

## Effects of Transcranial Direct Current Stimulation on Response Inhibition in Healthy Populations

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### Abstract

Response inhibition refers to the ability to suppress inappropriate or currently unnecessary behaviors. Studies have demonstrated that response inhibition is primarily associated with the functional integrity of the inferior frontal gyrus, dorsolateral prefrontal cortex, and pre-supplementary motor area. Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique. In recent years, research employing tDCS to modulate response inhibition by stimulating relevant brain regions in healthy populations has proliferated; however, the primary findings remain inconsistent. Elucidating the specific neural mechanisms through which tDCS influences response inhibition, reducing heterogeneity across tDCS studies, exploring more effective tDCS stimulation protocols, and establishing age-dependent differences in tDCS efficacy have become pressing issues requiring immediate resolution.

### Full Text

## Effects of Transcranial Direct Current Stimulation on Response Inhibition in Healthy Populations

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**Abstract:** Response inhibition refers to the ability to suppress inappropriate or no-longer-needed behaviors. Research indicates that response inhibition is primarily associated with the functions of the inferior frontal gyrus, dorsolateral prefrontal cortex, and pre-supplementary motor area. Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that

has gained increasing attention in recent years for its potential to modulate response inhibition by targeting these brain regions in healthy populations. However, the main findings remain inconsistent. Elucidating the specific neural mechanisms through which tDCS influences response inhibition, reducing heterogeneity across tDCS studies, exploring more effective stimulation protocols, and determining age-dependent differences in tDCS effects have become urgent priorities.

**Keywords:** response inhibition, transcranial direct current stimulation, inferior frontal gyrus, dorsolateral prefrontal cortex, pre-supplementary motor area, stop-signal task, go/nogo task

## 1 Introduction

When a response is required, we initiate action; yet when that response becomes inappropriate or unnecessary, we must be able to suppress the impulse. Consider crossing an intersection when the light suddenly turns red, forcing us to inhibit the forward motion; or a driver suppressing the ongoing action of pressing the accelerator upon seeing a reckless pedestrian; or halting an email transmission upon realizing it is addressed to the wrong recipient. All these situations involve response inhibition—the capacity to suppress inappropriate or no-longer-needed behaviors to enable flexible, goal-directed responses to environmental changes. As a critical component of executive function, response inhibition represents one of the most essential cognitive abilities for healthy populations and is closely linked to numerous pathological conditions. Deficits in response inhibition have been documented in attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), schizophrenia, and substance addiction. Furthermore, response inhibition is associated with decision-making and working memory, constituting a fundamental ability for normal daily functioning.

Response inhibition also manifests in specific capacities that can be enhanced to improve related abilities. For instance, military personnel's response inhibition is relevant to combat effectiveness, with research demonstrating that improved response inhibition reduces shooting errors and significantly decreases civilian casualties in simulated combat scenarios. In recent years, investigating the neural mechanisms of response inhibition has attracted widespread research interest. The Go/Nogo task (GNG) and stop-signal task (SST) are common paradigms for studying response inhibition. Combined with neuroimaging, transcranial magnetic stimulation (TMS), and electroencephalography (EEG), extensive research has shown that response inhibition function is closely related to the prefrontal cortex (PFC) and basal ganglia, particularly the right inferior frontal gyrus (rIFG/rIFC), dorsolateral prefrontal cortex (DLPFC), and pre-supplementary motor area (pre-SMA).

