UNIVERSITÀ DEGLI STUDI DI PADOVA

Dipartimento di Psicologia dello Sviluppo e della Socializzazione
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Enhancing Working Memory: Exploring single-session tDCS Effects and Individual differences.

Relatore
Prof. Mario Dalmaso

Correlatore esterno
Prof.ssa Sara Assecondi

Laureanda: Elena Giovanazzi
Matricola: 2051769

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Index

Abstract

The aim of this thesis was to investigate the effects of non-invasive stimulation by tDCS on a working memory task, taking into account both stimulation protocols and individual differences, such as the use of strategies. Three tDCS stimulation protocols were used: placebo (placebo stimulation), F4 (stimulation of the right dorsolateral prefrontal cortex), and P4 (stimulation of the right posterior parietal cortex). Individual differences, such as the use of strategies, were taken into account. The results indicate that stimulation alone had no significant effect on performance. However, a significant correlation was found between the effectiveness of self-reported strategy use and performance. No interaction between strategy use and stimulation was observed, suggesting that the type of stimulation did not promote strategy use more than placebo in a single session. These results suggest that individual differences, particularly strategy use, play a crucial role in the performance of working memory tasks, while the specific single-session tDCS protocols tested do not provide a clear advantage over placebo, and further research is needed.

1. Introduction

1.1 What is Working Memory?

Recalling the instructions of a recipe during cooking, navigating whilst driving, following directions, conversing with others and solving mathematical problems are all daily tasks that necessitate working memory (WM) (Nolen-Hoeksema et al., 2014). This particular type of memory enables us to provisionally store a limited amount of sensory information among multiple simultaneous stimuli, primed semantic concepts, and more integrated data and eventually manipulate them. One commonly referenced model of working memory is Baddley's (1990) multicomponent model. In this model, working memory is seen as containing three components: the central executive, which functions as an attentional system that supervises and coordinates two subordinate systems, the phonological loop for linguistic processing and the visuospatial sketchpad for nonverbal material. This division into two subsystems is supported by the fact that verbal WM tasks are hindered by articulatory suppression, while nonverbal tasks are not affected. Conversely, tasks that require the use of the visuospatial system do not impair verbal tasks, but have negative effects on nonverbal working memory tasks (Làdavas & Berti, 2020).

The neural substrates of working memory are not limited to a single area of the cortex. While it has been observed, including through neuroimaging studies, that working memory is a prefrontal cortex function, activation of different areas is observed for slightly different tasks, suggesting that there may be areas in the parietal and temporal cortex involved in specific modes of working memory (Bear et al., 2016; e.g. Haxby et al., 2000). For example, Ray et al. (2008) conducted a study that observed bilateral activation of cerebral hemispheres in healthy participants, particularly in the frontoparietal regions, during visuospatial and verbal working memory tasks with identical stimuli through the use of fMRI. Notably, a distinct left frontoparietal activation was detected during the verbal task, which was absent during the spatial task. These findings imply the existence of specialized brain regions for specific tasks. Another piece of evidence supporting this is the existence of another area deep within the intraparietal sulcus, known as the lateral intraparietal cortex (LIP), which is specialized for vision and plays an important role in working memory. Studies examining delayed saccade tasks in macaques have shown that LIP is involved in the temporary retention of spatial information before initiating a motor response (Gnadt & Andersen, 1988). Taken together, this evidence suggests that the neural substrates of working memory are specific distributed networks rather than isolated areas. Another important aspect to consider is that working memory is linked to attention, with which it has a bond of mutual influence. The involvement of attention is necessary to store information in working memory. Since attention is a selective process, only what is deliberately chosen will be stored in WM. This implies that much of what we are exposed to will not even be deposited in working memory and, consequently, will not be available for later retrieval (Nolen-Hoeksema et al., 2014). Several studies (Broadbent, 1958; Darwin et al., 1972; Sperling, 1960; Treisman & Rostron, 1972) have demonstrated that subjects are not able to completely retrieve information that was irrelevant to the task and therefore not attended (Cowan et al., 2024). Attention, however, would not only play a filtration role but is involved in prioritizing the retention of certain items (Cowan & Morey, 2007; Hu et al., 2016; Lepsien et al., 2011), retaining only relevant information (Oberauer et al., 2012), recalling items from long-term memory (Barrouillet et al., 2011), and amplifying visual mental representations (Ricker & Vergauwe, 2022). Likewise, working memory influences attention as a filter. For example, it creates models of the environment around us and compares them with incoming stimuli; if something changes, it immediately captures our attention (Elliott & Cowan, 2001).

The defining characteristic of working memory, however, remains its limited nature. According to studies by Ebbinghaus, Miller, and Yu (Ebbinghaus, 1885; Miller, 1956; Yu et al., 1985), when we use phonological encoding (i.e. when we attempt to retain information through verbal items such as numbers, words, or single letters), we can hold only 7±2 items. This ability, which varies among individuals, is referred to as working memory span or capacity. The studies were designed to measure the capacity of WM alone by presenting items to be remembered at a speed that did not allow individuals to make connections. However, in more ecological situations, people use long-term memory to perform a process called chunking, which means that long-term memory is used to recode new material into larger and more meaningful units that take up "less space" in working memory. For instance, instead of remembering "1, 2, 0, 0, 1, 8, 9, 0," we will store "1200, 1890" to reduce the number of items to be remembered from eight to two. Ultimately, the capacity of our short-term memory can be defined as 7±2 chunks (Miller, 1956). Working memory and long-term memory are interconnected since one of the roles of working memory is to temporarily hold information for later transfer into long-term memory. In other words, information held in working memory can be encoded or transferred into long-term memory (R. C. Atkinson & Shiffrin, n.d.; R. M. S. Atkinson Richard C., 1971; Raaijmakers & Shiffrin, 1992)

Studying working memory is interesting since it allows us to better understand how this complex system works, individual differences (which I will discuss further below) and how to possibly improve it.

1.2 Working Memory Tasks.

Various tasks are available in the literature meant to test working memory (WM). The difference between these tasks lies in the cognitive process that is being investigated, e.g., the capacity of working memory or its relationship to attention. Below is a brief description of basic tasks found in the literature. It is important to note that for each type of task, many variations have been created from time to time to better suit the purpose of the specific research. Also, for the purposes of this thesis, I will provide additional details on the n-back task.

1.2.1 Simple span Task

The Simple Span task assesses the participant's capability to encode and retrieve a sequence of items from working memory. The subject listens or reads verbal items and then repeats them aloud or writes them down. The number of items in the list increases until the participant can no longer accurately remember them. Common types of this task include forward digit span, forward word span, and spatial location span, where lists are composed of numbers, words, or locations in space, respectively (Naveh-Benjamin et al., 2007). One possible variation of this type of task is the Digit span Backward, in which participants are asked to repeat the list in reverse order to test their ability to manipulate the items. For instance, when reporting the sequence " 1 , 2 , 6 " forwards, it should be presented as " 1 , 2 , 6 ", whereas when presenting it backwards, it should be reported as " 6 , 2 , 1 ".

