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Department of Brain and Behavioral Sciences (DBBS)

MSc in Psychology, Neuroscience and Human Sciences

MODULATION OF RESPONSE INHIBITION THROUGH TRANSCRANIAL DIRECT CURRENT STIMULATION ON THE RIGHT INFERIOR FRONTAL GYRUS

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Abstract

Response inhibition is the inhibition or cancellation of an initiated, planned, or prepotent response and involves different interrelated inhibitory mechanisms. The Stop Signal Task (SST) measures the ability of individuals to cancel a planned or initiated response. Right inferior frontal gyrus (rIFG) is evaluated as the key structure of the response inhibition. Still, it is debated whether the function of the right inferior frontal gyrus is inhibition or response updating. The present study aimed to clarify the function of the rIFG under the effect of different tDCS modulations. We examined the effects of computational-modelled high-definition (HD-tDCS) and conventional tDCS on participants' stop signal (SST) and double-response task (DRT) performance compared to sham condition. 42 healthy and young participants underwent each one of the 20-minute tDCS conditions in three sessions, at least 72 hours apart, and then performed the SST and DRT tasks within 20 minutes. Bayesian paired-sample T-Test is conducted to compare stop-signal reaction time (SSRT) and double-response latency (DRT2) across conditions. For all measurements, results predicted moderate evidence against a difference between HD-tDCS, conventional tDCS, and sham stimulation. These findings suggest that neither HD-tDCS nor conventional tDCS significantly improved response inhibition or response selection performance. Further research is needed to clarify the role of rIFG modulation in response inhibition and the efficacy of different tDCS parameters.

Keywords: right inferior frontal gyrus, stop signal task, tDCS, response inhibition, HD-tDCS

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I. Introduction

From a broad perspective, stopping in need is crucial for survival. While navigating the world around them, people often need to stop, change, or update their actions or behaviors to obtain their goals, fit in the environment, or behave in a way that no longer serves their initial purpose. This change of behavior relies on inhibition. The concept of inhibition or inhibitory systems, in terms of what it is, how it is expressed, its neural mechanisms, and how it is handled within different paradigms is widely discussed. Based on these discussions, this thesis aims to study the involvement of the right inferior frontal gyrus (rIFG) in the Stop Signal Task (SST) type response inhibition using transcranial direct current stimulation (tDCS).

1.Response Inhibition

1.1. The History and the Definition of Inhibition

Inhibition has various meanings in psychological research and neuroscience, from the level of neuronal communication to the behavioral outcome or a more general trait. The early theoretical approach by the philosophy to the inhibitory processes around the late 19th century was how it constituted the basis of will, and early psychiatric attempts followed this approach while defining the symptoms of "insanity" and healthy behavior; if the will were inhibited extensively the patient would be depressive, while if it was not inhibited sufficiently the patient would be excited, therefore healthy behavior was considered possible with the controlled balance of will and inhibition, where the control is dependent to self-awareness of the behaviors (Macmillan, 1996; cited by Bari and Robbins, 2013). On the other hand, Franz Gall proposed that if a particular faculty of the brain were more excited, the behavior related to that faculty would be more pronounced. Conversely, if a faculty were less excited, it would not produce the behavior. Therefore, instead of a separate mechanical control mechanism

between faculties, the difference in the degree of excitation was causing the inhibition (Macmillan, 1992).

In physiological research, Hall and Magendie demonstrated that central nerves had modulatory control over the contraction of heart muscles. Still, their propositions did not include an inhibitory mechanism because of the paradigm of that era: nerves can be excited or not, and they do not convey a message to stop (R. Smith, 1992). This point of view started to change with the discovery that vagus nerve stimulation can inhibit or stop heart muscle contraction by firstly Volkmann, who considered the results of an error related to the implementation of the method, and Weber, who used the term inhibition to describe central nerves' restraint control of heart muscles (Bari & Robbins, 2013; Hoff, 1940).

In psychological research at 20th century, inhibition was defined as *"some sort of interference exerted by one mental process upon another"* (Skaggs, 1929) or *" a condition of an organism characterized by various degrees of response decrement"* (Wenger, 1937); while Freud defined it in terms of ego withholding a function or itself, Pavlov defined with the withdraw from conditioned response (Wenger, 1937), and for Eysenck inhibition was a modulator of cortical arousal that determine the differences in extraverted and introverted personality traits (Eysenck, 1955). Every definition of inhibition had some differences from the others, as well as similarities. Therefore, the definitions of inhibition began to take on distinctive names depending on the studied paradigm. For example, Lubow and Moore (Lubow & Moore, 1959) defined the phenomenon of being exposed to a stimulus continuously with no reinforcement, which reduces the capacity to create other associations about that stimulus later as latent inhibition; Hull (1943) defined the result of stimuli closely related to the activation of a response becoming conditioned to the inhibition associated with its termination as conditioned inhibition. Posner and colleguaes (Posner et al., 1985) defined the relative blocking of processing stimuli that drew the attention a moment before as

inhibition of return. Before discussing the inhibition paradigms in detail later, in general, it can be seen that there are some common points on the definition of inhibition, as said by APA (2018), *"the process of restraining one's impulses or behavior, either consciously or unconsciously…"* or *"the suppression of covert responses to prevent incorrect responses"*.

Because it is defined as a conscious or unconscious restraint on behavior and response, inhibition is studied based on executive functioning/cognitive control (Friedman & Robbins, 2022). Cognitive control is the effortful maintenance of behaviors, responses, and thoughts to achieve goals (Diamond, 2013; Miller & Cohen, 2001). Friedman & Robbins (2022) indicate the components of cognitive control -based on the tasks that each component can be measured- as response inhibition and interference control, working memory, updating, shifting, cognitive flexibility, and decision-making; while the updating, shifting, and inhibition are the core elements that construct other components (Miyake et al., 2000; Miyake & Friedman, 2012).

It is necessary to define inhibition within an operational definition and the neural structures involved in studying psychiatric disorders associated with deficits in inhibition. According to Aron (Aron, 2007), inhibition as a term is overused; therefore, the meaning is expanded to the point of being vague and difficult to measure, exempting the inhibition of motor responses: response inhibition. In the next section, inhibitory taxonomy and related paradigms will be discussed with a focus on response inhibition.

1.2 Taxonomy of Inhibitory Systems and Response Inhibition

According to (Aron et al., 2014), inhibition is *"the suppression of inappropriate responses, stimulus–response mappings or task-sets when the context changes, and suppression of interfering memories during retrieval."*. Thus, inhibition encompasses a wide range of observable behaviors that can be measured using various tools, and the classification of the inhibitory mechanism is helpful in deciding which tool is beneficial for research

purposes. Nigg (2000) suggests that inhibitory systems can be classified based on whether they function automatically or effortfully. While automatic inhibitory systems are involved in attention orientation by suppressing the last observed stimuli and location, or the stimuli come out of the already attended zone (as in inhibition of return, see: (Posner et al., 1985); the effortful inhibitory systems regulate the motor or cognitive response towards an external stimulus as well as the thoughts and emotions.

According to Nigg (2000), the four effortful inhibitory systems are inference control, cognitive inhibition, oculomotor inhibition, and behavioral inhibition. The inference control allows the responses to the target stimuli while inhibiting the responses to noise stimuli (Eriksen & Eriksen, 1974). The critical component here is inference control happening between two competing stimuli or two components of one stimulus that arrive simultaneously, and one of them is irrelevant to the ongoing task and the desired response. Inference control can be measured with the Stroop and Flanker Tasks (Yeung et al., 2020). In both tasks, stimuli presented to the participant are either congruent or incongruent; in incongruent conditions, the mean reaction time (RT) is longer, and lower RT is considered an indicator of better inference control (Paap et al., 2020). In the literature, this kind of inhibition is also defined as cognitive inhibition (Audiffren et al., 2021), but Nigg (2000) further separated them into inference control when two external stimuli compete, and cognitive inhibition when suppression is addressed to internal stimuli, such as mental imagery or thoughts, to avoid interrupting ongoing working memory execution or attention. In this sense cognitive inhibition involves attention to process new information or focus on goal-related stimuli, rather than inhibition of a response (Tonev, n.d.)). Another effortful inhibitory system is oculomotor inhibition. Oculomotor inhibition is active when an eye movement is required against a salient stimulus and can be measured with an antisaccade task (Hallett & Adams, 1980). In this task, participants have to inhibit reflexive gaze to stimuli,

and effortfully look in the opposite direction of the stimuli; errors indicate a defect in inhibition ability (Everling & Fischer, 1998). Expression of inhibition between the oculomotor inhibition task and motor inhibition task was only different from each other in terms of graduality; therefore it is proposed that oculomotor inhibition can be categorized as a motor response inhibition (Aron, 2011; Wijnen & Ridderinkhof, 2007). The last effortful inhibitory mechanism defined by Nigg (2000) is behavioral inhibition, which involves the processes that withhold unwanted or inappropriate responses. Nigg (2000) and Harnishfeger (1995, cited by Aron, 2007) use behavioral inhibition as an umbrella term that covers impulse control, regulating actions, thoughts, emotions, and responses. While response inhibition is limited to the motor inhibition ability in certain tasks related to certain paradigms, behavioral inhibition is studied with personality traits and developmental psychopathologies. Later, Nigg (Nigg, 2017) defines behavioral inhibition as *"The bottom-up interruption of a behavior sequence in response to novel, ambiguous, or threatening stimulus"* and response inhibition as *"Top-down ability to intentionally or effortfully suppress a triggered behavior to sustain behavior toward a goal"*. Nigg's response inhibition covers a set of behaviors including inhibiting impulsive choices and inhibiting the motor outcome of a trigger, and might be sustained for a long time, for instance not checking a notification on the phone while studying to get a good grade. However, this example would not be considered as response inhibition according to a more recent division of inhibitory systems made by Bari & Robbins (2013). According to them, inhibitory control is a set of behaviors that share similar properties but different processes; instead of focusing on how effortful the mechanism is, they focused on the function of each mechanism and what it inhibits (See Fig 1.). In the example given earlier, the student prioritizes the delayed reward of achieving a good grade on her exam, requiring sustained focus and effort over time, by forgoing the immediate gratification and distraction of checking her phone (delay discounting) as well as the inhibition of the motor response

(reaching for the phone). Therefore the student is performing two processes of behavioral inhibition; response inhibition (inhibitory control of compulsive actions), and deferred gratification (inhibitory control of impulsive choices).

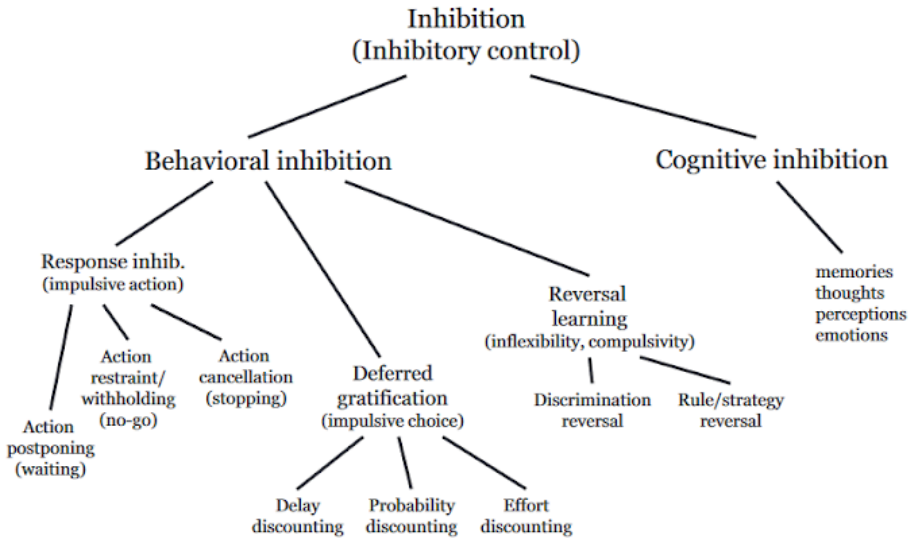


Fig 1. The cognitive processes forming inhibitory control (taken from Bari & Robbins, 2013)

Response inhibition is the capacity to abolish a prepotent (i.e., the most available or the well-coupled and dominant response to a specific stimulus), triggered, planned, or ongoing action when the action is or becomes irrelevant, unnecessary, or not serving the momentary purpose (Banich & Depue, 2015; Pouget et al., 2017; Tiego et al., 2018). Although the mechanisms used to perform response inhibition achieve similar behavioral outcomes, there are operational and physiologic differences between them. Action restraint is the inhibitory mechanism the student uses while resisting the urge to reach the phone or resisting going to the kitchen to find snacks to eat while studying. Thus, action restraint is inhibiting prepotent but not needed motor responses (He et al., 2018). Action cancellation (He et al., 2018 citing Barkley, 1997), on the other hand, is the ability to abolish an ongoing

or planned action when it becomes unnecessary (Raud et al., 2020). Following the example, if the student reaches for the phone to check the notification, and suddenly remembers that she needs to continue studying and pulls her hand away, the process here is action cancellation. The timing of inhibition distinguishes between the two processes. In action restraint, the action is inhibited before the response starts. At the same time, in action cancellation, the action is inhibited due to an additional stopping signal received after the action has been already planned or started.