The right inferior frontal gyrus is a crucial brain region for response inhibition. Studies of brain lesions and functional impairments provide strong support for rIFG's role in response inhibition. Research has shown that patients with

rIFG damage exhibit impaired performance on response inhibition tasks, and TMS-induced disruption of rIFG function similarly reduces response inhibition capacity. The dorsolateral prefrontal cortex also contributes to response inhibition, with high-frequency rTMS over the left DLPFC improving performance on continuous performance tests. Numerous studies have additionally implicated the pre-SMA in response inhibition processes, with fMRI revealing increased pre-SMA activation during successful inhibition and pre-SMA damage leading to impaired SST performance. The basal ganglia, a collection of subcortical nuclei including the caudate, putamen, globus pallidus, and subthalamic nucleus, represent an essential component of response inhibition neural circuits. Diffusion-weighted imaging has demonstrated white matter tract connections between the IFC, subthalamic nucleus, and pre-SMA. Researchers have proposed a frontal-basal ganglia model to explain the neural mechanisms of response inhibition, wherein rIFG and pre-SMA generate stop commands transmitted to the basal ganglia, which then reduce motor cortex drive through output nuclei to suppress motor impulses.

Non-invasive brain stimulation techniques such as TMS have been widely used in response inhibition research. In recent years, transcranial direct current stimulation (tDCS) has emerged as a novel non-invasive technique garnering increasing attention. Unlike neuroimaging and EEG, which primarily reveal correlational relationships, tDCS enables investigation of causal relationships between brain function and behavior. tDCS differs from TMS in several respects. Mechanistically, TMS uses a magnetic coil to induce electric currents in underlying brain tissue, whereas tDCS delivers weak direct current (typically 0.5–2 mA) through scalp electrodes, partially penetrating the skull to affect cortical activity. tDCS has two polarities: anodal stimulation generally increases cortical excitability, while cathodal stimulation decreases it. Regarding safety, both techniques are generally safe when applied within recommended parameters, though rTMS carries a minimal risk of serious adverse events such as seizures, whereas tDCS typically produces only mild sensory effects without reports of severe adverse events. tDCS is thought to exert its effects through non-synaptic mechanisms (altering resting membrane potential) and synaptic-level long-term potentiation/depression mechanisms, with longer or repeated stimulation producing lasting after-effects and plasticity changes. Overall, tDCS represents a safe, tolerable, non-invasive, portable, and convenient technique for modulating cortical function and cognitive abilities.

Fortunately, response inhibition is plastic and can be enhanced through cognitive augmentation techniques. Two main approaches exist for healthy populations: cognitive training, which is time-consuming and relatively inefficient, and non-invasive brain stimulation, particularly tDCS, which offers technical advantages. An increasing number of researchers are exploring whether tDCS targeting specific anatomical regions can enhance response inhibition in healthy populations—a question with significant implications for increasing resilience to psychiatric disorders and improving related abilities. This review examines studies investigating tDCS effects on response inhibition in healthy participants,

focusing primarily on rIFG, DLPFC, and pre-SMA stimulation, with behavioral outcomes measured through GNG and SST performance. Nogo error rates (or accuracy) serve as the primary GNG metric, while stop-signal reaction time (SSRT) is the main SST indicator. We first discuss findings from each stimulation target, summarizing parameters and positive or negative results to enhance understanding of previous research, then address limitations in existing studies, and finally explore future directions for more scientifically rigorous, efficient, targeted, and standardized tDCS protocols for enhancing response inhibition.

## 2 Effects of tDCS Over the Right Inferior Frontal Gyrus on Response Inhibition

The right inferior frontal gyrus represents a higher-order brain region for response inhibition. Aron et al. (2014) described the rIFC and its associated neural network (the frontal-basal ganglia network) as a “brake” upon which response inhibition depends. Numerous tDCS studies have targeted rIFG to investigate its impact on response inhibition function (Table 1).

Anodal tDCS over rIFG can enhance response inhibition capacity. Jacobson et al. (2011) applied tDCS to participants’ rIFG during SST performance, finding that anodal stimulation significantly reduced SSRT compared to sham stimulation, with no effect on a control task differing only by the absence of stop signals. This demonstrates region-specific modulation of response inhibition rather than general cognitive ability. Campanella et al. (2018) used conditional accuracy functions (CAF) to assess GNG performance, revealing that anodal rIFG stimulation reduced the accuracy decline typically observed with rapid responses, indicating improved inhibition efficiency. Additional studies have similarly demonstrated enhanced response inhibition following anodal tDCS over rIFG.