1.2.2 Complex span

This task entails administering items to the participant and prompting them to complete multiple mental operations before recalling them. The objective is to examine the individual's capability to manage a dual demand for attention, which involves performing an operation while retaining it in memory and encoding items to release attention. The Spatial Complex Span and Operation Span are two variants where, in the former, spatial locations and, in the latter, words to be remembered are followed by mathematical tasks before recollection (Naveh-Benjamin et al., 2007)**.**

1.2.3 Running span

In Running Span, individuals are asked to recall a series of items of unpredictable quantity, often beyond their capacity to memorize the entire list, which is presented rapidly. After the list's conclusion, the aim is to retrieve and recall as many items as possible, or a specific number, in reverse order from the end of the list. The aim is to get people to maintain vigilance and, at the end of the list, to move items from a passive memory stream to the focus of attention. Examples of this type of task include the running digit span, running location span, and running shape span (Naveh-Benjamin et al., 2007)

1.2.4 Dual task working memory

The point of the dual task is to require dual attention, as in complex span, and to encode information in a way that keeps attention free. Practically speaking, it is any combination of a task that requires memory for at least one set while sharing attention with another task (Naveh-Benjamin et al., 2007). The Brown-Peterson task is a typical example, in which the participant is presented with a set of letters to remember, then asked to count backwards, and finally to recall the letters on the list (Peterson & Peterson, 1959).

1.2.5 Item and biding tests

The item and binding test involves combining an item that designates the specific object in the set to be remembered and binding that reflects whether there is a specific pairing among the items to be remembered in the set. The cognitive processes being studied involve memory, which relies on basic methods to retrieve target objects for the item, while binding investigates the support of arbitrary associations that require attention. While individual words or items are easily remembered due to their association with long-term memory, it can be more challenging to recall the associations or bindings that connect these items. An example of this kind of task is identifying which object was presented (item) and what color it was (binding) (Naveh-Benjamin et al., 2007)**.**

1.3.6 The *N-Back* paradigm

The n-back paradigm constitutes a working memory task in which a series of items, for example, letters, are presented one at a time. Participants must determine whether each item matches the one presented a certain number (N) of times in the past. The difficulty of the task increases as N increases. The task requires maintaining a continuous list of recent items to be remembered and updating the list as one responds (Naveh-Benjamin et al., 2007). One additional challenge is to exercise caution and avoid false alarms on trials that match, for example, the second or fourth previous letter in a 3-back task, commonly known as recent lure trials. Effective executive control is required to successfully reject these lures. To prevent errors, individuals must recognize the conflict between the high familiarity of the current item and the controlled retrieval of the target item (Ralph et al., 2014). An example of a trial in a verbal 3-back type might be "a - b - c - d - **b** - *d* ", in which the bolded character is the match because it is identical to the item three times in the past, while the italic character is a lure because it would correspond to two items before. There are several versions of this type of task that change according to the type of item, e.g., digit n-back or spatial n-back (e.g. Laine et al., 2018; Stephens & Berryhill, 2016, respectively), or whether its difficulty changes according to individual performance or is fixed to certain level throughout the testing (e.g. Assecondi et al., 2021; Zarantonello et al., 2020, respectively).

The n-back paradigm's experimental design can significantly impact subject performance, indicating its importance. As Ralph et al. (2014) has noted in his dissertation, various factors, including the ratio of lure to target trials and the presence or absence of trial-by-trial feedback, may influence the control strategy employed by participants. In the context of working memory, two types of control strategies emerge: the proactive one, which involves activation of the task context in preparation for the upcoming stimulus, and the reactive one, which refers to transient activation of the context in response to the stimulus. In working memory experiments, the design is such that proactive rather than reactive control is favored.

1.3 Why Is Working Memory Related With Strategy?

As pointed out earlier, because working memory is not unlimited, we often implement strategies in an attempt to maximize the limited memory we have available. It has been observed in WM studies that the use of a strategy can have a positive influence on performance (Carretti et al., 2007; Laine et al., 2018; McNamara, 2001). In fact, according to a review conducted by (Ben Izhak & Lavidor, 2023), the use of strategy facilitates deeper item processing, thereby facilitating mental operations and information maintenance. Moreover, while people naturally rely on strategies during WM tasks, there are individual differences in choosing them and this consequently affects performance (Laine et al., 2018; McNamara, 2001).

Working memory is a core cognitive function, fundamental for everyday activities, that correlates with intelligence. It is thus not surprising that many studies have attempted to improve working memory capacity, through cognitive training. In these works, the increase in working memory capacity was studied by evaluating the effects of training on either a task structurally similar to the one used in the training or on a different one but still involving working memory, finding different results (e.g Traut et al., 2021). A role in explaining these conflicting outcomes could be played by the strategy devised by or even provided to participants. In the first case, we refer to internal strategies as they are self-generated by the participant. In the second case, we refer to external strategies as they are learned during the experiment. Both types of strategies can enhance performance on working memory tasks, however the positive effect of external one can also transfer to an untrained but similar task (Laine et al., 2018). According to the *Strategy Mediation Hypothesis* proposed by Laine et al. (2018), improvements in working memory training are caused by the adoption of specific cognitive strategies to efficiently undertake the tasks, rather than a general increase in working memory capacity. Laine's interpretation implies that these strategies significantly affect training results, often restricting improvements to the specific tasks trained and limiting transfer to wider cognitive skills.

1.4 What Type Of Strategy Exists?

According to the definition provided by Waris (Waris et al., 2021), strategies are conscious conceptual rules created to respond to a cognitive task that can modulate lower-level processes involved in the management of that task. This spontaneous method can rely on cognitive mechanisms responsible for problem-solving and may be the result of previous experience and thus memotechnics already used. When participants are asked to report the strategy they used in a given task, a variety of types can be observed. In the literature, these types are often categorized according to the categorization made by Morrison (Morrison et al., 2016) or the subdivision made by Laine (e.g. Fellman et al., 2020; Morrison et al., 2016). The Morrison's categorization includes a "*rehearsal"* strategy which consists in repeating the items of the task; *Grouping* is condensing several items into a single entity to remember them; *Updating* is memorizing an element and then updating the information as the task goes forward; *Grouping and comparison* means condensing a chunk of items and comparing them with the successive ones; *Semantics* means that the subject used the meaning of the item to remember it; *Phonology* consists of analyzing the way the items sound to memorize them; *Imagery* consist in creating, according to the meaning of the item, a visual image of it; *Familiarity* insists on relying on recognition memory, rather than trying to remember; *Guessing*, giving a random response; Other strategy, uncategorizable strategies and lastly No strategy.

However, because some strategies were rarer than others, in some studies (e.g. Forsberg et al., 2020; Laine et al., 2018) the types that represent 5% or less of the total were condensed into “other strategies”.