1.3. Response Inhibition Paradigms

Stop Signal Paradigm.

The classical stop signal task (SST) constitutes a choice reaction time (RT) task followed by a stopping cue. Participants were first asked to respond in a predetermined way according to task demand; such as the shape (Verbruggen & Logan, 2009a), location (Bartholdy et al., 2016), or direction (Senkowski et al., 2023) of the stimulus. The stopping cue is presented shortly after the choice RT task stimulus onset and may be presented in an auditory or visual way (Verbruggen & Logan, 2009b; Wessel, 2018). The time interval between go and stop signals is called stop-signal delay (SSD), which can be fixed or varied (Band et al., 2003). The task intends to measure the suppression of a started response (Band et al., 2003) by calculating the time needed for stopping (i.e., stop-signal reaction time, SSRT), which indicates cognitive control. The SSRT is calculated by finding the difference between a specific percentile of the go reaction time (go RT) distribution and the average SSD (Logan & Cowan, 1984). The stop signal paradigm is rooted in the horse-race model. According to this model, the behavioral outcome of responding or stopping (i.e., successful inhibition of the response) depends on which process concludes first, and can be affected by the duration of SSD, the frequency of the response, or the predictability of the stop-signal (Logan & Cowan, 1984; Verbruggen & Logan, 2009a). During the race, the go process starts

when a go stimulus is presented, and the stop process begins when a stop signal is presented. Suppose the stop process finishes before the go process (i.e., the go RT is greater than the sum of the SSRT and the SSD). In that case, the response is successfully inhibited, and no response is made. Conversely, if the go process finishes before the stop process (i.e., the go RT is less than the sum of the SSRT and the SSD), the response is not inhibited, and the response is incorrectly made. Therefore inhibition can be measured as a function of go RT, SSD, and SSRT as well as the probability of responding after the stop signal, and RT of go trials (Huster et al., 2013; Verbruggen & Logan, 2008, 2009a).

Go/No-Go Paradigm.

The Go/No-Go task constitutes an RT task where participants are presented with two different stimuli one by one, and they are asked to respond when a specific frequent stimulus (go cue) is presented, but not respond to the other stimuli which is less frequent (no-go cue) (Verbruggen & Logan, 2008a). There is also a variation in which the go stimulus is constantly presented, and occasionally an additional no-go cue is presented with the go stimulus at the same time (Littman & Takács, 2017). The commission error (participant responds while the no-go cue is presented) indicates failed response inhibition or impulsivity, while omission error (participant does not respond while a go cue is presented) is associated with a deficit in attention or disengagement from the task (Trommer et al., 1988). The dependent variables used in this paradigm are the amount of errors and error types, as well as the RT in go trials (Huster et al., 2013).

These two tasks differ in terms of the timing of inhibition, whether the inhibition process be automatized or not, and the measurements they provide to evaluate inhibitory control (Huster et al., 2013; Littman & Takács, 2017; Verbruggen & Logan, 2008). In the Go/No-go task, inhibition is observed as a proactive process that happens automatically after the participant decides whether the given stimulus is a "go" stimulus or a "no-go" stimulus; it

is a process that involves the participant forming a response tendency toward the go stimulus and then inhibiting that tendency, rather than inhibiting the response itself (Cunillera et al., 2016). As a result, performance may improve with learning or repetition and can depend on the motor preparation of the participant (Verbruggen & Logan, 2008; Wessel, 2018). The inhibition process can start even before the stimuli are presented (Ficarella & Battelli, 2019).

On the other hand, in the Stop-signal task, the stop signal comes after the action has started or after a cue has been given to start the action. Here, an action that has been initiated or is being prepared to be initiated is canceled or stopped. In this case, inhibition is not considered a process that can be automatized within the framework of this paradigm, and it requires constant effort (Logan, 1994) since it is not possible to foresee if there will be a stop signal or not, and the stop signal timing can change momentarily. Nevertheless, even though an automatic process can be involved in SST-type inhibition due to stimulus-response mapping (Verbruggen & Logan, 2008), it does not affect SST-type response inhibition (Best & Verbruggen, 2019.; Cohen & Poldrack, 2008). Participants may delay the start of the action in anticipation of a possible stop signal as a trade between speed and accuracy of stopping, indicated by slower GoRT after failure to stop (Bissett & Logan, 2011). However, this anticipatory behavior possibility can be eliminated in experimental setups where SSD takes varied intervals (Verbruggen et al., 2019; Verbruggen & Logan, 2009b).

Studies using these paradigms are used to detect response inhibition deficiency in clinical populations, as the failure of inhibition can be related to certain psychiatric disorders. For instance, it is argued that one of the explanations for obsessive-compulsive disorder (OCD), a condition characterized by intrusive thoughts and compulsive behaviors, is the impairments in cognitive and behavioral inhibition (Chamberlain et al., 2005). In two studies with the Go/No-Go Task, it was found that the OCD group performed worse than the control

group (Aycicegi et al., 2003; Martínez-Esparza et al., 2021). This effect could be related to the severity of the symptoms (Rosa-Alcázar et al., 2021).

Neurodevelopmental disorders like attention deficit and hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are being studied in relation to inhibition. Indeed, evidence showed that during the Go/No-go task, children with ADHD had pre-error slowing reaction time (RT) and took longer time for recovery after an omission error compared to children in the control group (Epstein et al., 2010); during the Stop Signal Task (SST) children with ADHD had longer stop-signal reaction time (SSRT), lower go accuracy and higher SST omission errors (Senderecka et al., 2012; Senkowski et al., 2023). In a study done by (Schmitt et al., 2018), using SST they found that the children with ASD had less inhibitory control on voluntary delaying the response; and more impaired control was related to more severe symptoms of repetitive behavior.

Eating disorders are another inhibitory control-related condition. Smith and colleagues ((K. E. Smith et al., 2020) found that during the days with lower momentary inhibitory control, individuals with anorexia nervosa binging-purging (AN-BP) type and individuals with bulimia nervosa (BN) were more prone to binge eating when they are negatively affected; while being in an adverse effect or momentary having less inhibitory control was not a moderator for the individuals with binge eating disorder (BED). In another study with adolescents, individuals who had disordered eating behaviors (DEB) had lower accuracy in SST, and they recruited more anterior cingulate cortex and medial prefrontal cortex structures than the control group during the errors(Bartholdy et al., 2019).

While discussing what inhibition elicits an ongoing debate, how these processes are executed is an important aspect to understand its dysfunctions and find ways to modulate when needed. The neural basis of response inhibition involves specific brain regions and networks that coordinate to manage these inhibitory actions effectively. This next section will

examine the brain's role in regulating these functions and the neural basis of response inhibition.

1.4. Neural Basis of Response Inhibition

The prefrontal cortex (PFC) is well known for its involvement in high-order cognitive functions, including cognitive control (Haddon & Killcross, 2006; Hwang et al., 2014; José et al., 2020; Miller & Cohen, 2001). Some theories try to understand the role of PFC on inhibitory control; one crucial concern is whether the PFC amplifies the relevant response (a global action selection network), or actively inhibits every irrelevant response (a specialized inhibitory network). This question arises from the similarity of brain regions and connectivities of action selection and response inhibition(Jasinska, 2013). A study addressing this question (Maizey et al., 2020) compared brain activation during a dual response task (DRT) and SST, considering the nature of response updating in these tasks, either with inhibition or without. They found more frontal region of rIFG (i.e., pars triangularis) activated during the inhibitory action updating (SST) and a common activity across both tasks in cortical and subcortical regions such as the pre-SMA and posterior right IFG (i.e., pars opercularis), but more activation in basal ganglia and thalamus regions during response inhibition compared to execution and anterior rIFG activation during inhibition, which means there may be a generalized response selection network but also that a right-centralized inhibitory network may be present in the brain.

Moreover, different sub-regions of rIFG are involved in different kinds of response updating. A study following the context-cueing paradigm of Verbruggen and colleagues (2010) found that, even in pars triangularis, there are functional subdivisions: the posterior portion supports action updating while the anterior portion supports solely response inhibition (Maizey, n.d.). The context-cueing paradigm (Verbruggen et al., 2010) is a neuropsychological task investigating the cognitive processes involved in response inhibition

and action updating. In this paradigm, participants are presented with a series of trials, each consisting of a context cue (e.g., a color or shape) followed by a target stimulus. The context cue signals whether a response is required (go trial), should be inhibited (stop trial), or should be updated by adding an extra thumb response. The tasks included in this paradigm are double-response task (DRT), ignore task (IT), and SST.

According to the Dual Mechanism of Control (DMC) framework, control of behavior is sustained in reactive (momentary) and proactive (prolonged) inhibitory ways (Braver, 2012). While sustained lateral PFC activation is related to proactive inhibition due to its involvement in maintaining goals (Chiew & Braver, 2013), the temporary activity in this region along with a wider network indicates reactive inhibition. A study utilizing a modified SST in a way that participants acknowledged the probability of receiving a stop signal demonstrated that both proactive and reactive inhibition share the dorsolateral prefrontal cortex (DLPFC)/anterior cingulate cortex (AAC) network, the ventrolateral prefrontal cortex (VLPFC)/pre-supplementary motor area (pre-SMA) /inferior parietal lobule (IPL) network, and the right ventrolateral prefrontal cortex (rVLPFC)/IPL network activations including inferior frontal gyrus. In contrast, the superior parietal lobule (SPL) activation was only observed in proactive inhibition, activation of right DLPFC/IPL regions, right frontal/ temporal regions, and rVLPFC/pre-SMA regions were only observed during the reactive inhibition (van Belle et al., 2014). Another study that used SST with three types of trials: go (press 1 for X, 2 for O), stop (withhold the response for red background), and switch (press 3 for blue background), they found that the effective connection from the inferior frontal gyrus (IFG) to the SMA is associated with reactive inhibition, while the connection from the caudate to the IFG is associated with proactive inhibition. The indirect DLPFC-caudate-IFG-SMA-subthalamic nucleus(STN)-primary motor cortex (M1) pathway is involved in proactive modulation, and the hyperdirect pathway bypasses the striatum (F.

Zhang & Iwaki, 2019). This framework demonstrates that according to the inhibition's timing and the inhibition's attentional load, the activated network would be different. In the sense of response inhibition; action restraint can be provided in reactive and proactive ways because it includes a top-down control of constant monitoring of the goal and is still dependent on no-go signal, while action cancellation is uniquely stimulus-dependent by the definition of a bottom-up fashion, and therefore only can be provided reactively.

The IFG is a brain region extensively studied for its role in inhibitory control (Tabibnia et al., 2011). However, a debate occurs on its actual function: whether it is the coordinator of the inhibitory control, or rather a key component within a larger network responsible for saliency detection or response updating. Hampshire and colleagues (Hampshire et al., 2010) showed that the rIFG is involved in variations of stop signals, even when stopping is not necessary. Their study used three scanning blocks based on the SST design for different purposes. The results suggest a broader role of rIFG in detecting important task cues. Additionally, the study found that inhibition tasks involve a wider brain network and the lack of increased interaction between rIFG and STN during inhibition which challenges the idea of a specialized inhibitory function for rIFG. Instead, according to them, rIFG contributes to general executive control and is not specialized in only response inhibition (Hampshire & Sharp, 2015). A recent study focusing on temporal activation of rIFG and pre-SMA during a selective stopping task revealed that rIFG is responsible for stopping and irrelevant to the attentional demands of the task (Schaum et al., 2020), while another one points out that the activation of pre-SMA preparing the network to stop, rIFG can be responsible for the stop operation (Swann et al., 2012). The theory of (Aron et al., 2014) is based on these findings. It focuses on action cancellation type response inhibition and proposes a pathway consisting of the rIFG, STN, and supplementary motor area pre-SMA (Fig.2). While the other studies mentioned discussed that response inhibition is the function

of differentiating wide regions, Aron et al. (2014) propose that response inhibition is the function of the specialized pathway mentioned above: rIFC is essential in stopping initiated responses (Aron et al., 2007), especially its pars opercularis subregion (Brown et al., 2023), along with the insula and inferior frontal junction (IFJ), activating during the stopping process. The rIFG likely facilitates inhibition through the STN (Aron & Poldrack, 2006; Zhuang et al., 2023). The preSMA is also involved in stopping, with structural and functional connections to the rIFC (Swann et al., 2012). The fronto-basal-ganglia network affects the premotor and primary motor cortex to implement inhibition.

