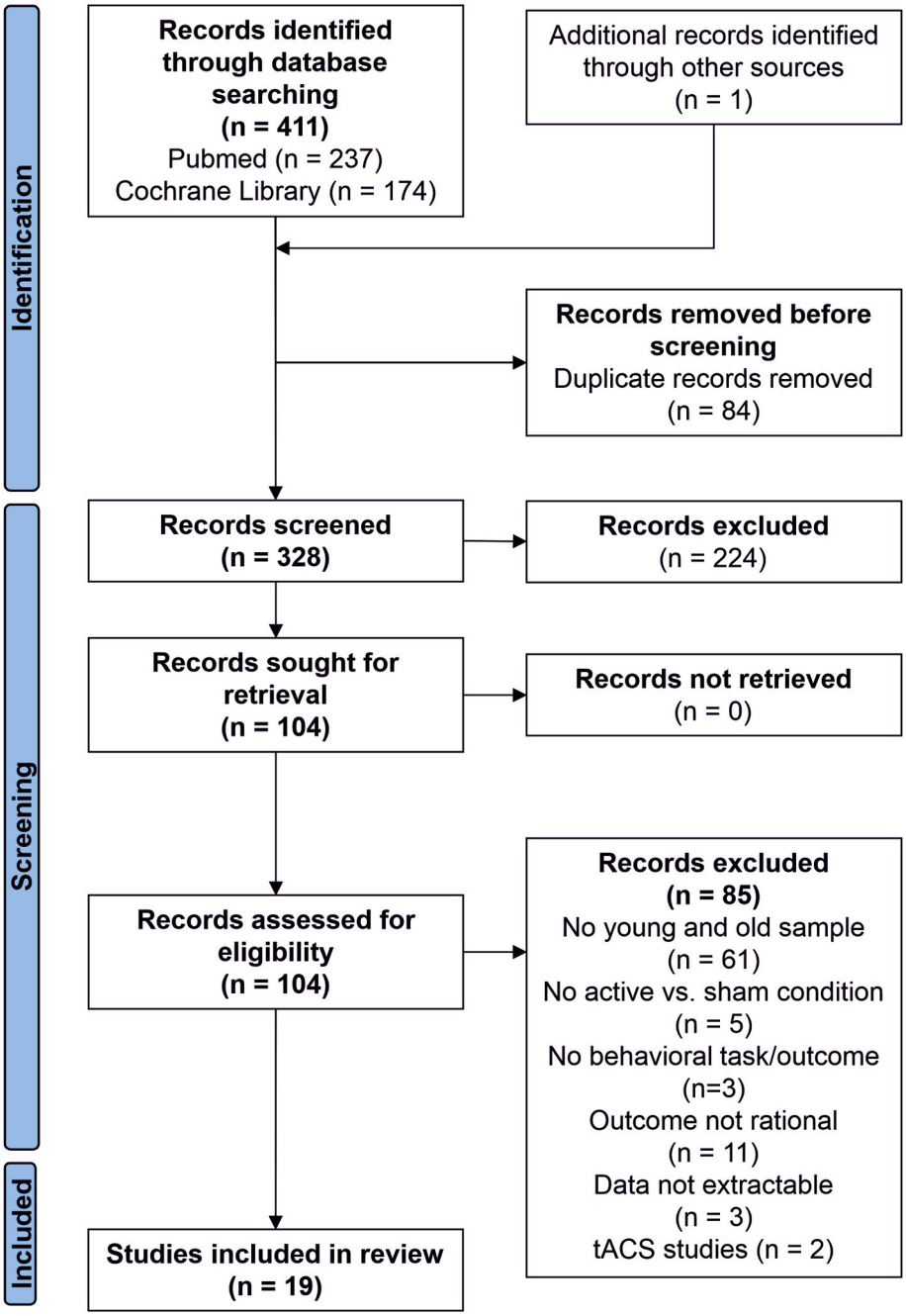

Fig. 1. PRISMA flowchart for the study identification procedure.