Neuroimaging research indicates that tDCS affects response inhibition at both behavioral and neurophysiological levels. Sandrini et al. (2020) conducted two experimental sessions, first establishing baseline SST performance, then administering anodal or sham tDCS over rIFC following resting-state fMRI. Post-stimulation fMRI and event-related fMRI during SST revealed that anodal tDCS significantly shortened SSRT, enhanced connectivity between pre-SMA and subthalamic nucleus during stop trials, and altered intrinsic connectivity among rIFC, caudate, pre-SMA, and right DLPFC.

Combining anodal tDCS with response inhibition training may produce superior enhancement effects. Ditye et al. (2012) investigated SST training combined with anodal tDCS over rIFG, administering 8 minutes of training and 15 minutes of tDCS (1.5 mA) daily for four days. Results showed that while training alone improved response inhibition, the combination with tDCS produced greater enhancement. Hogeveen et al. (2016) compared conventional tDCS, high-definition tDCS (HD-tDCS), and sham stimulation over rIFC during SST training versus control task training. Both active stimulation groups showed

improved response inhibition when combined with SST training but not with control training, suggesting that task relevance influences stimulation effects, possibly because tasks more closely related to response inhibition pre-activate corresponding neural populations, making them more susceptible to external current modulation.

Interestingly, researchers have distinguished between reactive and proactive inhibition, proposing that rIFG participates in both processes. Proactive inhibition is indexed by increased go-trial reaction times, while reactive inhibition is measured by SSRT reduction. Cunillera et al. (2014) applied tDCS to rIFC using a combined GNG-SST task, finding that anodal stimulation increased go-trial reaction times while decreasing SSRT, demonstrating dual effects on both inhibition types. However, Cunillera et al. (2016) failed to replicate these findings, observing increased go-trial reaction times but no significant SSRT changes. Another study targeting rIFG with SST found SSRT reduction during and after anodal stimulation without significant differences in go-trial reaction times. Given the limited research and inconsistent results, whether rIFG possesses dual inhibitory functions requires further investigation.

Although most studies demonstrate improved response inhibition following anodal rIFG stimulation, some report null effects, likely due to heterogeneity in stimulation parameters (current intensity, location, reference electrode position, polarity, duration), response inhibition measures, and population characteristics. For example, one recent study using dual-tDCS over rIFG and right DLPFC with 9 cm<sup>2</sup> electrodes found no behavioral changes, possibly because proximal stimulation sites and large electrode areas caused current dispersion. Methodological differences, such as using the relatively simple GNG task versus the adaptively difficult SST, may produce ceiling effects. Campanella et al. (2018) suggested that overall error rates lack sensitivity for detecting subtle GNG performance changes, which may explain negative findings in Campanella et al. (2017). Fujiyama et al. (2021) demonstrated age-dependent tDCS effects, with anodal rIFG stimulation reducing SSRT in young adults ( $24 \pm 4.9$  years) but not older adults ( $69 \pm 5.8$  years). These findings underscore the need to consider multiple factors to reduce experimental heterogeneity.

**Table 1** Effects of tDCS on response inhibition function in the right inferior frontal gyrus region

| Study                  | Task | Stimulation | Current Intensity | Duration | Main Effects  |
|------------------------|------|-------------|-------------------|----------|---|
| Jacobson et al. (2011) | SST  | A/C/S       | 1 mA              | 10 min   | Anodal stimulation reduced SSRT; cathodal had no significant effect |