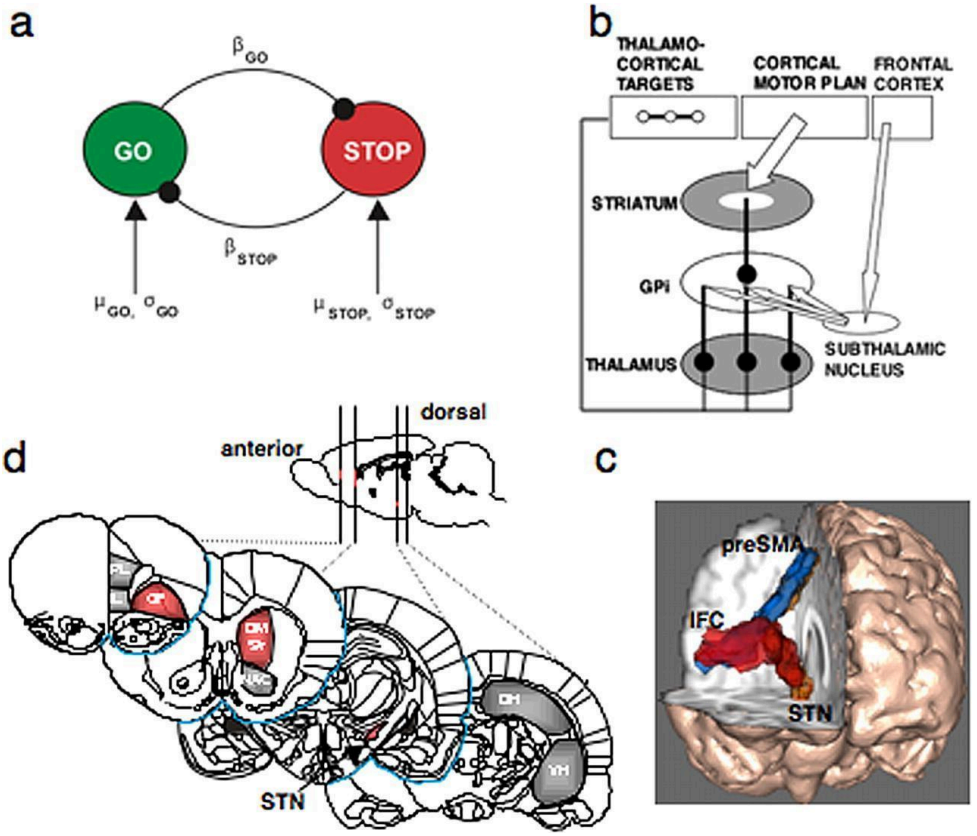


Fig.2 "*A, The interactive race model between Go and Stop processes (Boucher et al., 2007). The parameters were estimated by fitting the model to thousands of behavioral trials from a monkey neurophysiology study. B, Schematic of fronto-basal-ganglia circuitry for Going and Stopping. The Go process is generated by the premotor cortex, which excites the striatum and inhibits globus pallidus, removing inhibition from thalamus and exciting motor cortex (see text for details). The stopping process could be generated by inferior frontal cortex leading to activation of the subthalamic nucleus, increasing broad excitation of pallidum and inhibiting thalamocortical output, reducing activation in motor cortex. C,*

Diffusion-weighted imaging reveals putative white matter tracts in the right hemisphere between the dorsomedial preSMA, the ventrolateral PFC or IFC, and the putative region of the STN. Reproduced with permission from Aron et al. (2007). D, Regions of the rat brain implicated in behavioral stopping. Stopping is significantly impaired following excitotoxic lesions within the regions highlighted in red, whereas lesions within the gray-colored regions do not affect stopping. OF, Orbitofrontal cortex; IL, infralimbic cortex; PL, prelimbic cortex; DM Str, dorsomedial striatum; NAC, nucleus accumbens (core); DH, dorsal hippocampus; VH, ventral hippocampus; GPi, globus pallidus pars interna." (Taken from Aron et al., 2007).

While the stop signal task induces brief global motor suppression, selective stopping can also occur, involving the rIFC, striatum (King et al., 2012), and pallidum, suggesting the use of the indirect pathway (Fig.3) (Jahfari et al., 2011). Consequently, response inhibition appears to be mediated by a right-lateralized fronto-cortical network. The IFG produces inhibitory stop signals projected to the motor cortices using the cortico-striatal-thalamic-cortical path (Aron et al., 2014).

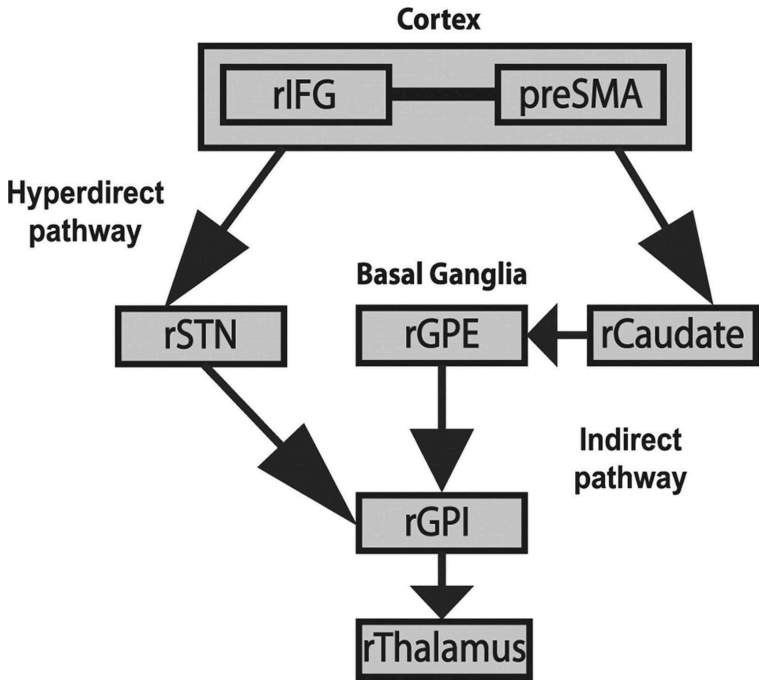


Fig. 3 Indirect and Hyperdirect pathways of response inhibition (Taken from Jahfari et. al., 2011)

This neural communication facilitates the suppression of prepotent motor responses, and the evidence for this theory comes from neuroimaging and neuromodulation studies. A study on monozygotic twins investigating which brain regions show reliable activations and if there are genetic influences on response inhibition, (Korucuoglu et al., 2021) demonstrated that inferior/middle frontal gyri, superior parietal gyrus, and precentral gyrus had test-retest reliability on response inhibition while proposing that this effect is dependent on task demands. In a meta-analysis (R. Zhang et al., 2017), researchers compared the neural correlates of response inhibition across different paradigms: interference control, action withhold (Go/No-Go), and action cancellation (SST). They found that independently of task type, areas including the IFG, insula, the right median cingulate, paracingulate gyri, and the right superior parietal gyrus were consistently activated. For action withholding/restraint, activation was primarily in the fronto-parietal network, which involves the dorsolateral frontal cortex and temporal-parietal junction. Action cancellation activated both the ventral attention network and the fronto-parietal network, indicating higher inhibitory demands (R. Zhang et al., 2017). These results suggest that while there is a shared neural network for general response inhibition that always includes rIFG, distinct areas are recruited depending on the specific inhibitory process, again, due to different cognitive demands and mechanisms involved in each type of task. When the task is switched to Go/No-Go, there will be other regions activated in addition to the shared network.

For instance, a meta-analysis on the Go/No-Go task revealed that different brain regions were engaged during simple and complex tasks, with increased working memory demands activating the right dorsolateral prefrontal and inferior parietal areas. Simple and complex Go/No-go tasks activated the pre-SMA and left fusiform gyrus. Since the pre-SMA is associated with response preparation and selection, the findings suggest it has a role in choosing the correct behavior, whether it involves executing a proper response or inhibiting

an incorrect one (Simmonds et al., 2008). Similarly, another meta-analysis on simple and complex Go/No-Go tasks using activation likelihood estimate revealed a network of brain regions consistently activated during the no-go trial performance, including the rIFG, right middle frontal gyrus (rMFG), and supplementary motor complex (SMC) and while the task is complex other regions including DLPFC and ACC were also activated probably due to higher demand of other cognitive processes (Criaud & Boulinguez, 2013).

The evidence discussed so far seems to ensure that the rIFG has a definite role in response inhibition, either as a break or a supporter of action selection, such as selecting to stop the response. Therefore, as well as imaging studies, non-invasive brain stimulation (NIBS) techniques are enlightening in revealing the relationship between response inhibition and rIFG. The following section will discuss the role of NIBS techniques in researching response inhibition, focusing on transcranial direct current stimulation.

2. Non-Invasive Brain Stimulation

Neuroscience research extensively employs brain imaging techniques to provide real-time visualization of brain activation, facilitating the understanding of the structure and function of diverse brain regions. These correlational data allow for inferences regarding the association of neural activations with distinct behavioral and clinical outcomes. However, it is crucial to acknowledge that such associations do not invariably indicate causality. The NIBS techniques are employed to overcome this issue due to their modulatory effect on the brain and behavior (Polanía et al., 2018). Though transcranial electrical stimulation (tES) techniques and transcranial magnetic stimulation (TMS) are commonly used to investigate cognitive functions, mood, and motor activities in both healthy and clinical populations (Antal et al., 2022; Begemann et al., 2020; Clark et al., 2012; Flöel, 2014), they differ in their benefits and limitations due to differences in principles they rely on (Fig. 4).

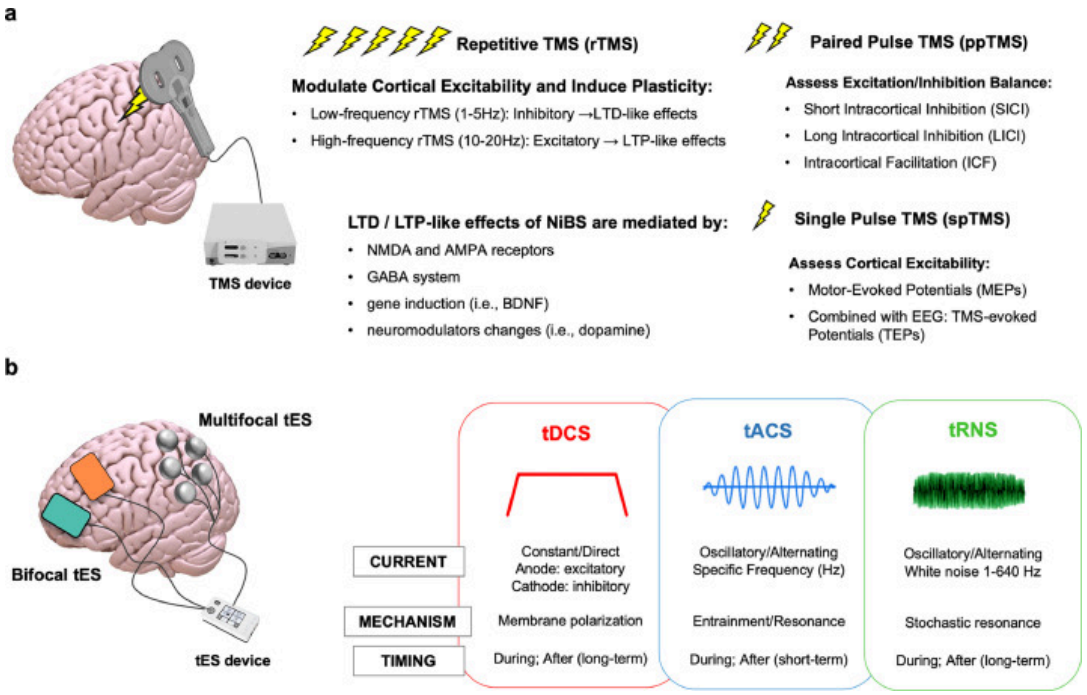


Fig. 4 Comparison of TMS and tDCS. a) mechanism of action and stimulation types of TMS; b) mechanism of action and stimulation types of tES (Sprugnoli et al., 2021)

2.1 Transcranial Magnetic Stimulation

TMS uses a brief high-intensity electrical current produced in the coil to create an intense magnetic field that penetrates the application area and induces action potential (Valero-Cabré et al., 2017). Depending on the stimulation method, duration, and amount, this method can activate or inhibit the stimulation area temporarily (Banerjee et al., 2017). TMS can be administered as single pulses, paired pulses, or repetitive TMS (rTMS), with each method serving different research and therapeutic purposes (Barker et al., 1985; Hallett, 2007).