Laine (2018), moreover, divided the strategies according to how detailed the descriptions were in a three-point system. A strategy with zero points was an answer not given, with one point being a vague or non-specific strategy, a clear strategy with one detail obtained two points and with three points a well-described strategy with two details. For example, “I didn’t use a strategy”, “I stayed more concentrated than usual” and “I have tried to remember three items and then compare them to the next tree” would have been categorized as zero points, one and three respectively. (Laine et al., 2018) Laine also distinguished between strategies generated by the participant during the task and those provided by the investigator. The former are referred to as *internal strategies*, as they are self-generated by the In the second case, we refer to *external strategies* as those learned during the experiment. As mentioned earlier, it was observed that both types of strategies can improve performance in working memory tasks, however, the external one also has a positive result in an untrained but similar task (Laine et al., 2018).

1.5 Strategy, Working Memory And Tdcs:

Over the past few years, technology and techniques to improve cognitive performance have evolved. The field of neuropsychology refers to these interventions and technologies as neuroenhancement, which are used to improve human performance beyond normal abilities, as defined by Antal (Antal et al., 2022). This objective can be achieved through a variety of interventions, from using legal drugs such as nicotine, to energy drinks containing high levels of caffeine or stimulants, to more sophisticated brain stimulation technologies. Non-invasive brain stimulation techniques (NIBS), such as repetitive transcranial magnetic stimulation (rTMS) and low-intensity electrical stimulation (tES), including transcranial direct current stimulation (tDCS), can be used to improve cognitive abilities (Antal et al., 2022). Transcranial direct current stimulation (tDCS) administered while performing a cognitive task, has the potential to improve task performance. For instance, (Stephens & Berryhill, 2016) found that 2mA anodal tDCS targeting the right prefrontal cortex improved on WM performance, compared with sham stimulation or with the same stimulation at a lower intensity. This method of stimulation involves administering a low electric current to the scalp that it is hypothesized to cause modulations in neuronal membrane potentials, which can affect the likelihood of neurons firing over time. These changes preferentially impact the networks of neurons that are already active, as compared to the networks that are in a resting state (Gill et al., 2015). Thus, it has been argued that, the use of technologies such as TDCS coupled with cognitive training may be beneficial to performance because the neural mechanism thought to underlie tES techniques involves modulating the patterns of ongoing neural activation, strengthening or weakening these patterns through the Hebbian synaptic mechanism of neuroplasticity, in which ongoing patterns of neural activity are selectively modulated or strengthened by stimulation (Antal et al., 2022; Gill et al., 2015; Jackson et al., 2016; Kronberg et al., 2020; Reato et al., 2013). In other words, the effect of tDCS to produce long-term potentiation (LTP) in the brain through modulation of synaptic plasticity depends on the fact that tDCS boosts Hebbian plasticity by modulating pyramidal neuron membrane dynamics linked with input associativity and input specificity of the ongoing endogenous Hebbian plasticity. In detail, the effect of tDCS depends on input specificity, which refers to the boost in strength of only the relevant synaptic inputs. These are the inputs that are already activated and undergoing endogenous plasticity. Input associability, the other key mechanism, refers to the fact that tDCS helps weak inputs to be associated with strong inputs. This is a cellular mechanism that allows linking two pieces of information that were not related before. For these two mechanisms, the effects of tDCS are task-specific and may be most effective when paired with learning tasks that induce plasticity. Thus, the potential of tDCS in enhancing cognitive functions is contingent upon targeted stimulation of specific synaptic pathways (Kronberg et al., 2020).

One of the aspects to consider when thinking about an intervention or experiment using the tDCS technique is the timing of stimulation, as there are two experimental designs, defined as online and offline. Experiments conducted online involve an exercise during stimulation, while experiments conducted offline involve the task being performed after and/or before stimulation (Thair et al., 2017). However, in a study conducted by Martin (2014), it was observed that participants achieved better skill acquisition using a working memory task and online stimulation of the left dorsolateral prefrontal cortex. In addition, it is important to emphasize that in order for stimulation to be effective, it must be applied consistently to the area responsible for the cognitive skill in question. In this regard, the study conducted by Ruf (2017) compares three conditions, task-congruent, task-incongruent, and sham stimulation, with two WM tasks, one spatial mediated by the right dlPFC and one verbal mediated by the left dlPFC. Results suggest that anodal tDCS needs to stimulate the domain-specific active dlPFC to be effective. In a different study conducted by Gill (2015), it was noted that the potential for improvement resulting from tDCS depends on the task performed during stimulation (Gill et al., 2015). The positive effect is produced when the task sufficiently activates the cognitive demand and related brain regions, which is in line with other experiments that found no improvement with the use of tDCS alone (Andrews et al., 2011). These three aspects align with the concept of activity selectivity, which refers to the fact that tDCS modulates an already activated neuronal network preferentially, while it does not modulate separate neuronal networks that are inactive (Bikson & Rahman, 2013).

Furthermore, Jones et. al. (2015) conducted a study pairing tDCS on the left prefrontal cortex with strategy instruction, and discovered that providing a strategy while using tDCS benefits performance, especially in individuals with higher working memory capacity. On the other hand, a study conducted by Assecondi (2021), where younger participants underwent a working memory training paired with tDCS, suggests that using a combined strategy with stimulation to the right dorsolateral prefrontal cortex is particularly beneficial for those participants with low working memory. The differences between those studies, such as the stimulation parameters, the task used, and how they manipulated the strategy (i.e., between individuals or within the same person) can be the reason for these two different results. However, from these two studies, it can be hypothesized that the use of the strategy may act as a booster of non-invasive brain stimulation on memory tasks.

It is noteworthy that Wang, Itthipuripat and colleagues (2020) also discovered that the effects of transcranial direct current stimulation (tDCS) applied to the right posterior parietal cortex (PPC) are mediated by encoding strategy in verbal working memory. These findings are consistent with the meta-analysis conducted by Wang, He and colleagues in 2019, which identified the brain regions involved in working memory. In fact, the meta-analysis was based on functional neuroimaging studies of WM and the n-back paradigm. The researchers identified six cortical regions that exhibited consistent activation throughout the task: bilateral middle frontal gyrus (BA 10); bilateral inferior parietal lobule (BA 40); bilateral precuneus (BA 7); left superior frontal gyrus (BA 6); left anterior insula (aI) (BA 13); bilateral thalamus. Moreover, the same study demonstrated that 2-back increased activation in the left middle frontal gyrus, left inferior frontal gyrus, and left aI relative to 1-back (H. Wang et al., 2019). Furthermore, in the spatial version of the n-back task, activation was observed in the following brain regions: left superior frontal gyrus, bilateral middle frontal gyrus (BA 6), bilateral medial frontal gyrus (BA 8, 32), bilateral inferior parietal lobule (BA 40), bilateral superior parietal lobule and right precuneus (BA 7, 19). Additionally, the authors propose that the DLPFC is engaged during the encoding phase of structured sequences, where it plays a role in strategic recording of information from memory and the implementation of strategies to enhance memory (also Bor et al., 2004; Fletcher et al., 1998). Conversely, the parietal cortex is known to be involved in a wide range of cognitive functions. Its activation depends on WM load and is related to the visuospatial aspects of the task. It is also known to interact with the prefrontal cortex and appears to be related to the selection and switching of behavioral components during the planning phase of the task. This may help to explain some of the conflicting results observed. Experiments targeting different brain areas may have stimulated different aspects of the strategies, thus leading to different effects, although these were all derived from the same network.