| Study                    | Task    | Stimulation | Current Intensity | Duration  | Main Effects  |
|--------------------------|---------|-------------|-------------------|-----------|---|
| Ditye et al. (2012)      | SST     | A/S         | 1.5 mA            | 15 min    | Training reduced SSRT; anodal stimulation enhanced training effects     |
| Cunillera et al. (2014)  | GNG-SST | A/S         | 1 mA              | 18 min    | Anodal stimulation reduced SSRT and increased GoRT                      |
| Dambach et al. (2015)    | GNG     | A/C/S       | 1 mA              | 21.75 min | No significant differences in Nogo error rates across groups            |
| Stramaccia et al. (2015) | SST     | A/C/S       | 1 mA              | 20 min    | Anodal stimulation reduced SSRT; cathodal had no significant effect     |
| Cai et al. (2016)        | SST     | A/S         | 1 mA              | 15 min    | Anodal stimulation reduced SSRT and increased GoRT                      |
| Cunillera et al. (2016)  | GNG-SST | A/S         | 1 mA              | 20 min    | Anodal stimulation had no significant effect on SSRT but increased GoRT |

| Study                        | Task | Stimulation | Current Intensity | Duration | Main Effects   |
|------------------------------|------|-------------|-------------------|----------|--|
| Hogeveen et al. (2016)       | SST  | A           | 1.5 mA            | 20 min   | HD-tDCS combined with SST training reduced SSRT; HD-tDCS with CRT training had no effect |
| Castro-Meneses et al. (2016) | SST  | A/S         | 1 mA              | 15 min   | Anodal stimulation reduced SSRT; GoRT showed no significant difference                   |
| Campanella et al. (2017)     | GNG  | A/S         | 1.5 mA            | 20 min   | No significant difference in Nogo error rates between anodal and sham                    |
| Campanella et al. (2018)     | GNG  | A/S         | 1.5 mA            | 20 min   | Anodal stimulation reduced accuracy decline during rapid responses                       |
| Leite et al. (2018)          | GNG  | A/S         | 2 mA              | 30 min   | No significant difference in Nogo accuracy between anodal and sham                       |

| Study                         | Task               | Stimulation | Current Intensity | Duration     | Main Effects   |
|-------------------------------|--------------------|-------------|-------------------|--------------|--|
| Li et al. (2019)              | SST                | A/C/S       | 1.5 mA            | 4 min 12 sec | Anodal stimulation reduced SSRT; cathodal had no significant effect                |
| Chen et al. (2019)            | modifiedA<br>SST   | A           | 1.5 mA            | 20 min       | Anodal stimulation reduced SSRT  |
| Sandrini et al. (2020)        | SST                | A/S         | 1.5 mA            | 20 min       | Anodal stimulation shortened SSRT  |
| Thunberg et al. (2020)        | SST                | A/S         | 1.5 mA            | 20 min       | No significant difference in SSRT between anodal and sham                          |
| Friebs, Brauner et al. (2021) | SST                | A/C/S       | 1.5 mA            | 20 min       | No significant differences in SSRT across groups                                   |
| Fujiyamam et al. (2021)       | modifiedA/S<br>SST | A/S         | 1.5 mA            | 20 min       | Anodal stimulation significantly reduced SSRT in young adults but not older adults |

*Note: A: anodal stimulation; C: cathodal stimulation; S: sham stimulation; GNG: go/nogo task; GoRT: go-trial reaction time; SST: stop-signal task; modified SST: SST variant; SSRT: stop-signal reaction time; GNG-SST: combined GNG and SST task*

### 3 Effects of tDCS Over the Dorsolateral Prefrontal Cortex on Response Inhibition

The dorsolateral prefrontal cortex is associated with numerous cognitive functions including working memory, attention, decision-making, and cognitive control, but it also represents an important region for response inhibition. In recent years, DLPFC has become a key target for tDCS studies of response inhibition function (Table 2).