2.1.1. TMS research on response inhibition.

In basic and clinical research, TMS is used for various purposes, including understanding the function of the regions, improving or disrupting functions to understand their principles, and determining whether this can be used in rehabilitation and therapeutic settings.

For example, one study (Obeso et al., 2013) aimed to understand the distinct function of pre-SMA and its connectivity with rIFG and used a modified SST, which includes switching the response trials. They obtained structural MRI from each participant to determine the location of pre-SMA and rIFG in each participant's brain, and they applied offline continuous theta burst stimulation (a repetitive TMS technique) over rIFG and online single-pulse TMS over pre-SMA. They found that in both single-pulse stimulation of pre-SMA and cTBS on rIFG conditions, participants worsened inhibitory control, but this was not valid for switching trials. They also found that proactive inhibition is affected more by pre-SMA stimulation and not by rIFG stimulation. However, they couldn't answer the question of the interplay between these regions. Another one (Allen et al., 2018), that was specifically looking for answers to the question of temporal primacy between these regions, employed MEG and TMS using SST, pointing out that there were no temporal differences between the regions, meaning the regions were activated simultaneously.

TMS is helpful in accurately targeting specific brain regions and observing immediate effects on behavior and cognitive processes, especially when it is used with a neuronavigation system (Nieminen et al., 2022). Moreover, TMS studies propose improvements in the conditions of patients when applied in therapeutic settings (Cavicchioli et al., n.d.; Chang et al., 2020; Kesikburun, 2022), and approved by the FDA for the treatment of drug-resistant depression(George, 2010). However, TMS is an expensive method that comes with adverse effects, such as severe headaches after stimulation, discomfort during the stimulation, and the risk of seizures (Sandrini et al., 2011).

2.2. Transcranial Electrical Stimulation (tES)

tES involves the application of a weak electrical current directly to the scalp via electrodes. The main types of tES include Transcranial Direct Current Stimulation (tDCS), which applies a constant current; Transcranial Alternating Current Stimulation (tACS), which

uses oscillating currents; and Transcranial Random Noise Stimulation (tRNS), which delivers random noise currents (Fig. 4.b). tDCS is a widely used form, primarily for modulating cortical excitability (Nitsche & Paulus, 2000). tACS and tRNS modulate brain oscillations and network connectivity, though they are less commonly applied than tDCS (Antal & Herrmann, 2016), also in response inhibition studies. tES, while less focal than TMS, is more accessible due to its lower cost, ease of use, and portability. It can be applied in a wide range of settings, including at-home use for certain conditions. The limited sensations during the stimulation, combined with minimal side effects, make tES particularly attractive for long-term therapeutic interventions, such as stroke rehabilitation and cognitive enhancement in healthy individuals (Brunoni et al., 2012). However, the electric fields generated by tES are weaker and diffuse compared to TMS, making it harder to target specific brain regions precisely. The variability in individual responses to tES, influenced by factors such as skull thickness, brain anatomy, and cellular morphology, further complicates its application (Li et al., 2015). Moreover, while tES has shown promise in various clinical trials, its efficacy is still debated, with some studies reporting inconsistent results (Horvath et al., 2014). Due to this inconsistency, it is necessary to develop standardized protocols and conduct more research to understand the underlying mechanisms of tES fully.

2. 2.1. Transcranial Direct Current Stimulation (tDCS).

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that applies a weak direct current (amplitude lower than 2mA) to the brain through electrodes attached to sponges soaked with saline solution (Nitsche & Paulus, 2000). The distance of the target region to the electrodes and the morphology of the neurons affect the stimulation's effectiveness (Das et al., 2016; Palm et al., 2016). During stimulation, the current forms a circuit by passing through the brain between the anodal and cathodal electrodes. The anode current depolarizes the resting membrane potential subthreshold, while

the cathode current creates hyperpolarization, but the excitability can vary in both polarities (Bikson et al., 2016; Paulus, 2003). While it is known that while stimulating the motor cortex, the outcome follows the anodal excitatory and cathodal inhibitory (AeCi) effect, this effect varies when it comes to stimulating cortex areas involved in complex cognitive processes (Coffman et al., 2014; Jacobson et al., 2012; Sehatpour et al., 2020). This could be due to the fact that complex or higher-order cognitive functions are typically carried out through the coordination and simultaneous or sequential activation of different brain regions or networks. Therefore, stimulating any individual part during this process may produce a different outcome compared to when the entire process is stimulated, depending on the specific task and the role of the stimulated region in the sequence of operations. The modulation settings, such as duration and the intensity of the current, also affect the stimulation success and the aftereffects (Palm et al., 2016; Thair et al., 2017).

The lack of understanding of the physiological mechanisms of tDCS limits the effective use of tDCS (Filmer et al., 2020). Still, evidence points to the that tDCS influences intracellular plasticity by regulating intracellular Ca2+ concentration, potentially impacting both short-term and long-term synaptic facilitation and neuronal plasticity (Das et al., 2016; Vasu & Kaphzan, 2023). Furthermore, tDCS has been shown to alter the excitability of neuronal networks by modulating neurotransmitter release or receptor availability, with studies indicating that it decreases GABA levels in the case of anodal tDCS (atDCS) and decreases both GABA and glutamate in the case of cathodal tDCS (ctDCS) (Caumo et al., 2012; Das et al., 2016). Additionally, tDCS has been found to interact with neuromodulators (Adelhöfer et al., 2019; Jamil & Nitsche, 2017), with atDCS supporting the function of the serotonergic system and serotonin facilitating its effects, while serotonin reverses the function of ctDCS (Das et al., 2016). Furthermore, dopamine appears to show an opposing pattern in response to tDCS(Das et al., 2016).

Typical stimulation procedures involve the use of electrodes with opposite polarities, covered with sponges soaked in saline solution, and applied to the specific area of the person's scalp using a cap or elastic band. A current of two milliamperes (mA) or less is then delivered to the brain through these sponges. Although this technique has been increasingly used for both exploring possible clinical applications and behavioral research proposes (Brunoni et al., 2012; Coffman et al., 2014) due to its ease of application and low cost, there are differing findings about its effects and the extent of these effects.

In the classical setup of tDCS, the conventional tDCS, two large (between 25-35 cm^2) electrodes are used: an anodal and a cathodal electrode, which is one positioned over the target area for stimulation, and the other electrode, which serves as the return electrode, placed at a different location on the head or body (Thair et al., 2017). The placement of these electrodes is crucial for effective stimulation. If the electrodes are too close, the current may bypass the intended brain tissue and flow through the least resistant path (Reinhart et al., 2017), cerebrospinal fluid, to the receiving electrode, resulting in inadequate stimulation (Moliadze et al., 2010). Conversely, if they are too far apart, the current may disperse, leading to increased stimulation intensity for needed outcomes (Faria et al., 2011). In that case, the increased intensity brings safety questions (Nitsche & Bikson, 2017). In addition to the placement and distance of the electrodes, several other factors influence the optimal functioning and aftereffects of tDCS montages: current intensity (Dedoncker et al., 2016), duration of the stimulation (Vignaud et al., 2018), number and interval of the stimulation repetitions (Bastani & Jaberzadeh, 2014), and whether the current is administered during (online) or before (offline) the task or training. The skull thickness, scalp properties, brain anatomy, stimulated tissue, and the neuronal morphology of the stimulation area also affect the efficacy and the direction of the tDCS stimulation (Datta et al., 2013; Dmochowski et al., 2011; Seo et al., 2017). Despite its widespread use in studies, there are still conflicting

findings regarding conventional tDCS due to its limited focality, causing both target and non-target brain areas to be affected by the stimulation (Masina et al., 2021; Woods et al., 2016). The large electrodes make it difficult to control the direction of the current, especially when the area of interest in the brain is relatively small. Because of this, it is difficult to replicate findings (Masina et al., 2021). In order to overcome this limitation, high-definition tDCS (HD-tDCS) montages are recommended.

HD-tDCS employs small electrodes and a multi-electrode montage, usually placing four or more receiving electrodes arranged in a ring around a central active electrode and the most common type is called 4x1, which includes one active electrode surrounded by 4 return electrodes and limit the diffusion of electrical current under this ring (Turski et al., 2017). This setup allows for more focused stimulation of a specific cortical area by confining the electric field to a smaller region defined by the electrodes, thus increasing focality and prolonged aftereffects (Datta et al., 2009; H.-I. Kuo et al., 2013; Villamar et al., 2013). HD-tDCS's ability to minimize stimulation of surrounding tissues leads to more consistent and reliable outcomes compared to Conventional tDCS (H.-I. Kuo et al., 2013). The biggest drawback of HD-tDCS, which offers better focality compared to conventional tDCS, is that it opens up a higher level of interpersonal variability because the stimulated area is more focalized. When the stimulated area is smaller, and the neuroanatomy of each participant is different, the probability that the stimulated area is not the desired area increases (Mikkonen et al., 2020). At this point, researchers are getting help from brain imaging and computational neuroscience methods.

Computational models such as Finite Element Method (FEM) are useful to simulate how the current will flow during the stimulation and model accurate montage configurations (Datta, 2012; Nasimova & Huang, 2022). FEM was originally developed for solving engineering problems but has been adapted for use in biomedical applications like tDCS

(Friswell & Mottershead, 1995). This method allows researchers to predict the current distribution within the skin, skull, cerebrospinal fluid (CSF), and brain tissue based on stimulation parameters such as electrode placement and current intensity (Seibt et al., 2019). The process starts with creating a model of the head using MRI data. The model is divided into multiple compartments representing various tissue types, each with specific electrical conductivity properties. Then the electrodes are virtually placed on the model's surface, and the FEM simulation calculates how current flows through the brain. The accuracy of simulations depends heavily on the quality and resolution of the MRI data, on assumptions about tissue properties and boundary conditions, and demands computational expertise (Alam et al., 2016). Therefore, computational tools such as SimNIBS, COMETS, and ROAST (Realistic volumetric approach to Simulate Transcranial electric stimulation) help calculate the electric field distribution to control inter-individual differences (Datta, 2012; Huang et al., 2019; Molero-Chamizo et al., 2021). In a study (Alam et al., 2016) on HD-tDCS, researchers used MRI scans and FEM to test different HD-tDCS ring setups on individual differences. They found that larger rings produced a stronger electrical field but less focality, and using more than four electrodes did not improve focality. Despite individual variations in how electricity spreads in the brain, the study found consistent patterns in how the electric field behaves across the different head models used. This result means that while everyone's experience may slightly differ regarding the stimulation outcomes, the study's general trends are still relevant. Even so, replication problems still persist in tDCS studies due to stable factors that participants' nurture and nature, such as genetics and demographics; variable state-based factors, which are the factors participants bring to the experiment room momentarily, such as alertness or psychostimulant consumption; and experimental contextual elements that are the personal experience of the experiment by the participant such as task difficulty (Vergallito et al., 2022).

2.2.2. tDCS Research on Neuropsychology and Response Inhibition.