So far, no study has systematically examined and quantified age-related variability in response to tDCS. Greater variability within an age group would indicate more heterogeneous responses due to underlying biological factors, allowing a quantitative assessment of this hypothesized variability for the first time. To address this gap, we conducted a systematic review [43] to identify studies directly comparing young and older adults across motor and cognitive domains within the same experimental setup. Then, we quantified cognitive and motor performance variability using the log-transformed coefficient of variation ratio (lnCVR) to systematically assess age-related differences in tDCS response [44,45]. We hypothesized that age-related variability would differ substantially between young and older adults, with older adults exhibiting higher variability. Moreover, we hypothesized that this difference would be more pronounced in active tES than sham stimulation, allowing us to identify a unique factor distinct from any general differences in behavioral training effectiveness between age groups.

2. Methods

2.1. Search strategy and study selection

A comprehensive literature search was conducted in the PubMed and Cochrane databases from January to August 2024. The used search string was: "(transcranial electrical stimulation OR tES OR transcranial direct current stimulation) AND (old OR elder OR older) AND (young)." The reference lists of the retrieved studies were also checked for additional eligible studies. A total of 411 studies were identified through the database search, with one additional study found through reference checking (see Fig. 1).

Studies were included if they met the following criteria: (a) applied tDCS in young (YA, between 18 and 35 years) and older adults (OA, ≥60 years) using identical stimulation parameters and tasks, (b) involved only healthy participants to minimize variability related to pathological conditions, (c) included both an active (treatment) and a sham (placebo) group, (d) examined motor and/or cognitive functions operationalized by behavioral outcomes (e) single- and multisession tDCS studies, (f) that employed either cross-over or between-subject designs, (g) were published in peer-reviewed journals, (h) were written in English, and (i) were not case reports, case series, reviews or opinion pieces.

2.2. Data extraction

Following the PRISMA guidelines [43], two independent researchers (A.E.F and D.A.) conducted the literature search, study assessment and data extraction. We extracted the mean and standard deviation for motor and cognitive outcomes for both the active and sham stimulation conditions post-intervention, and the sample size. When numerical values were not provided in the manuscript, the "metaDigitise" R package (version 1.0.1) [46] was used to extract values from figures. Otherwise, authors were contacted directly (4, with all responding). Additionally, we extracted information on the study design, participant characteristics, stimulation parameters and electrode placement (Table 1). The final sample included 19 studies: 7 investigated motor and 12 cognitive functions. Please note that we used additional information from the following 2023 publication [16] to extract the contrast between older and young adults for Meinzer and colleagues (2012). The systematic review was not pre-registered.

2.3. Age-related response variability

Using the formula below, we calculated the log coefficient of variation ratio (lnCVR), which adjusts for mean differences between groups [39,44,45]. A lnCVR below 0 suggests higher variability in older compared to young adults, a lnCVR of 0 implies equal variability between young and older adults, and a value above 0 suggests lower variability in older compared to young adults. To facilitate interpretation, we converted the lnCVR into a percentage-based variability score using an exponential function [45].

$$lnCVR = \ln \frac{\frac{s_{young}}{\bar{x}_{young}}}{\frac{s_{old}}{\bar{x}_{old}}} + \frac{1}{2\,(n_{young}-1)} - \frac{1}{2\,(n_{old}-1)}$$

Note. lnCVR = Log coefficient of variation ratio; s = Standard deviation; $\bar{x}$ = Mean; n = sample size.

We pooled the lnCVR across all domains and conditions, with contrasting young and older adults to account for age-related variability in response to active and sham tDCS conditions. For additional exploratory analyses, we performed meta-regressions using mixed-effects models, including the task domain (cognitive or motor) as moderator in the lnCVR analysis. This approach allowed us to specifically assess the effect of task domain on response variability. We report the moderator estimates along with a 95 % confidence interval and the corresponding p-value.

We used the Higgins and Green I^2 test to assess heterogeneity, which quantifies heterogeneity as a percentage from 0 % to 100 %. According to guidelines, I^2 values of 25 %, 50 %, and 75 % correspond to low, moderate, and high heterogeneity levels, respectively [47,48].