1.6 Individual Differences (And Tdcs)

Evaluating individual differences is crucial to make inferences that accurately reflect the examined population. One model that serves this purpose well is the Aptitude by Treatment Interaction (ATI) model, developed in 1991 (Snow, 1991). The ATI was designed to systematically account for individual differences among treated individuals in treatment assessment. The aim is to evaluate whether alternative treatments have varying effects based on personal characteristics and to identify the most suitable treatment for an individual. In fact, in this theoretical model, the term 'attitude' is precisely defined by Snow as: *"any measurable person characteristic hypothesized to be propaedeutic to successful goal achievement in the treatment studied.*" Therefore, it is important to consider all relevant aptitudes to obtain a comprehensive and accurate understanding of the phenomenon under investigation.

Thus, it is clear that, whether training-related improvements in working memory are related to the use of a successful strategy or a genuine increase in working memory capacity, individual aptitudes may mediate the final outcome. This is framed in Lövdéns theoretical framework (Lövdén et al., 2010). In this framework two cognitive constructs can be identified: flexibility and plasticity. These processes respond to the need to adapt our resources and to meet an environmental demand when a mismatch (called supply-demand mismatch) occurs. Flexibility refers to the adaptation of pre-existing resources in an attempt to cope with different stimuli and resources requirements. One manifestation of flexibility is the acquisition of useful knowledge to complete a task. In this view, strategy can be seen as the utilization of preexisting resources to improve performance through the learning and use of task-relevant knowledge. The authors also suggest that mental strategies, explicit instructions, and identifying specific process combinations can enhance performance on particular tasks by increasing knowledge. The latter promotes greater flexibility by offering alternative representations of the environment and multiple approaches to a given stimulus, allowing the individual to perform better in similar tasks as well. Therefore, the efficiency of cognitive processes can be improved by the strategy without, however, enhancing it. Instead, a modification in cognitive functions, such as working memory, could be attributed to plasticity. Plasticity manifests itself in the change in performance but also in the change of the cognitive function itself (Lövdén et al., 2010). The author also emphasizes how plasticity can only be attributed to the exclusion of any process of flexibility, either the acquisition of knowledge or a better use of the cognitive process considered. Therefore, in this context, strategy plays an important role in working memory tasks as it can be considered a tool to elicit cognitive flexibility. This results in better performance by enabling participants to make the best use of the resources already available.

Another perspective on the relationship between strategy and working memory can be gained from the research conducted by H. Bailey and Dunlosky (2008). The author presents two hypotheses: strategy as a cause and strategy as an effect. The '*strategy-as-cause*' hypothesis argues that individuals who achieve higher performance are also more strategic. The '*strategy-as-effec*t' hypothesis states that the use of strategy is the result of improved working memory capacity. This perspective proposes that individuals with greater working memory capacity are more likely to use strategies effectively, increasing the likelihood of using strategies when performing tasks, which contributes to improved scores. Therefore, in this case, the author suggests a causal relationship between a higher working memory capacity and a higher probability of using strategies that affect performance results.
That is why cognitive strategies play a key role in determining the success of working memory implementation.

Variability permeates cognitive research and manifests itself in how individuals perform and the capacity of their working memory. Several variables, showing large interindividual variability, have been shown to impact working memory performance: age, education, motivation, baseline cognitive reserve, and baseline performance, to name a few.

1.6.1 High and low-capacity working memory individuals

If we were to subject a sample of people to a working memory task we might find individual differences in performance, even though this sample apparently shows no differences in age, schooling, motivation etc. One possible explanation for this difference is the different baseline level of working memory skills, with some individuals performing better (*high performers*) than others (*low performer*s) (Traut et al., 2021). This distinction is important because it may impact the outcome of cognitive training interventions, such as WM training or strategy instruction. Some studies found that high performers gain slightly more from the intervention (Jones et al., 2015), while, other studies report more benefits for the low performing individuals (Assecondi et al., 2021; Lövdén et al., 2012; Tagliabue et al., 2022). Differences in outcomes between low and high performers may be explained by the interaction between intervention type and individual response to intervention , namely Compensation and Magnification. Lövdén's (2012) research shows that compensation explains the reduced performance gap between high and low performers when a strategy is provided to the latter. In fact, since higher performers are already proficient at the task, they would not benefit significantly from adopting a different approach. However, the same study shows that when the intervention consists in the repetition, thus becoming practical, of the task, it is the high performers who improve, thus achieving a magnification effect on performance. These findings suggest that between-person differences decrease with compensation and age-group, and increase with practice.

1.6.2 Age differences

As previously mentioned, one of the most relevant differences between people is age, in fact, working memory is not stable during life, but it's subject to decline with aging. Seniority may also be the cause of the longer time required to process information (Salthouse, 2010). Other studies indicate age-related differences impacting both reaction time and accuracy in working memory tasks. Specifically, research demonstrates that elderly individuals tend to have longer reaction times, i.e., they are slower to respond, and are less accurate than younger subjects; further, reaction times begin to decline earlier, at about age 35, than accuracy, which starts to decline at around age 60 (Zarantonello et al., 2020)

One of the reasons may be that the functional integrity of certain brain regions, which are related to the storage, maintenance, and retrieval of information, are subject to individual and age-related differences (Grady, 2012).

On the other hand, there are individual and age-related differences in the use of strategy. While it is known that using an efficient strategy improves performance (Dunlosky & Kane, 2007), as suggested by (H. R. Bailey et al., 2014) aging can have an impact on the efficacy of a strategy. Moreover, the ability to employ effective strategies on a WM task can change while aging (Cokely et al., 2006; Dunlosky & Kane, 2007), and for older adults it can be difficult to produce spontaneous strategies (Ober, 1996). Furthermore, younger people are more likely than older individuals to develop spontaneous strategies in a memory task (Naveh-Benjamin et al., 2007).

Reasons for these differences were explored in a recent review (Ben Izhak & Lavidor, 2023). One possible explanation is the utilization deficiency: everyone develops associative connections to encode information using strategy, but older adults experience more difficulties in retrieving those connections. Based on the decoding deficiency, older adults have more trouble reaching the target memory while using the information encoding strategy, because the contexts they have created are less effective, although they recall them correctly. Eventually, there might be a retrieval deficiency that makes older people less likely to recuperate associative connections in a WM task. This suggests that the ability to employ effective strategies on a WM task changes while aging.

1.6.3 Motivation

In a study by Jones and collaborators (Jones et al., 2015), which used tDCS in combination with a working memory task, it was observed that one source of difference between individuals could be the level of motivation. Indeed, an economic reward, regardless of its amount, had a positive effect on performance, particularly on subjects with low working memory capacity. However, when this variable wasn't manipulated, the effect wasn't significant. (e.g. Assecondi et al., 2021).