Research demonstrates that tDCS over DLPFC can modulate response inhibition, with studies targeting both left and right hemispheres. Friehs and Frings (2018) targeted right DLPFC, finding that anodal stimulation reduced SSRT compared to sham. A subsequent study using an SST variant replicated this effect. In another experiment, cathodal stimulation over right DLPFC increased SSRT, indicating impaired response inhibition. Together, these findings suggest polarity-specific modulation: anodal stimulation enhances while cathodal stimulation impairs response inhibition. Nejati et al. (2018) applied anodal stimulation to left DLPFC, observing increased Nogo accuracy compared to sham, while other left DLPFC studies also reported SSRT reductions. These results indicate that both right and left DLPFC are involved in response inhibition, though the functional lateralization remains to be fully elucidated.

Combining tDCS with response inhibition training has yielded mixed results. Dousset et al. (2021) employed four days of tDCS combined with GNG training, finding that anodal right DLPFC stimulation produced the greatest improvement in Nogo accuracy at one-week follow-up. However, Sedgmond et al. (2019) found no significant effects of single-session tDCS combined with GNG training, possibly due to individual variability and unstable single-session effects, suggesting the need for more intensive investigation of combined protocols.

Despite evidence for tDCS effects on response inhibition, several studies report null behavioral outcomes. Lapenta et al. (2014) found no behavioral differences between anodal right DLPFC stimulation and sham on a modified GNG task, though EEG revealed reduced N2 amplitude and increased P3a amplitude, suggesting enhanced inhibition at the neurophysiological level. Stramaccia et al. (2015) observed no SSRT changes following right DLPFC stimulation, while anodal rIFG stimulation significantly reduced SSRT, possibly reflecting shorter-lasting DLPFC effects or differential contributions of distinct brain regions. Chen et al. (2021) reported that both anodal and cathodal stimulation over right DLPFC reduced SSRT, contrasting with Friehs and Frings (2019) who found cathodal stimulation increased SSRT. These discrepancies may stem from differences in reference electrode placement and resulting indirect modulatory effects on adjacent frontal regions.

Individual differences substantially influence tDCS effects on response inhibition. Nieratschker et al. (2015) found that cathodal tDCS over left DLPFC impaired response inhibition only in COMT Val homozygotes, not Met allele carriers, suggesting genetic modulation via prefrontal dopaminergic activity. However,

Plewnia et al. (2013) found no COMT genotype interaction, indicating the need for further investigation. Weidacker et al. (2016) demonstrated that higher cold-heartedness scores predicted better performance under cathodal stimulation, potentially reflecting restoration of excitatory-inhibitory balance. Wu et al. (2021) showed that baseline performance level moderated tDCS effects, with cathodal stimulation improving Nogo accuracy in low-baseline participants while impairing high-baseline performers, resulting in null group-level effects. These findings highlight the importance of considering individual variability in experimental design, analysis, and application to reduce heterogeneity and advance personalized neuromodulation approaches.

**Table 2** Effects of tDCS on response inhibition function in the dorsolateral prefrontal cortex

| Study                      | Stimulation | Target      | Current Intensity | Duration | Main Effects  |
|----------------------------|-------------|-------------|-------------------|----------|---|
| Plewnia et al. (2013)      | A/C/S       | left DLPFC  | 2 mA              | 20 min   | No COMT genotype difference in tDCS effects on Nogo accuracy                            |
| Lapenta et al. (2014)      | A           | right DLPFC | 2 mA              | 30 min   | No behavioral difference between anodal and sham; EEG showed neurophysiological changes |
| Nieratschker et al. (2015) | C           | left DLPFC  | 2 mA              | 20 min   | Cathodal stimulation reduced Nogo accuracy only in COMT Val homozygotes                 |
| Stramaccia et al. (2015)   | A/C/S       | right DLPFC | 1 mA              | 20 min   | No significant SSRT differences from sham   |