2.4. Variability and stimulation effect within age groups

We conducted additional analyses within each age group. To investigate the link between variability and stimulation effects across different age groups, we calculated the lnCVR and the standardized mean difference (SMD) by comparing active and sham conditions for each study. A lnCVR below 0 indicates reduced variability under active stimulation, values around 0 indicate no difference, and values above 0 indicate increased variability under active stimulation. SMD values below 0 indicate a reduced effect under active stimulation, 0 reflects no difference, and values above 0 indicate a higher effect under active stimulation. Finally, we used the extracted effect sizes for a Pearson correlation analysis to explore potential associations between variability and stimulation effects within each age group.

All analyses were conducted in R (4.4.1, https://www.R-project.org/), using the "metafor" package for lnCVR and SMD analyses [45,49]. All effects are reported with 95 % confidence intervals.

3. Results

3.1. Descriptive statistics

A total of 19 studies were included in this meta-analysis, with 7 studies investigating motor functions [24,50–55] and 12 studies examining cognitive functions [29,56–66]. Motor functions included learning new skills [24], eye-movement testing [50] or visuomotor tracking [54], Go/NoGo tasks [51,53], postural control tasks, [52], proprioceptive assessment task [55] and treadmill walking [63]. Cognitive functions included memory paradigms, such as language learning [29,58,60,64,66,67], visual working memory tasks [56] or naming tasks [57,61,62,65].

Two were multisession studies [24,29], while the remaining studies applied active tDCS once. Five studies were between-subject studies [24,29,59,63,64] and the remaining 19 were cross-over designs. All participants were healthy, with no history of neurological or psychiatric disorders or use of psychoactive medications. For older adults, normal cognitive functioning was confirmed using standard screening tools (e.g., Montreal Cognitive Assessment, Mini-Mental-Status-Test) with established cut-off scores.

Overall, 774 subjects were included, comprising 384 young adults (mean ± SD age: 24 ± 3 years) and 390 old participants (67 ± 5 years). For an overview of the study characteristics of the included studies, see Table 1. For further information on the extracted mean and standard deviation, see Table S1.

Table 1
Study characteristics of included studies for quantitative synthesis.