It is noteworthy that some research, such as that of Jaeggi, indicates that intrinsic motivation has a positive influence on the improvement of a task, the avoidance of dropout, and consistent engagement in the completion of training (Jaeggi et al., 2014). Further evidence of the effect of expectation and motivation was found by Parong and colleagues in 2022, who discovered a possible effect on working memory, but also on fluid intelligence and cognitive flexibility. The researchers observed a positive effect of positive expectation on performance on the post-test task (Parong et al., 2022). Another study conducted by Mohammed et al. (2017) involving 127 students had also found an effect of motivation in training. In this study, participants were randomly assigned to two conditions: a normal n-back or a gamified version of the task to enhance motivation. The latter group demonstrated greater commitment and engagement, although no significant differences were found between the two groups at post-test. It is also noteworthy that the observed benefit did not manifest until the third session (Mohammed et al., 2017). The authors posit that the positive effect of motivation may only become apparent after the learning phase of the task (Mohammed et al., 2017).

Collectively, these findings suggest that motivation is a crucial variable that must be rigorously examined when conducting research in cognitive training and working memory experiments.

1.6.4 Education

Education may also influence working memory, in favour of those who have higher education (Morais et al., 2018). For example, people that complete middle school degree or higher education are faster in working memory tasks and starting from high school education level even the accuracy is better (Zarantonello et al., 2020).

Another interesting individual difference that involves education is linked with tDCS. Berrhyl and Jones (2012) found beneficial effects of the stimulation to the left or right PFC only on more educated participants.

1.6.5 Cognitive reserve

Cognitive reserve (CR) is a construct introduced to explain why some people are more resilient to brain aging, disease or brain damage than others. CR is not static but changes depending on factors such as education, occupation, exercise and social interaction. CR is an active model of reserve, which implies that cognitive and functional brain processes are dynamic and capable of coping with changes or damage to the brain. CR can help understand how some people maintain cognitive and functional abilities despite age or disease-related brain changes (Stern et al., 2020). Nonetheless, it is not possible to measure it directly, consequently, researchers often use a proxy based on life-long education level, work experience, and leisure activities (e.g. Frankenmolen et al., 2018).

An intriguing study conducted by Zarantonello (2020) examined the correlation between CR and a working memory task. After being assessed to determine their cognitive reserve, participants were instructed to complete a working memory task using an n-back paradigm. This task established three levels of difficulty: low demand (1-back), high demand (2-back), and control (0-back). The findings indicate that there is a positive impact of CR on accuracy, irrespective of the level of difficulty, albeit not on reaction time. Additionally, individuals with a moderate level of CR exhibit better agility in inhibiting responses for non targets and respond more efficiently to targets.

To sum up, individual differences in CR could be one of the possible variables influencing the task to be taken into consideration.

1.7 Hypothesis And The Aim Of The Thesis

The main aim of my thesis is to investigate if tDCS targeting different nodes of the fronto-parietal network (namely the dorsolateral prefrontal cortex or the posterior parietal cortex) can modulate performance in a challenging working memory task in young adults. In particular, we will compare two stimulation protocols: one involving the right parietal cortex (anode on P4 and cathode on Fp1 in the 10–20 system) the other the right frontal cortex (anode on F4 and cathode in Fp1 in the 10-20 system). We hypothesize, in agreement with previously published work, that tDCS targeting the FPN during the cognitive task will increase performance, although we do not make strong predictions on the role of a specific node (DLPFC or PPC). Secondly, we aim to disentangle the relation between stimulated brain area, cognitive performance, and strategy use

2. Method

2.1 Participants

A total of 47 participants were enrolled, including 31 females. The participants were young adults aged 20 to 30 years (mean age = 23.24, SD = 3.25). Recruitment was conducted through flyers, social media ads, SONA platform and posters. At the beginning of the experiment, participants gave informed consent to participate. Each was then reminded of their right to withdraw from the study at any time. The following inclusion criteria were considered: do not have epilepsy or familiarity with the condition, do not consume psychotropic drugs, have not been diagnosed with a mental disorder, do not have metal inserts in their body, have not consumed excitatory drugs or alcohol in the previous six hours. They also have normal vision, do not have dermatitis, have not been diagnosed with a neurological disorder, and do not have scars on their head or scalp. Additionally, participants were requested to refrain from consuming coffee for four hours prior to the session and slept for at least 6 hours the previous night. Participants were compensated 21 euros for their participation in the study.

2.2 Task

As previously mentioned, there are different types of tasks that can be used to measure working memory. For our study, we chose the n-back paradigm because it requires both the detection of the stimulus and its storage in working memory, as well as the manipulation of the information and its continuous updating. Additionally, this particular task is one of the most frequently utilized for working memory training. The type of variant utilized was non-adaptive and had a difficulty level of 3-back. In the n-back visuospatial task used, participants are presented with a circle lacking a perimeter on a dark background that is divided into eight segments. One segment is "colored" white at a time. Participants must compare the newly coloured segment with the one that appeared n times earlier, and decide if they are in the same (left arrow) or different (right arrow) position by pressing a key on the keyboard (see figure 2.1).

figure 2.1

The experiment consisted of 20 blocks, with each block comprising the presentation of 20 stimuli, 14 of which were non targets and 6 of which were targets. In addition, 3 foil targets were also presented. The duration of each stimulus presentation was 300 ms, while the inter-stimulus interval (ISI) was 1700 ms. The total duration for one trial was 2000 ms.

2.3 Questionnaires

A series of questionnaires were administered to all participants with the following objectives: to investigate individual differences, to investigate aspects related to task and stimulation perception, and to obtain general information about the participants. This section will provide a brief overview of the questionnaires used.

Demographic information questionnaire: The questionnaire collected demographic information such as age, years of completed education, gender, manual dexterity, and eyeglass use.

Hospital Anxiety and Depression Scale (HADS): The HADS questionnaire investigated participants' level of anxiety and depression.

Familiarity with Technology: This questionnaire investigates each subject's experience with digital technologies, specifically whether they were familiar with computers, smartphones, Internet banking and online shopping, e-health applications, ATMs, video games, and ticket machines. The questionnaire comprises a series of questions designed to investigate perceived memory performance in everyday life.

Every Day Memory Questionnaire (EMQ). This questionnaire consists of a series of questions designed to investigate perceived memory performance in everyday life.

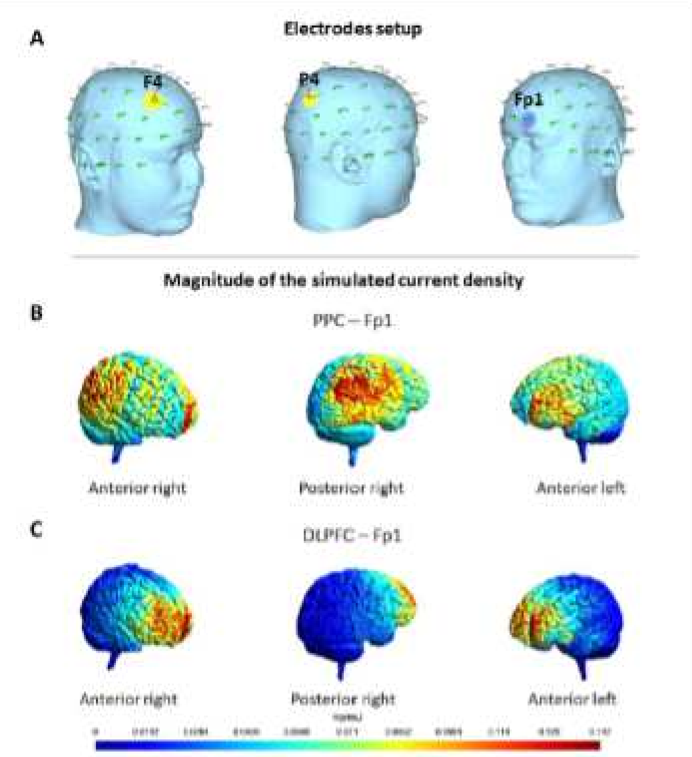
Strategy Use. The questionnaire investigated the use of strategies to perform the n-back task. Additionally, it inquired about the specific types of strategies employed. The aforementioned questionnaire was also administered at the conclusion of the third session.