| Study                  | Stimulation | Target      | Current Intensity | Duration | Main Effects   |
|------------------------|-------------|-------------|-------------------|----------|--|
| Weidacke et al. (2016) | A/C/S       | right DLPFC | 1 mA              | 20 min   | Higher cold-heartedness scores predicted better performance under cathodal stimulation |
| Mansouri et al. (2017) | A           | left DLPFC  | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT under fast-paced music                                 |
| Nejati et al. (2018)   | A/C/S       | left DLPFC  | 1.5 mA            | 20 min   | Anodal stimulation increased Nogo accuracy   |
| Wang et al. (2018)     | A           | right DLPFC | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT  |
| Friebs & Frings (2018) | A           | right DLPFC | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT  |
| Fehring et al. (2019)  | A           | left DLPFC  | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT  |
| Friebs & Frings (2019) | C           | right DLPFC | 1.5 mA            | 20 min   | Cathodal stimulation increased SSRT  |
| Sedgmond et al. (2019) | A           | right DLPFC | 1.5 mA            | 20 min   | No difference in Nogo accuracy between anodal and sham with training                   |

| Study                         | Stimulation | Target      | Current Intensity | Duration | Main Effects   |
|-------------------------------|-------------|-------------|-------------------|----------|--|
| Chen et al. (2021)            | A/C/S       | right DLPFC | 1.5 mA            | 20 min   | Both anodal and cathodal stimulation reduced SSRT compared to sham |
| Dousset et al. (2021)         | A           | right DLPFC | 1.5 mA            | 20 min   | Anodal stimulation with training reduced GoRT and Nogo error rates |
| Friebs, Brauner et al. (2021) | A/C/S       | right DLPFC | 1.5 mA            | 20 min   | No significant SSRT differences across groups                      |
| Friebs, Dechant et al. (2021) | A           | right DLPFC | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT                                    |
| Wu et al. (2021)              | A/C/S       | right DLPFC | 1.5 mA            | 20 min   | No group-level differences in Nogo accuracy or SSRT                |

*Note: A: anodal stimulation; C: cathodal stimulation; S: sham stimulation; DLPFC: dorsolateral prefrontal cortex; GNG: go/nogo task; PGNG: parametric go/nogo task; modified GNG: GNG variant; SST: stop-signal task; modified SST: SST variant; GoRT: go-trial reaction time; SSRT: stop-signal reaction time*

#### 4 Effects of tDCS Over the Pre-supplementary Motor Area on Response Inhibition

The pre-supplementary motor area is a critical neural substrate for response inhibition and an important node in the frontal-basal ganglia model, making it

a popular target for tDCS research (Table 3).

Extensive behavioral evidence demonstrates that anodal tDCS over pre-SMA enhances response inhibition. Hsu et al. (2011) applied anodal, cathodal, and sham stimulation to pre-SMA during SST performance. Compared to other conditions, anodal stimulation significantly reduced stop-trial error rates, though SSRT did not differ significantly. This may reflect the use of a fixed SSD determined from pre-testing without accounting for tDCS-induced changes. Kwon and Kwon (2013a, 2013b) replicated these findings, showing that anodal pre-SMA stimulation reduced SSRT compared to sham, with effects persisting during and after stimulation. Fujiyama et al. (2021) demonstrated that anodal pre-SMA stimulation significantly reduced SSRT in older adults ( $68.5 \pm 5.3$  years), confirming pre-SMA as an important target for modulating response inhibition.

Anodal tDCS over pre-SMA shows neurophysiological as well as behavioral effects. Liang et al. (2014) replicated Hsu et al.'s findings while additionally demonstrating SSRT reduction. Multiscale entropy analysis of EEG signals revealed that higher entropy correlated with better inhibition performance and that anodal tDCS further increased entropy. Yu et al. (2015) similarly found SSRT reduction following anodal pre-SMA stimulation, accompanied by increased blood oxygen level-dependent (BOLD) responses in pre-SMA and ventromedial prefrontal cortex (vmPFC). The tDCS-induced BOLD signal increase correlated positively with improved inhibition efficiency and enhanced pre-SMA-vmPFC functional connectivity.