Study	Parameters	Design and Domain	Task	Outcome	Sample
Study 1: Arciniega et al., 2018 10.3389/fnagi.2018.00057	2 mA 20 min frontoparietal cortex	CrossS ingle-sessionC ognitive	visual working memory	accuracy (%)	Young 22 ± 3 Old 67 ± 5
Study 2: Chen & Machado 2017 10.16910/jemr.10.3.5	1 mA 10 min dorsolateral prefrontal cortex	Cross Single-session Motor	eye movement testing (prosaccade + antisaccade blocks)	RT (ms)	Young 23 ± 1 Old 67 ± 2
Study 3: Conley et al., 2016 10.3389/fnhum.2016.00384	1 mA 20 min motor cortex	Cross Single-session Motor	Go/NoGo task	RT (ms)	Young 22 ± 3 Old 60 ± 11
Study 4: Craig & Doumas 2017 10.1371/journal.pone.0170331	2 mA 20 min primary motor cortex	Cross Single-session Motor	postural control task	length (cm)	Young 21 ± 3 Old 73 ± 5
Study 5: Fertonani et al., 2014 10.3389/fnagi.2014.00131	2 mA 5 min dorsolateral prefrontal cortex	Cross Single-session Cognitive	picture-naming task	RT (ms)	Young 22 ± 1 Old 67 ± 11
Study 6: Fiori et al., 2017 10.1016/j.bbr.2016.12.044	2 mA 20 min temporal cortex	Cross Single-session Cognitive	language learning (pseudoword-picture pairs)	correct response (%)	Young 29 ± 6 Old 72 ± 6
Study 7: Fujiyama et al., 2022 10.1016/j. neurobiolaging.2021.09.014	1.5 mA 20 min pre-supplementary motor area	Cross Single-session Motor	Flashing grid task combined with perceptual decision-making task and Stop Signal Task	RT (ms)	Young 25 ± 5 Old 66 ± 6
Study 8: Goodwill et al., 2015 10.1016/j.clinph.2015.01.006	1 mA 15 min motor cortex	Cross Single-session Motor	visuomotor tracking task	MEP (%)	Young 26 ± 2 Old 66 ± 1
Study 9: Habich et al., 2020 10.1155/2020/8896791	1 mA 20 min dorsolateral prefrontal cortex	Cross Single-session Cognitive	verbal episodic memory task	correct response (#)	Young 25 ± 3 Old 68 ± 5
Study 10: Kaminski et al., 2021 10.1038/s41598-021-82275-4	1 mA 20 min primary motor cortex	Between Multisession Motor	arc pointing task	accuracy (%)	Young 28 ± 4 Old 68 ± 6
Study 11: Leach et al., 2019 10.1093/geronb/gby003	1.5 mA 25 min dorsolateral prefrontal cortex	Between Single-session Cognitive	Associative memory (face-name) task	correct response (SDT)	Young 23 ± 5 Old 68 ± 5
Study 12: Manenti et al., 2013 10.3389/fnagi.2013.00049	1.5 mA 6 min dorsolateral prefrontal cortex	Cross Single-session Cognitive	verbal episodic memory task	RT (ms)	Young 24 ± 3 Old 68 ± 5
Study 13: Martin et al., 2017 10.1162/jocn_a_01166	1 mA 30 min primary motor cortex	Cross Single-session Cognitive	semantic word generation task	errors (#)	Young 27 ± 4 Old 69 ± 6
Study 14: Meinzer et al., 2012 10.1523/ JNEUROSCI.4812–11.2012 Meinzer et al., 2013 10.1523/ JNEUROSCI.5743–12.2013	1 mA 20 min inferior frontal gyrus	Cross Single-session Cognitive	semantic word generation task	RT (ms)	Young 27 ± 4 Old 68 ± 6
Study 15: Muffel et al., 2019 10.3389/fnagi.2019.00264	1 mA 15 min primary somatosensory cortex	Cross Single-session Motor	proprioceptive assessment task (KINARM)	error (degree)	Young 27 ± 3 Old 70 ± 5
Study 16: Orcioli-Silva et al., 2021 10.3389/fnagi.2021.739998	0.6 mA 20 min prefrontal cortex and vertex	Between Single-session Cognitive	Treadmill walking task	errors (%)	Young 21 ± 3 Old 67 ± 6
Study 17: Perceval et al., 2020 10.1016/j.bandl.2020.104788	1 mA 20 min inferior frontal gyrus	Between Multisession Cognitive	language learning (pseudoword-picture pairs)	correct response (#)	Young 22 ± 4 Old 68 ± 6

(*continued on next page*)

Table 1 (*continued*)

Study	Parameters	Design and Domain	Task	Outcome	Sample
Study 18: Peter et al., 2019 10.1007/s00429-019-01946-1	1 mA 15 min dorsolateral prefrontal cortex	Between Single-session Cognitive	verbal episodic memory task	correct response (#)	Young 25 ± 3 Old 69 ± 6
Study 19: Ross et al., 2011 10.3389/fnagi.2011.00016	1.5 mA 15 min anterior temporal lobe	Cross Single-session Cognitive	name recall task	correct response (%)	Young 19–37 Old 65 ± 4

Note. The table summarizes the characteristics of the studies for quantitative synthesis, including key parameters and outcomes for the transcranial direct current stimulation (tDCS) intervention. The reference, including the DOI, is listed in the "study." "Parameters" contains information regarding the stimulation intensity (in mA), stimulation duration (in minutes) and the stimulation location. "Design and Domain" contain information regarding the study design, hence cross-over studies (cross) or between-subject studies (between), the number of sessions (single- or multisession studies) and the task domain (cognitive or motor). More information on the paradigm can be found in "Task" and the corresponding extracted variable in "Outcome." The sample describes the age distribution of the young and older participants. The Age is described with mean ± standard deviation or age range if there was no information on the mean.