In addition to the aforementioned questionnaires, other questionnaires were utilized to investigate other individual differences (e.g., the Motivation and Expectation Questionnaire and the Health Status Questionnaire), to collect feedback on treatment and performance (e.g., the NASA Task Load Index and the Attitude Questionnaire), and to ensure that participants met the inclusion criteria (e.g., the Eligibility and Safety Questionnaire and the Daily Safety Questionnaire). However, these questionnaires will not be analysed in this thesis.

2.4 Protocol Of The Study

This study has a crossover design where each participant experiences three conditions in a randomized order: frontal stimulation with the anode located on F4, parietal stimulation with the anode targeted at P4 or sham stimulation with the anode randomly placed on either F4 or P4 (see figure 2.2). The study consists of three sessions spaced seven days apart, which incorporates a washout period to eliminate any potential residual effect of the previous stimulation (as recommended by i.e. Bergmann & Hartwigsen, 2021). The experiment was conducted using a single-blind method, meaning that the participants were unaware of the type of stimulation they received while the experimenters were aware. Each session started with participants completing a set of questionnaires. In the first session participants provided informed consent and at the end of the final session individuals were debriefed and had a chance to ask specific questions about the study. After completing the questionnaires, the participant underwent electrode placement before initiating the stimulation and the task. The experiment lasts roughly 20 minutes, with 20 blocks of 20+n stimuli each, with short self-paced breaks between blocks.

Figure 2.2



A computational model of the suggested configuration (Software SimNIBS) is presented in Panel A. To stimulate the DLPFC, the anode (yellow) was placed at F4, while for PPC stimulation, the anode (yellow) was placed at P4. In both configurations, the reference electrode or cathode (blue) was placed on the opposite side in fp1 (left). Panels B and C illustrate the current density module achieved by simulating stimulation using the proposed configurations at 2 mA. A higher current density (shown in red) indicates a greater current flow in the stimulated area or in the vicinity of the stimulation.

2.5 Stimulation Parameter.

TDCSs was delivered via a battery-powered constant current device (BrainStim, E.M.S. s.r.l., Bologna, Italy), which complies with the Medical Device Directive 93/42/EC. Two circular electrodes with a diameter of 2.5 cm were used, one cathode and one anode, with the anode placed at F4 or P4 and the cathode at Fp1 as previously described (10-20 international EEG coordinate system) via a conductive gel (SignaGel) between the rubber electrode and the scalp. In the active stimulation mode, a continuous current of 2 mA was applied for 20 minutes, preceded by an upward ramp from 0 mA to 2 mA of 30 seconds and followed by a downward ramp of 30 seconds (for a total stimulation time of 21 minutes), so that the electrode current density was 0.40 mA/cm². In the sham mode, current was delivered only during the first and last 30 seconds of the total 21 minutes, with an upward ramp from 0mA to 2mA at the beginning, no current delivered, and a 30-second ramp at the end, to simulate the sensation of stimulation without altering cortical activity. Prior to initiating the stimulation protocol, the stimulator (BrainSTIM) automatically assessed the impedance of the electrodes to ensure that the current intensity set in the protocol could be delivered. If the impedance was deemed sufficient, stimulation began.

To ensure the blind condition three electrodes were always mounted on the cap: one in F4, one in P4 position and one on Fp1; however only the Fp1 and one of the other two, depending on the protocol condition, were effectively connected to the tDCS device. For this reason, the stimulator was stored in a custom-made box that prevented the participant noticing which electrode was disconnected.

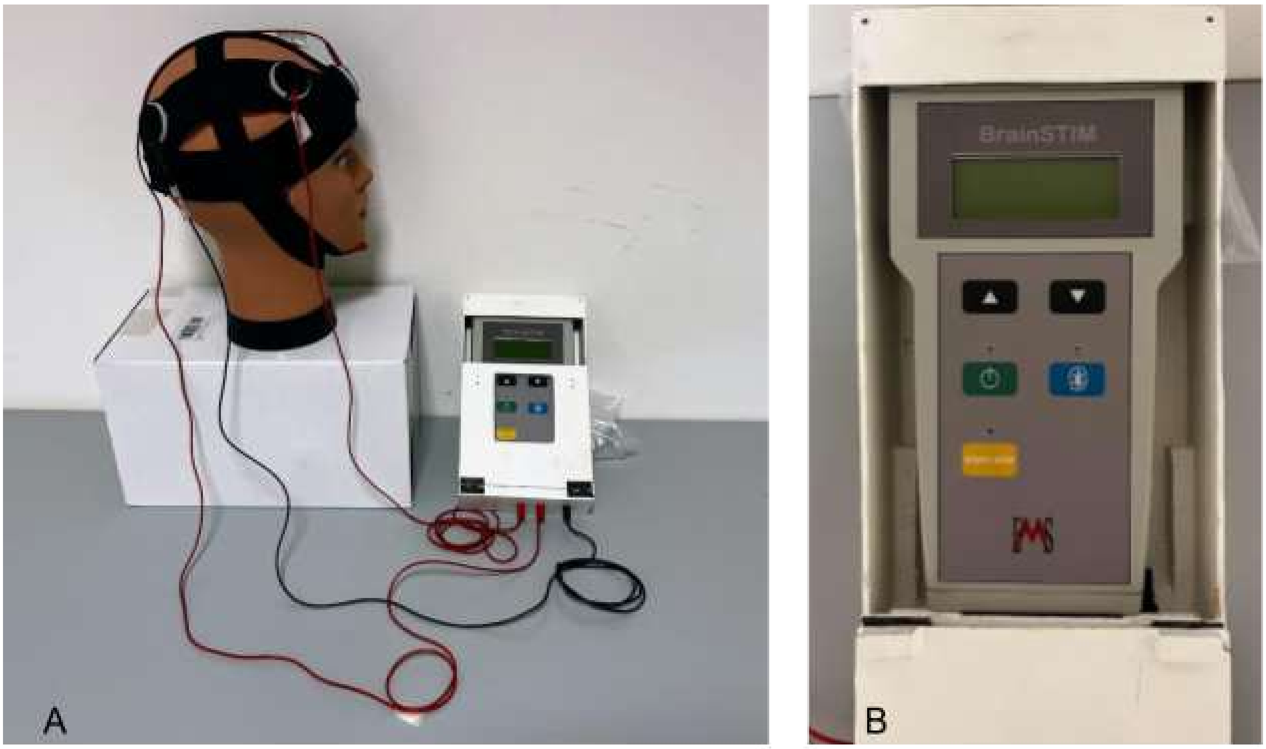


Figure 2.3

***Panel A** depicts the electrode configuration. The two red electrodes on Fp1 and, in this case, F4 (International EEG System 10-20), respectively, represent the two leads that were actually connected to the device. The black electrode was disconnected, as can be seen in **Panel B**. This setup was employed to ensure that the participant remained blind to the stimulation condition.*