Research on transcranial direct current stimulation (tDCS) and response inhibition includes both clinical and basic science investigations. Clinically-oriented research explores the use of tDCS in studies involving participants with various psychopathologies and neurological disorders (Rezakhani et al., 2024; Richardson et al., 2014; Wang et al., 2024) since the usage of the tDCS was aimed to its usage as a clinical treatment (Esmaeilpour et al., 2017) and it has a potential to alter the pathological plasticity (M.-F. Kuo et al., 2017). Major depressive disorder (MDD) is the psychiatric condition on which the effects of tDCS have been most researched, and had the most consistent evidence (Kekic et al., 2016; Yokoi & Sumiyoshi, 2015); and the application on left dlPFC of patients with MDD shown moderate evidence on improving cognition and symptoms (Bennabi & Haffen, 2018; Moffa et al., 2020), but there is no consensus on the effective therapeutic procedure of this method as well as the effectiveness in regards to MDD (Razza et al., 2020; Woodham et al., 2021), due to the vagueness of the determinants of the effect (Moffa et al., 2020)m. Still, it is found that HD--montage on dlPFC induces more change in the neural structure of patients with depression (Jog et al., 2023); symptoms like sleep disturbances can moderate the efficacy of the stimulation (Rezaei et al., 2021), and the improvements of the symptoms are more persistent when the stimulation is coupled with therapy (D'Urso et al., 2013). Anxiety disorders have also been studied in the context of tDCS stimulation of this region, as it is known to be associated with DLPFC functions (Stein et al., 2020). A study using conventional anodal tDCS on dlPFC for five sessions to test whether there will be any improvement in patients with generalised anxiety disorder (GAD) could not detect any improvement of anxiety symptoms except the physical stress symptoms (de Lima et al., 2019). Another one solely focused on social anxiety disorder and stimulating lateral and medial PFC found that 10 sessions of conventional tDCS reduced fear and avoidance symptoms, and these

improvements lasted two months when the stimulation was 2mA rather than 1 mA (Jafari et al., 2021). These effects are supported by the fact that anodal dlPCF stimulation improves a set of working memory and executive functions (Andrews et al., 2011; Fregni et al., 2005; Ruf et al., 2017), even with neurological conditions such as Alzheimer's disease and Parkinson disease (Boggio et al., 2006; Flöel, 2014).

Lastly, cravings, addictions, and substance abuse disorders were also considered for tDCS, including therapy. These disorders are also defined as impulse control disorders (Lapenta et al., 2018) Again, conventional bipolar tDCS stimulation on dlPFC was found effective on alcohol, tobacco, and food cravings(Lapenta et al., 2018; Lupi et al., 2017). This effect is associated with a change in decision-making styles (Salmani et al., 2024) or a change in cue saliency evaluation (Shahbabaie et al., 2014). However, these improvements might not be behavioral; a study focusing on food cravings reported that the improvements provided by tDCS did not change the food intake amount, but the participant self-report was pointing an improvement in cravings and participants who already had a lower level of impulsivity had more improvement (Goldman et al., 2011; Kekic et al., 2016). This extensive interest in dlPFC may be overshadowing the studies focused on other regions related to inhibitory control and executive functions (Chen et al., 2019). For example, obsessive-compulsive disorder cathodal tDCS over SMA improved the symptoms of drug-resistant OCD patients (Silva et al., 2021). This evidence aligned with a recent literature review (Brunelin et al., 2018), and results were valid when the application area changed to the pre-SMA and cerebellum (Bation et al., 2019; Brunelin et al., 2018). A recent study (Breitling et al., 2020) compared the effects of applying HD-tDCS and conventional tDCS on rIFG to children with ADHD on their working memory. They measured participants' 2-back performances during the application of an online 4x1 ring HD- montage and online conventional montage. They found that while the children's N200 and P300 signals were more alike with the normally

developed children, there was no behavioral outcome of these differences as a group; instead, they found that the effect of tDCS was dependent on how severe the symptoms were.

Regarding rIFG in one study, they measured whether applying anodal transcranial direct current stimulation (tDCS) over the right inferior frontal gyrus (rIFG) could help improve inhibitory control in individuals with restricted eating (RE) behaviors (Schroeder et al., 2023). Even though they were not able to identify a change in cravings, anodal tDCS significantly improved SST performance in the RE group. This improvement was not that volumed in unrestricted eaters, conversely to the literature that identified improved SST performance also in healthy populations (Borgomaneri et al., 2020; Schroeder et al., 2020). For example, Jacobson and colleagues (2011) investigated whether stimulating the right inferior frontal gyrus (rIFG) with anodal tDCS could enhance response inhibition and which montage induced a better outcome in healthy participants. Participants performed the SST after receiving tDCS unilateral or bilateral and anodal or cathodal stimulation, and results showed that anodal unilateral rIFG stimulation significantly improved response inhibition compared to a sham condition. The tDCS did not affect response time on go trials or performance on a control task, and stimulation of a control site, the right angular gyrus, did not demonstrate the same effects.

3. Aim and Hypothesis

The aim of this study is to compare the effects of two different tDCS montages, conventional tDCS and HD-tDCS montage built upon an optimized computational model of electric field distribution, implemented in the ROAST software (Huang et al., 2016, 2019), on response inhibition performance and to observe whether there is a difference between these montages in terms of both basic science and future clinical outcomes. Because conventional tDCS is an effortless and low-budget method, it is weak in terms of whether the output behavior is related to the stimulated region due to the width of the stimulated area, whether

the current at the required level for the output reaches the targeted region due to the spread of the electrical stimulation over a wide area. However, although HD-tDCS is more promising in terms of focality, it has limitations, such as requiring more decisive neuronavigation techniques in practice due to being more open to interpersonal differences and requiring more and more sensitive equipment. First of all, this comparison will allow a cost-effective comparison between the two montage types. Another aim of this study is to clarify whether the role of rIFG in response inhibition is a brake or a response selector. As discussed above, rIFG has been found to be related to response inhibition, especially SST-type action cancellation, in many studies; therefore, it has been characterized as a brake. At the same time, it has been discussed in another branch of the literature that it is related to response selection along with inhibition. Therefore, it is effective in response selection tasks such as DRT that do not involve inhibiting a response but involve performing an additional response. In order to shed light on this discussion, the DRT task was chosen as the control task as opposed to SST, which was chosen as the response inhibition task due to its well-documented connection with rIFG and response inhibition. If rIFG has a purely inhibitory function, the modulation of neurostimulation will be limited to SST performance only, but if it has a function related to response selection, DRT performance will also be affected by this performance. Based on these aims, we hypothesize that both conventional and HD-tDCS stimulations will improve SST performance compared to sham stimulation. Also, we expect that the improvement in SST performance will be greater in the HD-tDCS condition than in the Conventional tDCS condition. Therefore thealternative hypothesis is that data will show evidence of SSRT differences between HD-tDCS, Conventional tDCS, and Sham stimulation conditions, with the following direction: SSRT being faster in HD conditions than Sham stimulation (H1a); SSRT will be faster in Conventional conditions than Sham stimulation (H1b); and SSRT will be faster in HD condition than Sham stimulation (H1c). Conversely,

the null hypothesis (H0) will constitute no difference between conditions (H0a) and outperforming sham stimulation over HD condition and Conventional condition (H0b), or outperforming conventional condition over HD condition (H0c). For DRT we expect that there will not be enough evidence to reject the null hypothesis which will constitute no difference in double-response latency (DRT2; i.e., RT of the additional response from the onset of the double-response signal) between conditions (H0a) and outperforming sham stimulation over HD condition and Conventional condition (H0b), or outperforming of conventional condition over HD condition (H0c). Conversely, the alternative hypothesis will be that the data will show evidence of DRT2 differences between HD-tDCS, Conventional tDCS, and Sham stimulation conditions; with DRT2 will be shorter in HD condition than in Sham stimulation (H1a); DRT2 will be shorter in Conventional condition than Sham stimulation (H1b); and DRT2 will be faster in HD condition than Sham stimulation (H1c).

II. METHODS

1. Ethical Approval

The study was approved by the Ethics Committee of Istituti Clinici Scientifici Maugeri SpA SB, Pavia, Italy, according to the latest version of the Declaration of Helsinki and guidelines for the safe application of tDCS (Antal et al., 2017). All participants provided informed consent and agreed to the confidential processing of their data for research purposes before their participation.

2. Participants

The study planned to recruit participants based on a Bayesian sequential design with a maximal *N* (Schönbrodt & Wagenmakers, 2018). Using a Bayes Factor Design Analysis with Fixed *N*, it was estimated that at least 48 observations would be necessary to achieve a Bayes factor larger than 10 with a probability of p=0.8, assuming an expected effect size of δ=0.65 (Schroeder et al., 2020). A minimum sample size of 20 participants was determined before activating the stopping rule (i.e., data collection could stop if the evidence threshold determined by a BF_{10} = 10 was reached at 20 participants). Forty-seven right-handed healthy young adults aged 20-39 were recruited for the study by the end of the current academic year. However, data from 5 participants were excluded: 2 participants dropped out before completing all sessions, 2 participants exhibited a mean stopping rate higher than 0.75, which met the exclusion criteria, and 1 participant experienced technical issues that prevented the recording of responses. The final sample included 42 participants, of which 30 were women, and 12 were men. The mean age of the women was 25.20 years (SD = 3.22), with an age range of 20 to 37 years. The mean age of the men was 24.67 years (SD = 2.31), with an age range of 20 to 29 years. Only participants who completed all sessions were included in the analysis. Eligibility for participation was assessed by filling out questionnaires before the first session. Exclusion criteria were the following: color-blindness; reporting being ambidextrous

or not being dominantly right-handed (Edinburgh Handedness Inventory score < 0.8 (Oldfield, 1971); reporting having poor sleep quality during the last month (Pittsburgh Sleep Quality Index score (Buysse et al., 1989) > 5); having either one or more of the following conditions: susceptibility to, or history of, seizures or migraine; history of neurological or psychiatric disorders; history of substance abuse or dependence; history of brain surgery, tumor or intracranial metal implantation; current use of psychoactive medications; current or suspicion of pregnancy; presence of pacemaker or other implanted devices. Every participant was asked to stop consuming any psychostimulant, including alcohol and coffee, twenty-four hours and five hours before the experiment, respectively. The participants were not informed of the study's primary purpose until the end of the third session, when they were provided with information on the purpose, content, and expected results. Participation was voluntary, but psychology students at the University of Pavia were awarded 3/4 credits for their participation.

3. Instruments

3.1. Self-Reported Instruments

Edinburgh Handedness Inventory (Oldfield, 1971).

In this study, the inventory was used to determine which hand participants use dominantly. The inventory consists of ten different daily life scenarios in which participants evaluate how often they use each hand. They can give two points for the hand they always use when doing the action in question, and one point if they use both hands occasionally. The original English version of the inventory was used for participants who do not speak Italian, while the Italian translation was used for Italian-speaking participants. The study did not include participants who scored less than 0.8 on this inventory.

Pittsburgh Sleep Quality Index (PSQI;(Buysse et al., 1989)).

This tool assesses participants' sleep quality over the last month. It generates a global score based on the participants' responses to 16 items comprising seven components. The global score is calculated by adding the component scores, and if the global score is higher than five, it indicates poor sleep quality. For participants who do not speak Italian, the original version of the index was used, while for Italian-speaking participants, the Italian version (Palagini et al., 2016), which has been tested for reliability and validity, was used. The study did not include participants with a global score higher than five.

Morningness-Eveningness Questionnaire (MEQ (Horne & Ostberg, 1976)).

The questionnaire aims to determine participants' chronotypes regarding their circadian rhythms. The score is calculated based on the participants' responses to 19 items asking about when they sleep and wake up and at what time they do during the day when they need to or want to engage in an activity. The questionnaire divides participants into five chronotypes based on their responses: definite evening (16–30), moderate evening (31–41), intermediate (42–58), moderate morning (59–69), and definite morning (70–86). In this study, the questionnaire scores were used to determine the time period in which the participants were alerted, and their performance would reach the peak. Participants were invited to the laboratory for the experiment at their peak alertness time interval. While the English version of the questionnaire was used for non-Italian-speaking participants, the reliable and validated Italian version (Palagini et al., 2016; Terman & Terman, 2005) was used for Italian-speaking participants.

Transcranial Magnetic Stimulation Adult Safety Screen (TASS) (Keel et al., 2001).

The form primarily aims to ensure the safe application of Transcranial Magnetic Stimulation (TMS). However, it is also widely used in studies involving other brain

stimulation techniques. In this study, the form was used to screen whether tDCS was safe to apply to participants. Participants with conditions that could compromise safety were not included in the study. The original English version of the form was used for participants who do not speak Italian, while the Italian translation was used for Italian-speaking participants.

3.2 Behavioral Tasks

SST.