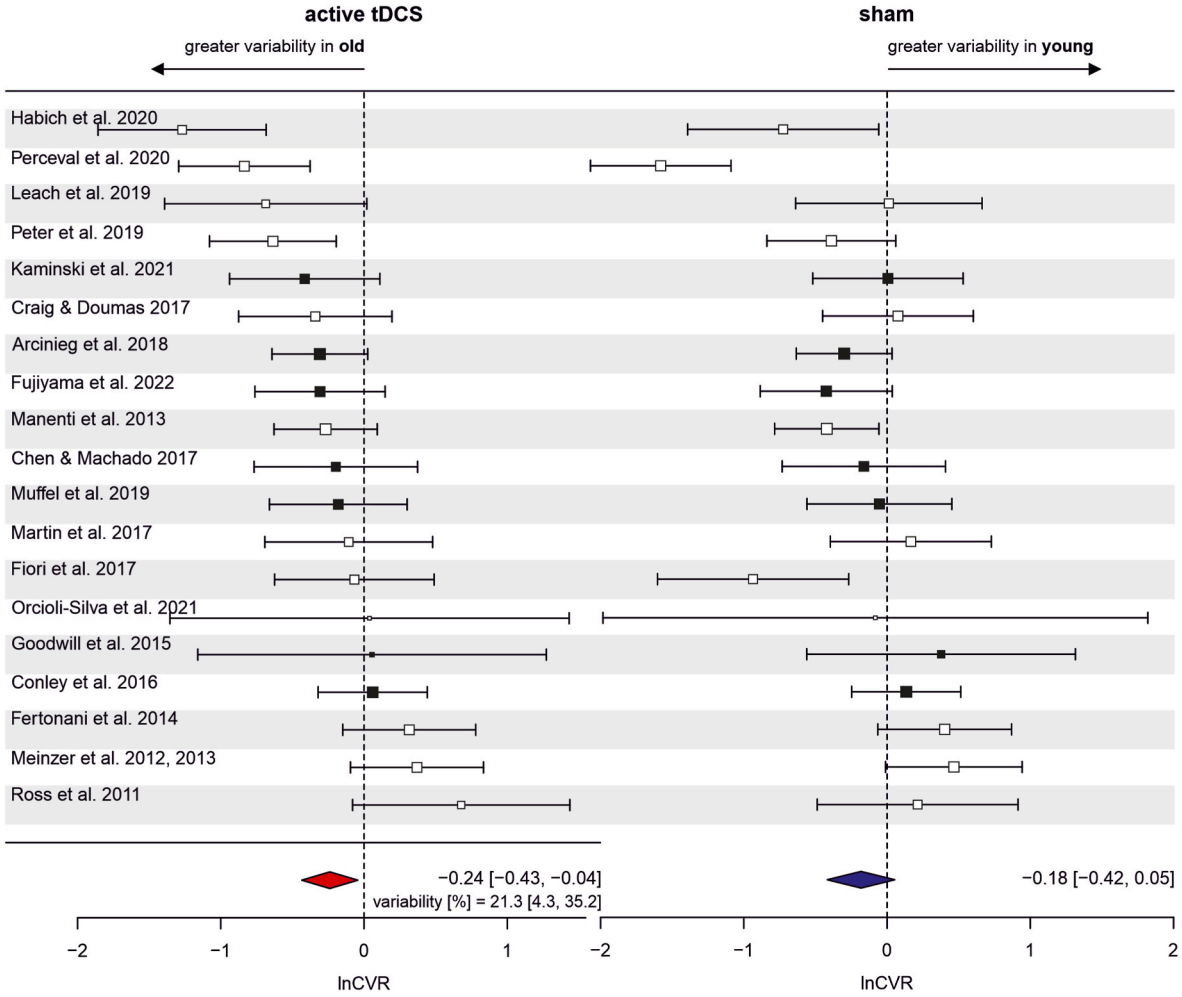

Fig. 2. Age-related response variability. Left panel: Forest plot illustrates the log coefficient of variation ratio (lnCVR) comparing the active young sample to the active older sample. Values below 0 indicate greater variability in the older sample under active transcranial direct current stimulation (tDCS). Effects are displayed as squares (black representing motor domain, while white represent cognitive domain) with 95 % confidence intervals. The overall effect was: $lnCVR_{active} = -0.24$ [-0.43, −0.04], p = 0.02. The lnCVR was converted into a percentage-based variability score using an exponential function to facilitate its interpretation: 21.3 % (95 %CI: [4.3, 35.2]). Additional analyses on the task domain revealed a more consistent pattern of age-related variability for motor tasks respectively ($lnCVR_{active\_motor} = -0.19$, 95 % CI: [-0.38, 0.00], p = 0.053; $lnCVR_{active\_cognition} = -0.25$, 95 % CI: [-0.56, 0.06], p = 0.11). Right Panel: Forest plot illustrates the lnCVR comparing the sham young sample to the sham older sample. Values below 0 indicate greater variability in the older sample under sham tDCS. Effects are displayed as squares (black representing motor domain, while white represents cognitive domain) with 95 % confidence intervals. The overall effect was: $lnCVR_{sham} = -0.18$ [-0.42, 0.05], p = 0.13. Additional analyses on the task domain revealed no difference between motor and cognitive tasks ($lnCVR_{sham\_motor} = -0.04$, 95 % CI: [-0.23, 0.15], p = 0.70, Cognition: $lnCVR_{sham\_cognition} = -0.27$, 95 % CI: [-0.63, 0.08], p = 0.13). Studies were ordered according to the degree of variability under active tDCS. tDCS, Transcranial direct current stimulation. lnCVR, log coefficient of variation ratio.

3.2. Age-related response variability

Under active tDCS, older adults exhibited higher variability compared to young adults ($lnCVR_{active} = -0.24$ [−0.43, −0.04], p = 0.02), although moderate heterogeneity was detected ($I^2 = 62.30$ % [31.21, 83.93]). This finding represents a 21 % higher variability in older adults compared to young adults (95 % CI: [4.3, 35.2]). In contrast, no age-related difference in variability was observed under the sham condition ($lnCVR_{sham} = -0.18$ [−0.42, 0.05], p = 0.13). Again, the heterogeneity was moderate ($I^2 = 73.39$ % [50.56, 87.51]), indicating that the observed variability may differ across studies. See Fig. 2 for the forest plots.