2.6 Data Analysis

The collected data showed a prominent within-subject learning effect, therefore as a first approach and for the purposes of this thesis, I will focus on the first session of the experiment. As such, the experimental design is a single-session between-subject comparison. This allows us to explore the effect of stimulations, without the confounder of the learning effect. As previously stated, the study employed three treatment groups: a placebo stimulation group (sham), a parietal stimulation group (P4), and a frontal stimulation group (F4). The sham and F4 groups each comprised 16 participants, while the P4 group had 15 participants due to ongoing data collection.

Statistical analyses were conducted using R, and Rstudio software.(R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.)

Dependent variables were performance indices as d-prime value (D'), reaction time (RT), the false alarm rate (pFA), and the hit rate (pH). The latter is the proportion of true positives, representing the probability of recognizing a target stimulus. In contrast, the proportion of false negatives, or pFA, is the probability of mistakenly recognizing a target stimulus when it is not present. With regard to reaction time, that is, the interval between stimulus presentation and behavioral response, only responses classified as hits and corrected rejections were included in the analysis. The value D' was calculated as follows: $D' = Z(pH) - Z(pFA)$, where Z is the inverse function of the standard normal distribution. We employed linear mixed models (LMM) to analyze the data. Model assumptions were evaluated through visual inspection of residual plots for normality and homoscedasticity. Age and education were included as covariates in the analysis. The LMM analysis was conducted using R version 4.0.3, and the nlme package (Pinheiro et al., 2021) Significance was calculated through Wald's test to estimate degrees of freedom and generate p-values for fixed effects.

Given that the effect elicited from tDCS begins only after 5 minutes of stimulation (Jackson et al., 2016) it was possible to consider the first two blocks as baseline performance since they were completed in these time frames. Therefore, as a preliminary step, the mean performance for each individual in the first two blocks was calculated. This value will serve as a baseline for subsequent analyses.

2.7 Experimental design.

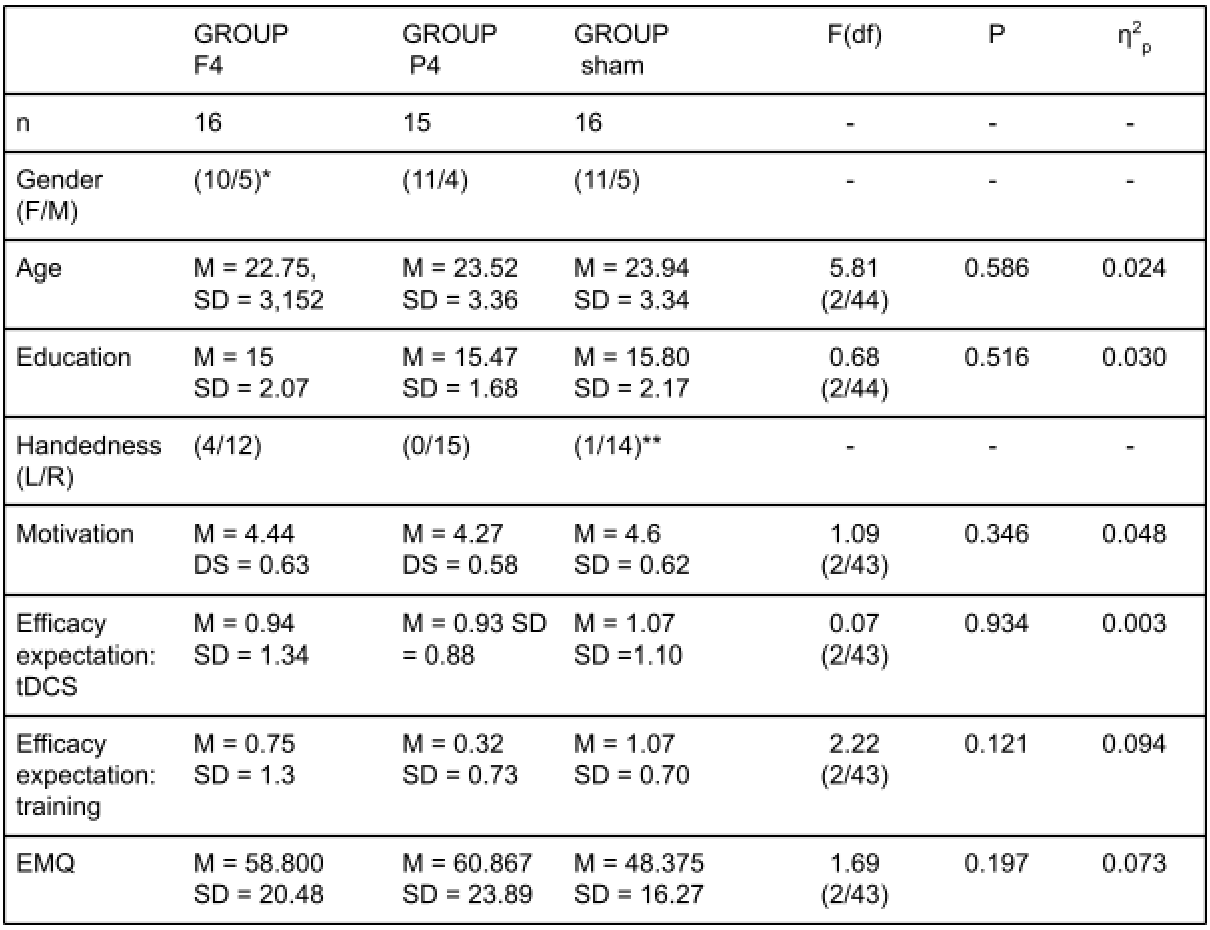
As previously stated, the present thesis will focus on the first session of the experiment. Therefore, the experiment is a single-session, between-subject design. A total of 47 subjects, including 31 females, aged 20 to 30 years, participated in the study. Each subject was randomly assigned to one of three stimulation groups: sham, p4, or f4.