In this study, we used the SST with a visual stop signal to measure how rIFG modulation using conventional or HD-tDCS affects response inhibition. The participants were instructed to determine the direction of the arrow on the screen and respond according to the direction as fast and accurately as possible (“go” response) when the arrow was green, but to suppress this response when, in a minority of trials (25%), the arrow turned red (“stop” signal). The SSD was adjusted based on each participant's responses to control the task difficulty. The task design, in accordance with recommended practices (Verbruggen et al., 2019), included a low probability of inhibition, rapid trial progression, and personalized SSD adjustments to ensure a strong motor response tendency. Each trial began with a fixation cross (lasting 500-1500 ms), followed by a green arrow inside a black circle (Fig. 2.1.). Participants were instructed to respond as quickly and accurately as possible by pressing the corresponding keys on the keyboard ("j" for left, "k" for right), using their right index finger for "j" and middle finger for "k." In 25% of the trials, the stop signal, marked by the arrow turning from green to red, was introduced after a variable SSD. Participants were informed that both the speed and accuracy of their responses, as well as their ability to stop successfully, were equally important and that they would not get any feedback regarding their correct or incorrect responses. The SSD was initially set at 200 ms and adjusted in 50-ms increments or decrements based on the success of the stop response to maintain a stopping probability (p(stop|signal)) of approximately 0.5. Participants completed 200 trials (150 go

and 50 stop) divided into three blocks, with SSD adjustments continuing throughout the blocks. The SSRT was calculated as the primary outcome of the task.

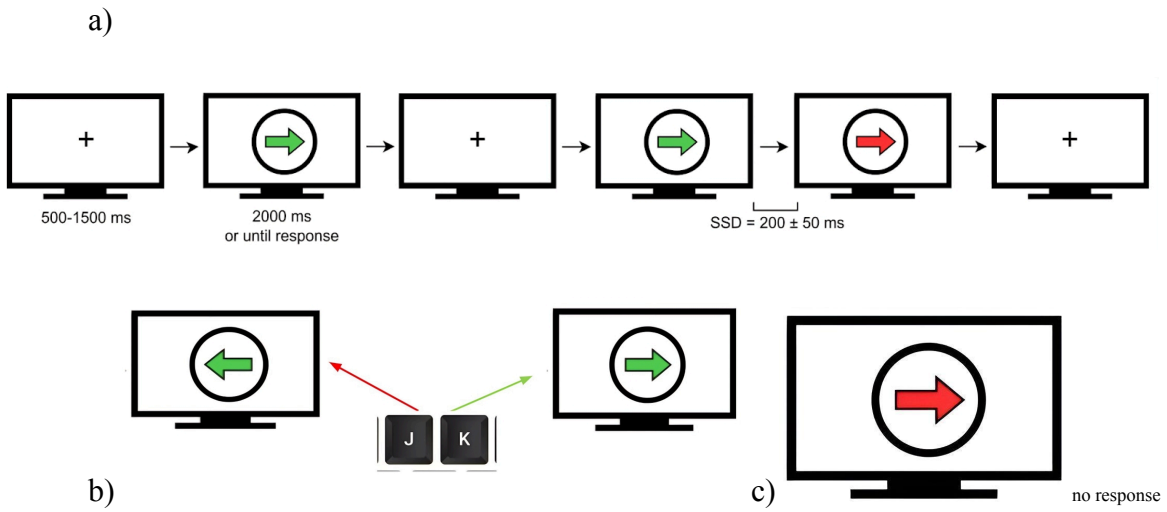
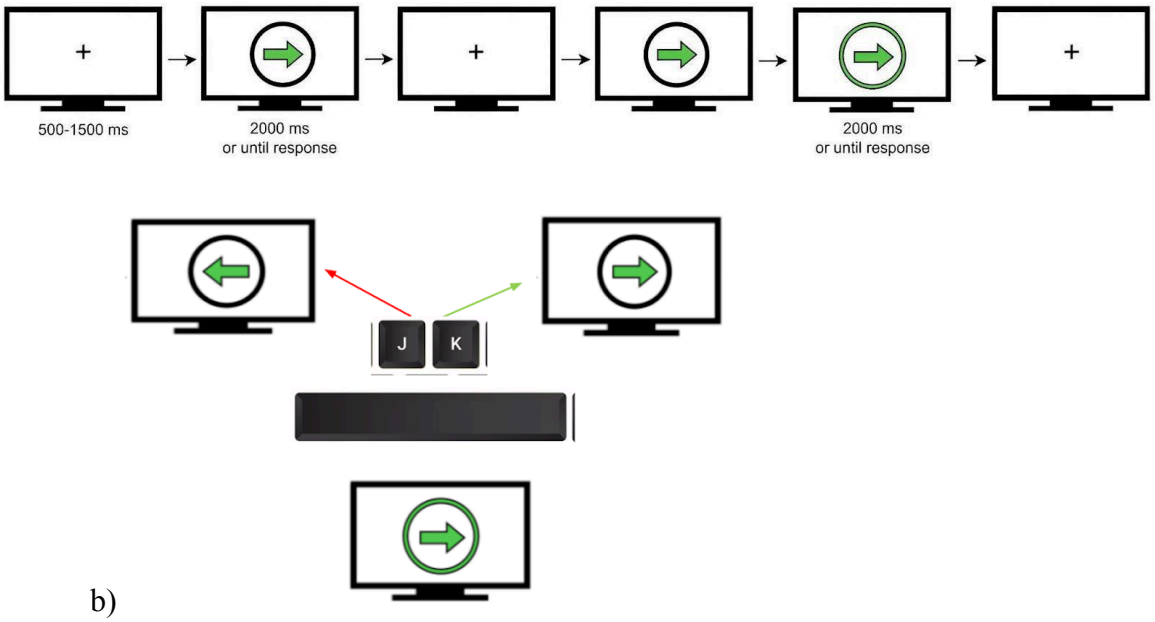


Figure 2.1. a) SST; b) and c) demonstrate the correct responses for trials.

Double Response Task (DRT).

(DRT) was implemented as a control task to distinguish non-inhibitory action updating from response inhibition, both processes linked to the right inferior frontal gyrus but different sub-regions (rIFG) (Maizey et al., 2020; Verbruggen et al., 2010). In this task, participants were instructed to make an additional, less frequent response by pressing the spacebar with their right thumb after the initial "go" response, triggered by the circle around the arrow turning from black to green (i.e., the double-response signal), regardless of the arrow's direction (Fig. 2.2.). Participants were informed that their responses' speed and accuracy were equally important and that they would not get any feedback regarding their correct or incorrect responses. The task consisted of 150 go trials and 50 double-response trials, mimicking the SST structure, totaling 200 trials divided into three blocks. The double-response reaction time counted as the primary outcome of the task.

a)



b)

Figure 2.2. a) DRT and b) Correct responses for trials.

3.3. tDCS

Conventional tDCS.

In this study, two large (5x5 cm²) pad electrodes and a battery-driven device (BrainStim, EMS, Bologna, Italy) were used (Fig. 2.3.) to deliver 2 mA anodal direct current over rIFG (crossing point between T4-Fz and F8-Cz; 10-10 EEG system), with the reference electrode located on the contralateral supraorbital area. The configuration protocol has been taken from a previous study that demonstrated successful modulation of rIFG and SST-type response inhibition (Jacobson et al., 2011).

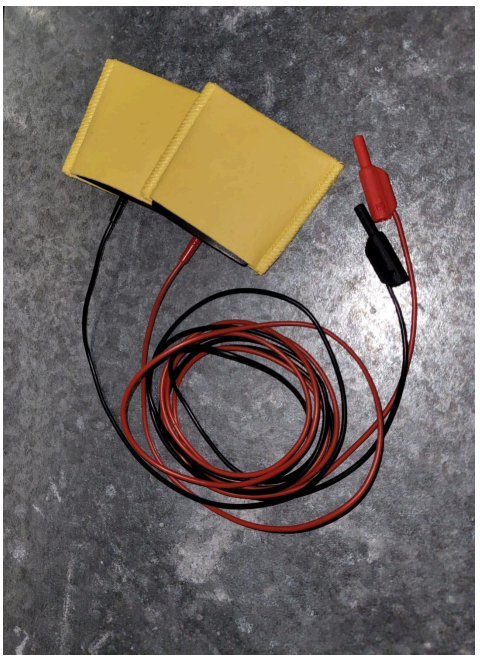
a)  b) 

Fig. 2.3. a) tDCS device b) large (5x5 cm) square electrodes in sponge envelope

HD-tDCS.

In this study, six small electrodes and three battery-driven devices (BrainStim, EMS, Bologna, Italy) connected to each other with triggers, each electrode delivering 0.667 mA (total current=2mA; density=0.23 mA/cm2) were used to modulate rIFG (Fig. 2.4.).

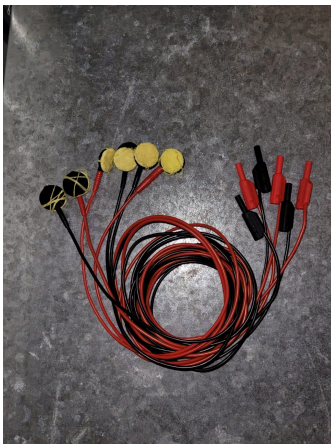
a)  b) 

Fig. 2.4. a) tDCS and trigger devices b) small electrodes attached to sponges.

For the configuration protocol, we employed the ROAST toolbox (Realistic Volumetric Approach to Simulate Transcranial Electric Stimulation), a computational tool

designed to model and simulate the effects of transcranial electrical stimulation on the brain (Huang et al., 2016, 2019). The ROAST is commonly used to optimize electrode placements by considering the anatomical and electrical properties of brain structures using high-resolution MRI data. Our current study used it to accurately target the right inferior frontal gyrus (rIFG) by refining electrode positions and current distributions. This was achieved by modeling the scalp location of 6 small (9.5 mm radius) circular electrodes, consisting of three anodes and three cathodes, based on the predicted location of rIFG at xyz=46 22 -2 (Neurosynth;(Yarkoni et al., 2011)). As a result, the electrodes were located at F4-F6-FC6 and F10-FT10-P10 sites according to the 10-10 EEG system.

4. Experimental Design and Procedure

The study employed a within-subjects design, where all participants underwent three different stimulation conditions: HD-tDCS, Conventional tDCS, and Sham stimulation. Each condition was administered separately, with at least 72 hours between sessions to minimize carryover effects. Before the first session, participants completed the MEQ, PSQI, and EHI before the experiment sessions were planned. At the beginning of only the first session, participants filled out the informed consent form, the privacy form, and TASS. Then, they read a presentation explaining the procedure, about the tDCS stimulation, and how they would do the tasks. After that, and upon arrival for two other sessions, participants were prepared for the stimulation. To prepare the participants for the stimulation, a 10-10 EEG cap was positioned on the participant's scalp. Specifically, the cap was aligned so that Cz corresponds to the midpoint of the distance between the nasion and inion, as well as the midpoint of the distance between the left and right pre‑auricular points. Afterward, electrodes previously soaked with the saline solution were placed on the participant's head, under the cap, and secured with an elastic tube bandage. In cases of high impedance, the hair under the electrodes were gently pushed, and saline solution was applied to the area. The electrode

configuration was set according to the condition they were assigned to that session. The order of the conditions and tasks was counterbalanced across participants to control for order effects, and both the participants and the experimenter administering the tDCS were blinded to the stimulation condition (real or sham). During the stimulation phase, both HD-tDCS and Conventional tDCS conditions involved 20 minutes of stimulation, with an additional 15 seconds for ramp-up and ramp-down phases before and after the 20-minute stimulation period. The Sham condition had the same duration, but, unknown to the participants, the intensity was ramped down to 0 mA after 30 seconds from the beginning of the stimulation, and ramped up again for 30 seconds at the end of the stimulation, to mimic the sensations of actual tDCS delivering . The electrode configuration for the Sham stimulation was identical to the HD-tDCS and Conventional tDCS setup, so that participants were randomly assigned to two subgroups, either with Sham conventional or Sham HD-montages. To control cognitive activity during stimulation, participants watched emotionally neutral video clips selected from a previous study (Mattavelli et al., 2022).