Subgroup analyses on task domain (cognitive versus motor) revealed a more reliable pattern of increased age-related variability in motor tasks compared to cognitive tasks (for more information see Supplements).

To further assess potential publication bias, we performed the Egger's test, which indicated no significant funnel plot asymmetry (z = 0.5, p = 0.62), with the intercept estimate supporting symmetry (b = −0.38, 95 % CI: [−0.98, 0.22]). Complementary Trim and Fill analysis identified five potentially missing studies on the left side of the funnel plot, suggesting underrepresentation of smaller studies with negative or null effects. After adjustment, the effect size remained directionally consistent and slightly stronger ($lnCVR_{active} = -0.41$, 95 % CI: [−0.63, −0.19], p = 0.0002), indicating that any publication bias may have led to an underestimation of age-related variability. High heterogeneity persisted ($I^2 = 75.5$ %), indicating that methodological variation across studies was the likely source of variability rather than publication bias (see Supplementary Fig. 1 for the funnel plot).

3.3. Variability and stimulation effect within age groups

In older adults, effect and variability did not differ substantially between active tDCS and sham (effect: SMDOA = 0.14 [−0.02, 0.31], p = 0.09, variability: $lnCVR_{OA} = -0.07$ [−0.18, 0.05], p = 0.27), showing a small heterogeneity (effect: $I^2 = 24.95$ % [0, 73.28] variability: $I^2 = 0$ % [0, 66.84]). In young adults, effect and variability differed between active tDCS and sham (effect: SMDYA = 0.27 [0.1, 0.45], p = 0.02, variability: $lnCVR_{YA} = -0.11$ [−0.22, 0.01], p = 0.06), showing moderate heterogeneity (effect: $I^2 = 32.16$ % [0, 80.72]), variability: $I^2 = 0$ % [0, 46.17]). Overall, a higher stimulation effect was associated with reduced variability in both age groups, but was statistically significant only for older adults ($r_{OA} = -0.78$ [−0.77, −0.03], p = 0.04, $r_{YA} = -0.38$ [−0.71, 0.08], p = 0.1).