Despite most studies demonstrating enhanced response inhibition following anodal pre-SMA stimulation, some report no behavioral improvement. Bender et al. (2017) found no differences in SSRT or inhibition success rates between anodal stimulation and control conditions, possibly due to lower current intensity and shorter duration compared to previous studies, or different reference electrode placement (right mastoid versus left cheek). Fujiyama et al. (2021) showed age-dependent effects, with anodal stimulation reducing SSRT in older but not younger adults ( $22.4 \pm 4.2$  years), potentially reflecting anatomical features affecting stimulation efficacy or true age-dependent effects. As reported in the literature, variations in current intensity, duration, reference electrode position, and population characteristics can produce different outcomes.

**Table 3** Effects of tDCS on response inhibition function in the pre-supplementary motor area

| Study                   | Task         | Stimulation | Current Intensity | Duration | Main Effects   |
|-------------------------|--------------|-------------|-------------------|----------|--|
| Hsu et al. (2011)       | SST          | A/C/S       | 1.5 mA            | 10 min   | Anodal stimulation reduced stop-trial error rates; no SSRT differences |
| Kwon & Kwon (2013a)     | SST          | A           | 1 mA              | 10 min   | Anodal stimulation reduced SSRT  |
| Kwon & Kwon (2013b)     | SST          | A           | 1 mA              | 10 min   | Anodal stimulation reduced SSRT during and after stimulation           |
| Liang et al. (2014)     | SST          | A           | 1.5 mA            | 10 min   | Anodal stimulation reduced both stop-trial error rates and SSRT        |
| Yu et al. (2015)        | SST          | A           | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT  |
| Bender et al. (2017)    | modified SST | A/C/S       | 0.7 mA            | 9 min    | No significant SSRT differences from sham                              |
| Fujiyamam et al. (2021) | modified SST | A/S         | 1.5 mA            | 20 min   | Anodal stimulation reduced SSRT in older adults but not young adults   |

*Note: A: anodal stimulation; C: cathodal stimulation; S: sham stimulation; SST: stop-signal task; modified SST: SST variant; SSRT: stop-signal reaction time*

## 5 Summary and Outlook

Numerous studies have examined tDCS effects on response inhibition by targeting different brain regions, yielding meaningful results that demonstrate tDCS' s potential as a tool for enhancing response inhibition in healthy populations. However, several limitations and unresolved issues remain.

First, the neural mechanisms underlying tDCS modulation of response inhibition are not fully understood. Two key questions persist: the precise physiological neural circuits of response inhibition, particularly the temporal dynamics of cortical region involvement, and the identification of critical brain regions whose stimulation produces maximal effects. While the frontal-basal ganglia model provides a framework incorporating rIFG, DLPFC, pre-SMA, and basal ganglia, it has notable gaps. The temporal sequence of cortical region activation remains unclear, with inconsistent reports about whether rIFG functions upstream or downstream of pre-SMA, or whether bidirectional connections exist. Methodologies such as electrocorticography may help clarify these temporal dynamics. Additionally, the current model does not adequately incorporate DLPFC, despite evidence for its involvement, suggesting more complex neural circuits remain to be elucidated. Furthermore, it is uncertain which brain region constitutes the critical target for tDCS modulation of response inhibition. While stimulation of rIFG, DLPFC, and pre-SMA all affect response inhibition, these conclusions derive from different experimental designs and parameters, preventing direct comparison. Future studies should employ rigorous controlled designs to compare different stimulation targets within the same experiment, combining behavioral, neurophysiological, and neuroimaging techniques to isolate the specific contributions of each region.