After the stimulation ended, behavioral tasks were administered within a 20-minute window to measure the aftereffects of the stimulation. The aftereffect period (i.e., from the end of the stimulation to the end of the task) was timed for each session. The order of the tasks was counterbalanced across participants to control order effects. After completing the tasks, participants completed a questionnaire (Fertonani et al., 2015) assessing their sensations during the stimulation to prevent adverse effects. Only after the last session participants filled out a form to measure their decision about whether the stimulation in each session they got was actual or not (i.e., placebo) and how confident they felt about their judgment, in order to check for the blinding procedure. Each session lasted approximately one hour, including the stimulation and completion of the tasks. Both the stimulation phase

and the behavioral task phase took place in an isolated booth, with researchers and participants communicating through a camera and a two-way microphone.

5. Statistical Analysis

The after-effects of stimulation on the SST were assessed by analyzing several measures: go-trial reaction time (GoRT), failed stop-trial reaction time (FsRT), the mean rate of stopping (p(stop|signal)), and stop-signal reaction time (SSRT). The first three values were used to ensure data quality, following the predictions of the race model (Verbruggen & Logan, 2008b), which posits that GoRT should be longer than FsRT, and that p(stop|signal) should approximate 0.5 due to the SSD staircase method. Participants with GoRT faster than FsRT, or with p(stop|signal) outside the 0.25 - 0.75 range (Verbruggen et al., 2019) were excluded from the analysis. SSRTs were calculated after excluding trials with reaction times higher than 2,000 ms (considered missing responses). The block-wise integration method was employed to estimate SSRTs for each block separately, and the average of these estimates was calculated, as this method is considered the most reliable for estimating the latency of response inhibition (Verbruggen et al., 2013).

Performance on the DRT was evaluated by measuring GoRTs and the latency of the additional response (DRT2). Statistical analyses were then conducted on SSRTs using Bayesian paired samples t-tests. Bayes Factors (BF) with informed priors were calculated to quantify the observed evidence, with a BF $\geq$10 indicating substantial evidence in favor of the alternative hypothesis (with conventional BF ranges interpreted as 1-3 = anecdotal, 3-10 = moderate, 10-30 = strong, 30-100 = very strong; Stefan et al., 2019). Separate paired-samples Bayesian t-tests were performed to compare the effects of HD-anodal and conventional anodal stimulation with sham stimulation on SSRTs, as well as to compare HD and conventional anodal stimulation directly.

For DRT, secondary analyses were conducted on DRT2 scores to determine whether any observed modulation was specific to response inhibition or related to non-inhibitory action updating (Verbruggen et al., 2010). Bayesian t-tests, similar to those used for SSRTs, were applied to compare anodal HD-tDCS with sham, conventional tDCS with sham, and anodal HD-tDCS with conventional tDCS.

III. RESULTS

1. Descriptive Statistics

Table 1 displays the observed mean SSRT of 42 participants. The observed means SSRT of the sham condition was equal to 303.167 (*SD* = 127.856), of the HD condition was equal to 304.214 (*SD* = 148.562), and of the conventional condition was 305.405 (*SD* = 140.879).

Table 1. *Descriptive Statistic*

	ssrt_sham	ssrt_HD	ssrt_bipolar
Valid	42	42	42
Mean	303.167	304.214	305.405
Std. Deviation	127.856	148.562	140.879
Minimum	144.000	107.000	158.000
Maximum	668.000	619.000	695.000

Table 3 displays the observed mean DRT2 of the sham condition was equal to 459.476 (*SD* = 139.617), of the HD condition was equal to 461.902 (*SD* = 105.214), and of the conventional condition was 453.195 (*SD* = 91.13). Missing data for each dependent variable was excluded from the analysis. All analyses were conducted on JASP (Version 0.18.3) computer software.

Table 3. *Descriptive Statistics*

	doubleRT_correct_sham	doubleRT_correct_HD	doubleRT_correct_bipolar
Valid	42	41	41
Missing	0	1	1
Mean	459.476	461.902	453.195
Std. Deviation	139.617	105.214	91.130
Minimum	320.000	307.000	354.000
Maximum	1.214.000	931.000	873.000

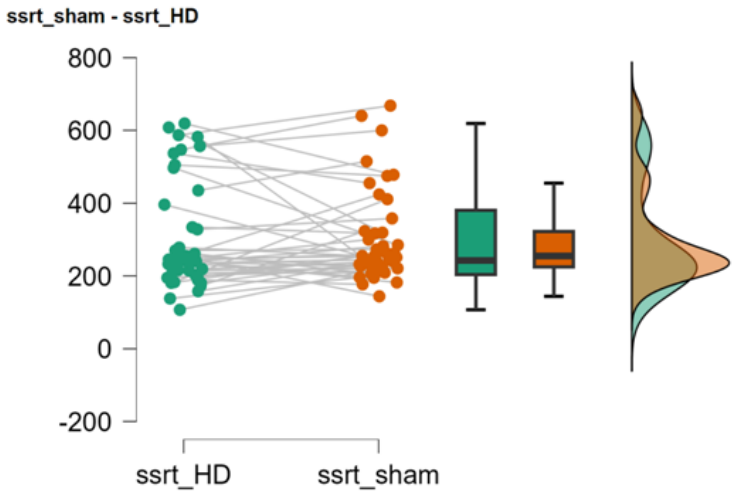
1.1 Blinding Effects

Participants' decision about whether the stimulation in each session they got was actual or not (i.e., placebo) and how confident they felt about their judgment. Results show

that participants' overall accuracy rate was 7.32%, while the accuracy rate for sham stimulation was 16%. The results indicate that the blinding technique was effective.

2. Difference Tests for SSRT

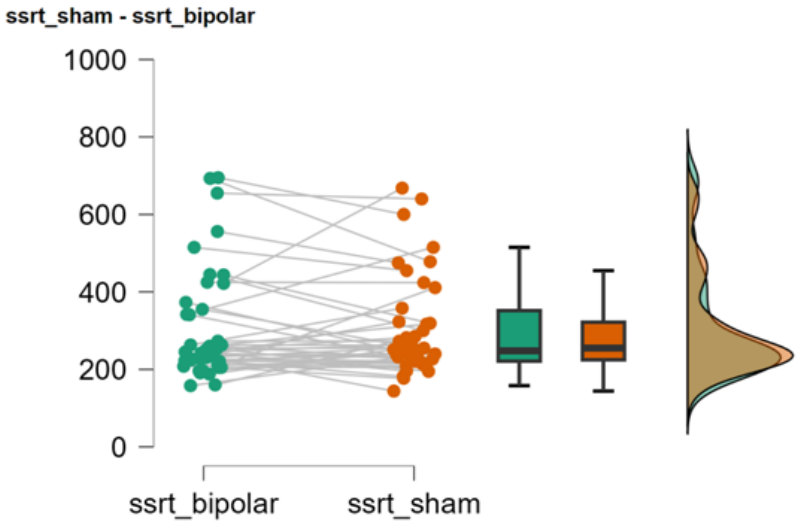
Bayesian paired samples T-tests were used to determine if there was reliable evidence indicating a difference between the conditions regarding SSRTs (For the distribution, Graph 1.), and the results summarized in Table 2. The data was examined using a prior informative criteria set to t(μ = 0.35, df = 3, r = 0.102), to compare whether the data fit under the alternative hypothesis or the null hypothesis. Firstly, to test whether HD-anodal stimulation of the rIFG modulates SST performance (i.e., stop signal reaction times (SSRTs)) compared with sham stimulation (H1a), a Bayesian paired sample T-Test was conducted. The test revealed BF_{10}=0.153 and BF_{01}=6.547 with a 95% CI [-.104, .396], indicating that there is moderate evidence in favor of the null hypothesis.



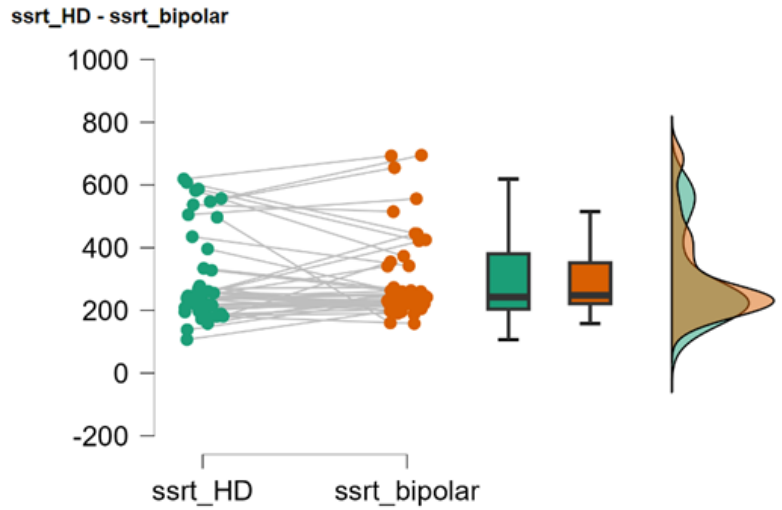
Graph 1. the distribution of SSRTs of participants in HD- and Sham conditions.

Similarly, to test whether conventional bipolar anodal stimulation of the rIFG modulates SSRT (For the distribution, Graph 2) compared with sham stimulation (H1b), a Bayesian paired samples T-Test was conducted. The test revealed BF_{10}=0.137 and BF_{01}=7.308

with a 95% CI [-.120, .390]; indicating that there is moderate evidence in favor of the null hypothesis.



Graph 2. the distribution of SSRTs of participants in Bipolar and Sham conditions.



Graph 3. the distribution of SSRTs of participants in Bipolar and HD- conditions.

Lastly, to test whether HD-anodal stimulation of the rIFG elicits a stronger modulation of SSRT (For the distribution, Graph 3) compared with conventional bipolar

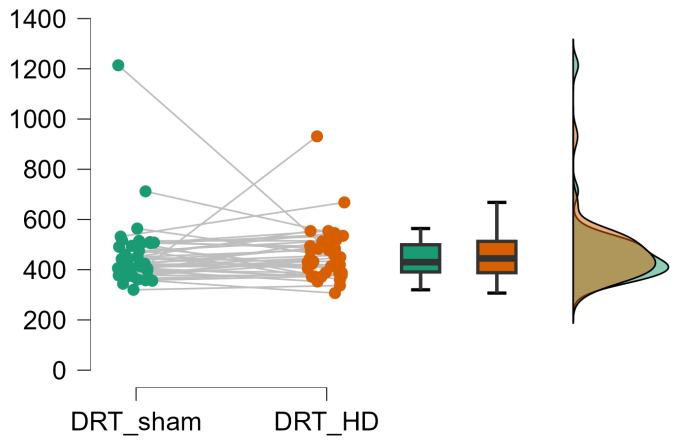
anodal stimulation (H1c) a Bayesian paired sample T-Test was conducted. The test revealed BF_{10}=0.151 and BF_{01}=6.638 with a 95% CI [-.105, .395], indicating that there is moderate evidence in favor of the null hypothesis. These results suggest that, in all conditions, there was moderate evidence against the alternative hypothesis, which means either tDCS stimulations did not modulate a difference in SSRTs or the effect was not strong and systematic enough to consider.

Table 2. *Bayesian Paired Samples T-Test*

Measure 1		Measure 2	BF_{10}	error %
ssrt_sham	-	ssrt_HD	0.153	0.062
ssrt_sham	-	ssrt_bipolar	0.137	0.053
ssrt_HD	-	ssrt_bipolar	0.151	0.061
doubleRT_correct_sham	-	doubleRT_correct_HD	0.120	0.041
doubleRT_correct_sham	-	doubleRT_correct_bipolar	0.068	3.943×10^{-4}
doubleRT_correct_HD	-	doubleRT_correct_bipolar	0.161	0.067

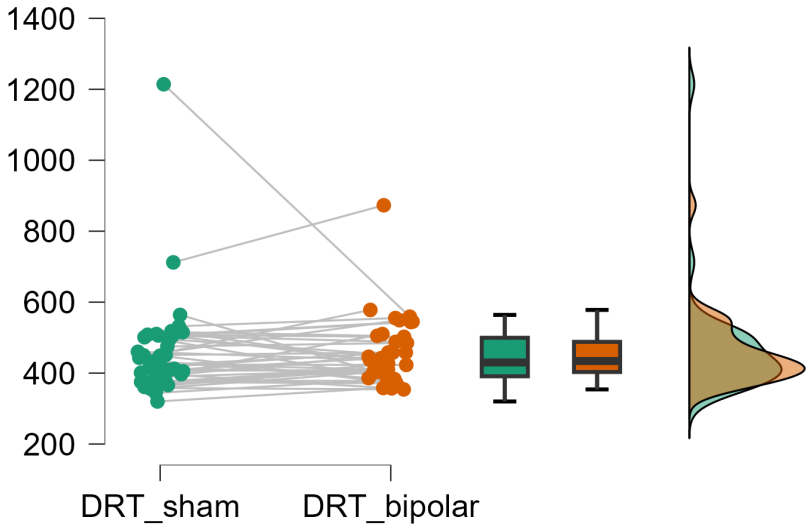
3. Difference Tests For DRT

Bayesian paired sample T-tests were used to determine if there was reliable evidence indicating a difference between the conditions regarding DRT2s, and the results summarized in Table 2. The data were examined using a prior informative criteria set to t(μ = 0.35, df = 3, r = 0.102), to compare whether they fit under the alternative hypothesis or the null hypothesis.