4. Discussion

This meta-analysis aimed to systematically assess age-related differences in tDCS response variability across motor and cognitive domains. Our results revealed that older adults exhibited substantially higher response variability than young adults during active, but not sham, tDCS. This effect was consistent across motor and cognitive domains. Moreover, lower response variability was associated with enhanced treatment efficacy. These results highlight the critical need to understand and address variability in tDCS applications to maximize their therapeutic potential.

Research investigating response variability in noninvasive brain stimulation remains limited [41,68]. Our findings diverge from previous meta-analyses, which indicated minimal response variability under active stimulation for disease-related outcome variables in psychiatric populations [41] or showed no variability in response inhibition among healthy and pathological participants [68]. Such discrepancy may arise from differences in study populations [41] and methodological focus, as previous analyses emphasized task type and stimulation protocols rather than biological factors such as age, sex and health status [68]. Homan et al. (2021) investigated treatment variability in psychiatric disorders by using questionnaires focused on symptom reduction, primarily for transcranial magnetic stimulation (TMS, which comprised 82 % of the included studies) and tDCS. Most participants received additional medication. Their results showed consistently low variability in treatment effects, except for schizophrenia, suggesting a potential need for personalized approaches in pathological populations. However, they did not consider moderators such as age or sex, which limited their ability to identify biological contributors to variability [41]. Similarly, a recent meta-analysis examined tDCS effects on response inhibition and found no difference in variability between active tDCS and sham conditions, indicating that inter-individual variability may not significantly contribute to the heterogeneity observed in this domain [68]. Again, this study primarily focused on methodological variations, such as differences in stimulation intensity and duration, rather than on biological characteristics of participants, like age and sex [69].

In contrast, our findings revealed an increased variability with age, which likely reflects an interaction between stimulation effects and age-related structural and functional brain changes [3,23,70,71]. Compared to young adults, older individuals may show greater within-group differences in skull thickness, sulcal morphology, and brain tissue composition, which can result in more variable electric field distributions under identical stimulation settings [35,36,72]. For example, increased cerebrospinal fluid (CSF) volume disperses current away from the cortex, reducing field intensity at the target site [36,69,73] and also creates more diffuse and inconsistent field patterns in older adults [36, 69]. Moreover, CSF amplifies the impact of sulcal morphology on current flow, further increasing current-flow variability between individuals [35]. This interaction between stimulation application and age-related anatomical heterogeneity may amplify variability in stimulation-induced behavioral outcomes in older adults, challenging the reliability and effectiveness of standard stimulation protocols [74, 75].

Domain-specific variability in stimulation outcomes likely reflects age-related neurobiological changes that alter brain network function. Structural decline is often accompanied by functional reorganization to maintain performance, often through compensatory mechanisms such as bilateral activation or the recruitment of alternative networks [76–78]. This reorganization complicates the identification of optimal stimulation targets [72,79], as – in addition to more variable neural networks in older adults – older compared to young adults may engage different networks for the same task [23,80]. Age-related differences in network integration are further supported by studies showing that identical tDCS targets can produce opposing changes in functional connectivity across different age groups [16,61,81]. Moreover, individual connectivity profiles have been linked to behavioral outcomes in older adults [12,82]. These findings underscore the importance of individualized stimulation approaches, which may be informed by functional connectivity analyses [81,83,84].

An optimal approach to enhance performance more uniformly in older adults likely depends on multiple interacting factors, including cognitive domain, baseline performance, and individual network integrity [3,23,36]. For instance, individuals with lower baseline learning capacity may derive a greater benefit from stimulation, highlighting the relevance of stratifying participants based on pre-intervention performance metrics [29,30,85]. In addition, domain-specific compensatory strategies, such as increased reliance on executive control in memory tasks, may shape not only behavioral outcomes but also the neural susceptibility to tDCS modulation [3,86, 87]. Further fluctuations in alertness, attentional engagement, and general health status dynamically influence cortical excitability and, consequently, the brain's responsiveness to stimulation [32,88]. For instance, older adults may show more variability in tDCS responses because they often experience fluctuations in attention and vigilance [4, 88,89]. Hence, the interaction of state-dependent factors and tDCS adds another layer of complexity to its application across diverse populations [37,88,90].