Second, research findings exhibit substantial heterogeneity. While most studies demonstrate tDCS can modulate response inhibition, null results also emerge due to individual differences, stimulation parameters (current magnitude, duration, electrode size, position), and behavioral task characteristics (analysis methods, difficulty). Notably, different analytical approaches to the same data can yield inconsistent results. Campanella et al. (2017) found no group differences using traditional error rate analysis, yet Campanella et al. (2018) detected improved performance using conditional accuracy functions on the same dataset. Similarly, drift diffusion model reanalysis of existing data revealed that anodal stimulation increased inhibition tendency while reducing impulsivity. Future research must carefully control for these factors to reduce heterogeneity and improve reproducibility. We recommend: (1) Controlling individual differences through homogeneous sampling and within-subject designs, while addressing potential blinding issues through realistic sham protocols and post-stimulation questionnaires; (2) Using standardized tDCS parameters, with electrode placement guided by the 10-20 system or fMRI, current intensities of 0.5–2 mA, durations of 20 minutes, and computational modeling to verify electric field distribution; and (3) Optimizing behavioral tasks to prevent ceiling/floor effects, using adaptive difficulty adjustment, standardized protocols, and consensus guidelines

for task implementation and analysis.

Third, tDCS research requires improved spatial resolution. Most studies use conventional tDCS with large rectangular electrodes (25–35 cm<sup>2</sup>), resulting in low spatial resolution and diffuse current spread that complicates mechanistic interpretation. High-definition tDCS (HD-tDCS) using small circular electrodes in a 4×1 montage provides higher spatial resolution and more focal stimulation, producing more robust behavioral and neurophysiological effects. However, few studies of response inhibition in healthy populations have employed HD-tDCS. Future research should increasingly utilize HD-tDCS to enhance spatial precision, simplify mechanistic interpretations, and improve result reliability.

Fourth, the combination of tDCS with response inhibition training requires further investigation. While both training alone and tDCS alone can enhance response inhibition, combined approaches may be more effective. Studies have employed online (simultaneous) and offline (sequential) combination protocols with inconsistent results. Ditye et al. (2012) found offline combination superior to training alone, while Hogeveen et al. (2016) demonstrated online combination benefits. However, Sedgmond et al. (2019) found no effect of online combination, and protocols vary in stimulation frequency and timing. Future research must systematically investigate optimal combination approaches, including online versus offline protocols and stimulation parameters.

Fifth, different stimulation protocols warrant exploration. Most studies employ single-session stimulation with effects lasting approximately 90 minutes, though HD-tDCS effects may persist for 2 hours. Multi-session stimulation can produce longer-lasting effects and has been safely applied in other domains, yet few studies have examined repeated stimulation for response inhibition in healthy populations. Future research should investigate the efficacy and long-term effects of multi-session protocols. Additionally, combining tDCS with other stimulation methods, such as transcutaneous auricular vagus nerve stimulation (taVNS), may produce synergistic effects. Multi-site stimulation targeting multiple brain regions simultaneously represents another promising approach that has shown benefits in motor and working memory studies but remains unexplored for response inhibition.

Finally, research across different age groups is limited. Most studies recruit young adults (20–30 years), with minimal research in children and only one study in older adults. Fujiyama et al. (2021) demonstrated that while older adults showed preserved plasticity, tDCS effects were evident only for pre-SMA stimulation, not rIFG, suggesting age-dependent differences in stimulation efficacy. Given that response inhibition declines with age and develops throughout childhood, investigating tDCS effects across the lifespan is both theoretically important and clinically relevant. Future studies should include diverse age groups to understand developmental and aging-related differences and develop age-appropriate protocols.

In summary, tDCS is a safe and effective non-invasive brain stimulation tech-

nique that can modulate neural activity in brain regions involved in response inhibition to affect cognitive function. However, current research has limitations that must be addressed. Future studies should elucidate neural mechanisms, reduce heterogeneity, increase spatial resolution through HD-tDCS, optimize combination with training, explore multi-session and multi-site protocols, and investigate effects across different age groups. Such advances will provide stronger evidence for optimizing tDCS applications to enhance response inhibition in healthy populations.

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