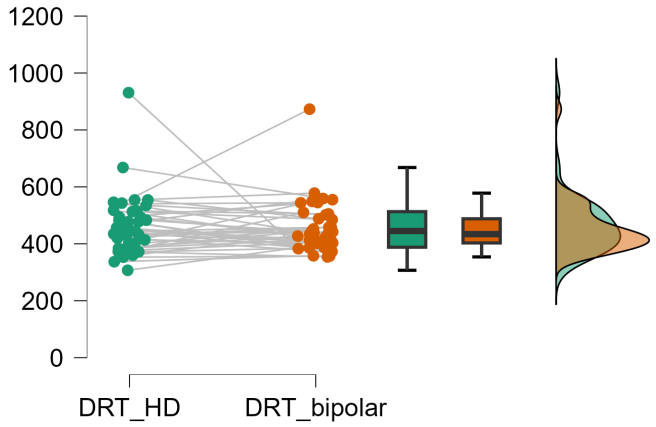
Graph 4. the distribution of DRTs of participants in HD- and Sham conditions.

Firstly, to test whether HD-anodal stimulation of the rIFG elicits a modulation of dual-response latency (i.e., DRT2 scores; for the distribution Graph 4) compared with sham stimulation (H1a), a Bayesian paired samples T-Test was conducted (For the distributions, Graph 4.). The test revealed BF_{10}=0.120 and BF_{01}=8.36 with a 95% CI [-.145, .383], indicating that there is moderate evidence in favor of the null hypothesis.



Graph 5. the distribution of DRTs of participants in bipolar and sham conditions.

Similarly, to test whether conventional bipolar anodal stimulation of the rIFG modulates DRT2 (For the distributions, Graph 5.) compared with sham stimulation (H1b), a Bayesian paired sample T-Test is conducted. The test revealed BF_{10}=0.068 and BF_{01}=14.6006 with a 95% CI [-.337, .310], indicating that there was strong evidence in favor of the null hypothesis.



Graph 6. the distribution of DRTs of participants in bipolar and HD- conditions.

Lastly, to test whether HD-anodal stimulation of the rIFG elicits a stronger modulation of DRT2 scores (For the distributions, Graph 6.) compared with conventional bipolar anodal stimulation (H1c) a Bayesian paired samples T-Test was conducted. The test revealed BF_{10}=0.161 and BF_{01}=6.218 with a 95% CI [-.102, .401]; indicating that there is moderate evidence in favor of the null hypothesis. These results suggest that in sham- HD and sham-conventional comparisons, there was moderate evidence against the alternative hypothesis, which means either tDCS stimulations did not modulate a difference in DRTs or the effect was not strong enough to consider. For conventional-HD comparison, results predicted strong evidence in favor of the null hypothesis.

4. Comparison of GoRTs

Bayesian paired sample T-tests were used to determine if there was reliable evidence indicating a difference between the conditions regarding GoRTs, and the results summarized in Table 2. The data was examined using a prior informative criteria set to t(μ = 0.35, df = 3, r = 0.102), to compare whether the data fit under the alternative hypothesis or the null hypothesis. Firstly, to test whether HD-anodal stimulation of the rIFG elicits a modulation of reaction time to go stimulus compared with sham stimulation (H1a), a Bayesian paired

sample T-Test is conducted. The test revealed BF_{10}=0.092 and BF_{01}=10.866 with a 95% CI [-0.194, 0.363]; indicating that there is strong evidence in favor of the null hypothesis. Similarly, to test whether conventional bipolar anodal stimulation of the rIFG modulates reaction time to go stimulus compared with sham stimulation (H1b), a Bayesian paired sample T-Test is conducted. The test revealed BF_{10}=0.092 and BF_{01}=4.866 with a 95% CI [-0.066, 0.409]; indicating that there is moderate evidence in favor of the null hypothesis. Lastly, to test whether HD-anodal stimulation of the rIFG elicits a stronger modulation of GoRT compared with conventional bipolar anodal stimulation (H1c) a Bayesian paired sample T-Test is conducted. The test revealed BF_{10} = 0.423 and BF_{01} = 2.363 with a 95% CI [-0.194, 0.363]; indicating that there is anectodal evidence in favor of the null hypothesis. These results suggest that in sham- HD and sham-conventional comparisons, there was moderate evidence against the alternative hypothesis, which means either tDCS stimulations did not modulate a difference in DRTs or the effect was not strong enough to consider. For conventional-HD comparison, results predicted strong evidence in favor of the null hypothesis.

IV. Discussion

To assess the difference between conventional tDCS and HD-tDCS modulations over rIFG on response inhibition and assess the role of rIFG on response inhibition and non-inhibitory response selection, this study measured the participants' response inhibition and non-inhibitory response selection performances, i.e., SSRT and DRT2 performances, respectively, during the aftereffect period following the two stimulation conditions methods and sham stimulation. The results derived from this study are preliminary. The desired number of participants could not be reached due to time limitations. In this study, we controlled participants' chronotype, psychostimulant consumption, and sleep quality but not their experiment day calendar of the participants; the unforeseeable changes in their daily habits for the experiment days may also affect the overall results in all conditions.

In terms of response inhibition, contrary to our hypothesis and previous findings, our results suggested moderate evidence against the difference between stimulation types, meaning that tDCS on rIFG did not elicit a modulatory effect on SSRTs: For HD- and sham comparison null hypothesis was 6.547 times more probable than alternative hypothesis, for conventional and sham comparison null hypothesis was 7.308 times more probable than alternative hypothesis, and for HD- and conventional comparison null hypothesis was 6.638 times more probable than alternative hypothesis. These results contradict previous research on the topic, which points out that unilateral anodal conventional tDCS over rIFG improves inhibitory control as indicated by decreased SSRT(Hogeveen et al., 2016; Jacobson et al., 2011)), even if there is an extended delay after stimulation and before to do the task (Stramaccia et al., 2015). As for HD-tDCS, previous evidence presents improved response inhibition if the HD-tDCS is used over rIFG (Guo et al., 2022; Hogeveen et al., 2016). Further, as discussed above, it is evident that rIFG is involved in SST-type response inhibition (Aron et al., 2014). The methodological differences in study and interpersonal differences in

brain and skull anatomy may explain the contradicting results. First, tDCS is already known for its drawback to interindividual differences. To control this, we used a within-subject design, previously validated conventional montage, and computer-modeled HD-tDCS montage, but still, group-wise, the evidence could not present a difference compared to the sham condition. As discussed above, it is known that brain anatomy and cell morphology affect the direction and extent of the electric current spread during conventional tDCS stimulation. The current follows the direction of least resistance path, so both brain and cell structures, such as the distribution of cerebrospinal fluid, the sulcus and gyrus organization of the brain, and the direction of synapses, impact the modulation of tDCS, the peak current can diffuse to a further area or the wider flow can prevent the accumulation of the needed intensity for the stimulation area(Aberra et al., 2023; Das et al., 2016; Datta et al., 2009). While bipolar montage reduces the effect of sulcus and gyrus organization for motor functions, results differ for cognitive functions. Furthermore, the morphological structure of the stimulation area is highly varied in shape and location (Tomaiuolo et al., 1999). Thus, for the conventional condition, even when a montage and task combination was used that was previously effective, the modulation may not be reached to peak effectful impact on the rIFG, and a different outcome might be expected due to variations in participants. In terms of HD-tDCS, previously, it has been discussed that the higher focality brings more inter-individual differences due to less diffused electrical field if applied in 4x1 ring montage to the stimulation area (Mikkonen et al., 2020), and it is suggested to use personalized models of stimulation would provide better outcomes. In this study, a 3x3 unilateral montage was applied, which was modeled by the ROAST toolbox using already existing MRI data to calculate tissue density to calculate the optimum electrical field density for all participants, the MRI scan did not belong to the participants of our study as well as only one model was

used for all participants. Thus, the calculated model may not be the best fit for every participant due to morphological differences.

In terms of non-inhibitory response updating, our results again suggested evidence against the alternative hypothesis, in this case, aligning with our expectations: For HD- and sham comparison null hypothesis was 8.36 times more probable than alternative hypothesis, for conventional and sham comparison null hypothesis was 14.6 times more probable than alternative hypothesis, and for HD- and conventional comparison null hypothesis was 6.216 times more probable than alternative hypothesis. The narrative around the functions of rIFG in response inhibition and response updating is discussed above. Due to this debate, we compared the participants' DRT2 performances with the sham stimulation to reveal whether rIFG is involved in both response inhibition and response updating or solely involved in response inhibition. Results derived from our study predicted moderate evidence in favor of the null hypothesis, which points out that the modulation of rIFG did not affect the response updating performance, as expected. This result aligns with the previous studies and reviews. However, as discussed above, the rIFG stimulation is not managed. Therefore, the findings may imply that the lack of success in stimulating the targeted region could be the reason for our results, as opposed to the rIFG not functioning in response updating.

Considering the difference between HD-tDCS and conventional tDCS, against our expectations, our results suggested moderate evidence against a difference modulated by tDCS in none of the RTs and strong evidence against a difference in DRT2 condition. The power of the evidence predicted may be affected by the sample size since we could not reach the proposed number of participants by our prior calculations. However, the direction of the evidence may be rooted in our methodological differences from the previous studies. First of all, for the conventional condition, we used the same montage that was effective in modulating the rIFG in previous studies, but the stimulation parameters were different. In the

current study, we used an electrical current of 2 mA for 20 minutes in both conventional and HD stimulations. In their studies for conventional stimulation, Jacobson and colleagues (2011) utilized 1 mA for 10 minutes, and Hoogeveen and colleagues (2016) stuck with the current amount, increasing the duration of stimulation to 20 minutes. The difference in the magnitude of the current might have resulted in changes in the stimulation duration and density. As aforementioned, stimulation parameters change the aftereffect duration, peak electrical field time, and location. Another explanation would be that the HD-tDCS is more prone to modulation when it is applied according to a personalized model when it is used to modulate cognitive functions, and the model we used here was not personalized but optimized according to calculations of conductivity of different tissues at the skull and the brain.

One limitation of our study pertains to the 10:10 EEG caps utilized, which are available in standardized sizes. However, due to limited availability, we were constrained to only two sizes. Electrode placement was carried out in accordance with the 10:10 navigation system, but the variability in head sizes among participants meant that the caps did not fit uniformly. This issue was particularly prominent in the HD-tDCS condition, where the electrical field is comparatively focal, leading to variations in electrode placement. Furthermore, the differing cap sizes resulted in varying pressure on the electrodes, despite efforts to stabilize all electrodes with elastic tube bandages, potentially affecting the conductance of the sponges. Another limitation is that the sample size was smaller than initially calculated, and while it would not change the direction of the evidence, the power of the evidence could be greater.

V. Conclusion

In this study, we aimed to investigate the effects of two different tDCS montages on response inhibition, focusing specifically on the rIFG. We found that neither conventional nor HD-tDCS had a significant effect on SST performance compared to sham stimulation. It's important to consider the limitations of our study, such as the smaller sample size and variability in electrode placement and fit, which may have affected the distribution of electric fields across participants, potentially impacting our ability to detect stimulation effects.

Overall, our study makes an important contribution to the ongoing study of tDCS montages for influencing response inhibition. We compared the effects of a previously tested anodal bipolar conventional montage with a new montage determined using ROAST software on response inhibition. Our results suggest that tDCS is sensitive to individual differences. Despite an increase in current, we did not observe the previously observed modulations. Further research is needed to determine if this change is truly related to the current amount, which will help advance the development of tDCS as a reliable research and rehabilitation tool.

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