In summary, our meta-analysis demonstrated that tDCS induces more heterogeneous responses in older than young adults across motor and cognitive domains. Differences in neuroanatomy, functional reorganization, and brain state may drive this increased variability between age groups. Addressing these multifaceted challenges will require innovative, personalized approaches that integrate anatomical, functional, and state-dependent factors to optimize tDCS efficacy in aging populations [36,81].

4.1. Limitations and future directions

Some limitations of our study should be considered. The limited number of studies directly comparing young and older adults within the same experimental design constrains our sample size and analytical scope. The limitation precluded detailed subgroup analyses of different tDCS modalities and paradigms. Direct comparisons are crucial for isolating age-related effects on tDCS response, as they help control for confounding factors such as variations in study design, stimulation parameters (e.g., intensity, duration, electrode positioning), and task paradigms [32,34,91]. In addition, our analysis suggested the possibility of publication bias, as indicated by a small number of potentially missing studies. However, adjusting for this using a trim-and-fill method did not alter the direction of our findings, supporting the robustness of the main results. The absence of sex-stratified outcome data in the included studies limited our ability to examine potential sex differences in tDCS responsiveness. Anatomical factors such as skull thickness and porosity, which differ between sexes, can influence current distribution and affect stimulation efficacy [69,92]. Future research should address this gap by reporting outcomes separately for males and females and incorporating sex as a key biological variable. Additionally, research with larger datasets is needed to explore how stimulation modalities and task domains influence variability in response patterns across age groups, providing deeper insights into the factors driving age-related differences in tDCS efficacy.

This study offers a novel contribution as the first meta-analysis to systematically quantify age-related variability in tDCS responses. Our findings suggest that lower response variability is generally linked to greater stimulation efficacy, aligning with theoretical assumptions [23,35]. This may indicate that tDCS induces a more uniform and robust response in young adults, potentially explaining age-related differences in variability, though further empirical validation is needed. We encourage future research to adopt the lnCVR as a variability effect size in meta-analyses across cognitive domains such as working memory, attention, and learning. To reduce response variability in older adults, future research should investigate personalized strategies that consider age-related anatomical and functional changes. One approach might be to increase electric field strength to compensate for atrophy and altered current distribution in aging brains [36,82,93]. Increasing regional precision through individualized electrode positioning may further improve accuracy in targeting and stimulation effectiveness [94,95]. Additionally, combining structural modeling with functional connectivity analyses may help to identify task-relevant network nodes for more effective stimulation in older adults [12,83,84].

5. Conclusion

Our findings showed that behavioral responses during active tDCS were more variable in older than young participants, providing the first quantitative evidence for previous theoretical frameworks on increased response variability in older adults. Our study highlights the importance of personalized approaches to optimizing tDCS interventions, particularly in aging populations, to increase their benefit.

CRediT authorship contribution statement

Anna Elisabeth Fromm: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Conceptualization. **Catalina Trujillo-Llano:** Writing – review & editing, Writing – original draft, Visualization. **Ulrike Grittner:** Writing – review & editing, Methodology, Formal analysis. **Marcus Meinzer:** Writing – review & editing, Conceptualization. **Agnes Flöel:** Writing – review & editing, Conceptualization. **Daria Antonenko:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

Availability of data and materials

The data supporting this study's findings are available from the corresponding authors upon reasonable request.

Funding

The project was funded by the Deutsche Forschungsmeinschaft (DFG, project number: 497919823, AN 1103/4-1 to DA and Research Unit 5429/1, project number: 467143400, FL 379/34-1, FL 379/35-1 to AF, ME 3161/5-1, ME 3161/6-1 to MM, AN 1103/5-1 to DA, and project number: 539593253, AN 1103/6-1 to DA). CTLL is a PhD fellow funded by the "Deutscher Akademischer Austauschdienst" (DAAD), German Academic Exchange Service, scholarship: 91828451).

The funders had no role in the design and conduct of the study, data collection, management, analyses, and interpretation, manuscript preparation, review, or approval, or decision to submit the manuscript for publication.

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.

Acknowledgments

We would like to thank Daniel Schulze for the helpful methodical exchange.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2025.06.005.

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