3. Results

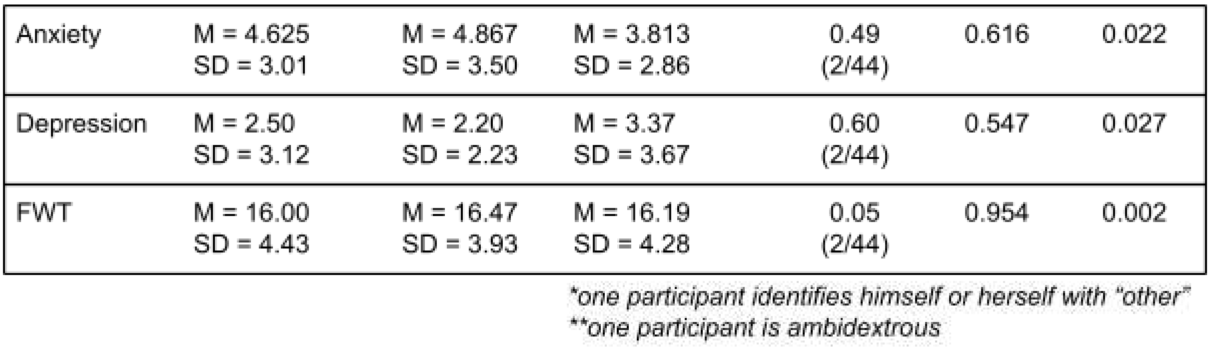
3.1 Baseline Differences

To ensure that all three groups were comparable at the baseline, a one-way independent ANOVA was conducted between groups (F4, P4, SHAM). Participants in the P4, F4, and sham groups exhibited no significant differences in age, years of education, motivation, expectation of TDCs or the training itself, anxiety or depression, familiarity with technology, and perceived memory health (all *ps* > 0.05, *ns*).

Table 3.1: baseline differences



	GROUP F4	GROUP P4	GROUP sham	F(df)	P	η^2_p
n	16	15	16	-	-	-
Gender (F/M)	(10/5)*	(11/4)	(11/5)	-	-	-
Age	M = 22.75, SD = 3,152	M = 23.52 SD = 3.36	M = 23.94 SD = 3.34	5.81 (2/44)	0.586	0.024
Education	M = 15 SD = 2.07	M = 15.47 SD = 1.68	M = 15.80 SD = 2.17	0.68 (2/44)	0.516	0.030
Handedness (L/R)	(4/12)	(0/15)	(1/14)**	-	-	-
Motivation	M = 4.44 DS = 0.63	M = 4.27 DS = 0.58	M = 4.6 SD = 0.62	1.09 (2/43)	0.346	0.048
Efficacy expectation: tDCS	M = 0.94 SD = 1.34	M = 0.93 SD = 0.88	M = 1.07 SD =1.10	0.07 (2/43)	0.934	0.003
Efficacy expectation: training	M = 0.75 SD = 1.3	M = 0.32 SD = 0.73	M = 1.07 SD = 0.70	2.22 (2/43)	0.121	0.094
EMQ	M = 58.800 SD = 20.48	M = 60.867 SD = 23.89	M = 48.375 SD = 16.27	1.69 (2/43)	0.197	0.073



Anxiety	M = 4.625 SD = 3.01	M = 4.867 SD = 3.50	M = 3.813 SD = 2.86	0.49 (2/44)	0.616	0.022
Depression	M = 2.50 SD = 3.12	M = 2.20 SD = 2.23	M = 3.37 SD = 3.67	0.60 (2/44)	0.547	0.027
FWT	M = 16.00 SD = 4.43	M = 16.47 SD = 3.93	M = 16.19 SD = 4.28	0.05 (2/44)	0.954	0.002

**one participant identifies himself or herself with “other”*
***one participant is ambidextrous*

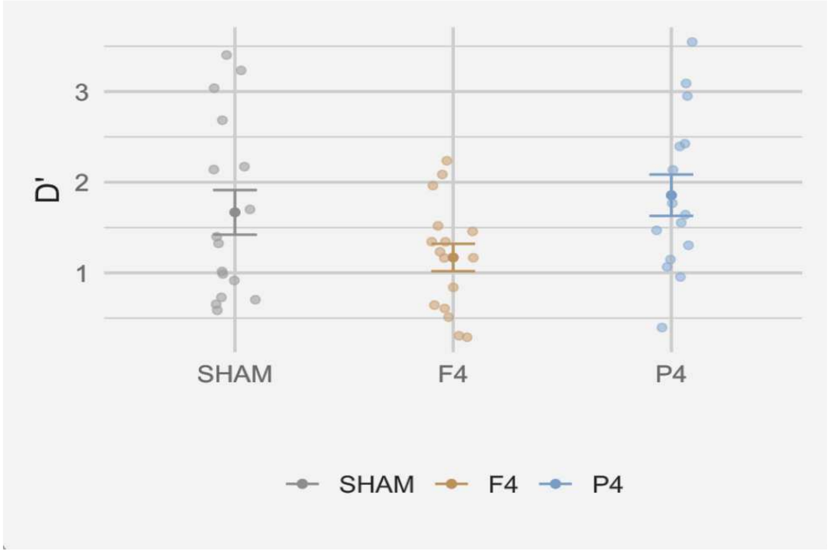
3.2 Effect Of Tdcs On Task Performance

We fitted four distinct linear mixed models to predict working memory performance (D', RT, pFA, and pH) with stimulation group (F4,P4, SHAM) as fixed factor, baseline performance, age, and education as covariates. The models included participant ID as random effects (random intercept).

The primary findings for each model will be presented in the subsequent sections.

3.2.1 D’.

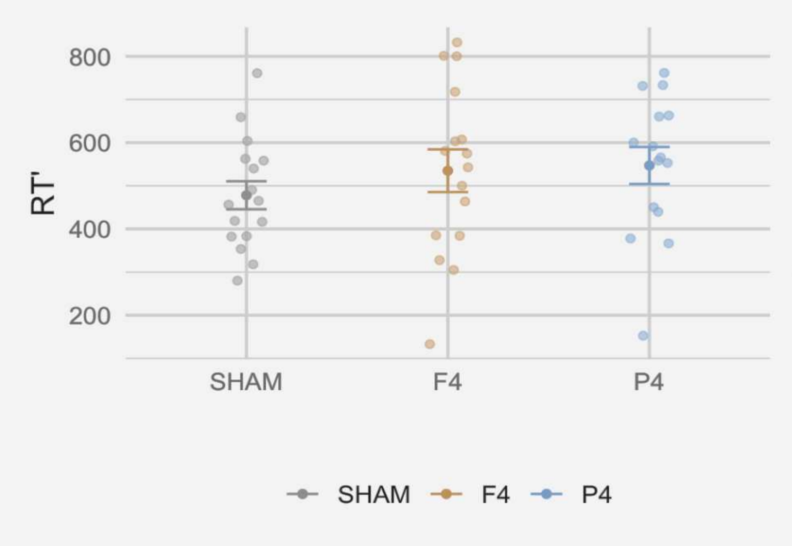
We found that performance was significantly predicted by the stimulation group (*F*(2,39) = 6.81, *p* = 0.003) and baseline performance (*F*(2,39) = 64.84, *p* < 0.0001). The results indicated that there was no interaction between the two variables. Nevertheless, we did identify a stimulation effect, although none of these survived the multiple comparisons test using the Holm method for three tests, (see table 3.2 in Supplemental Material).



Graph 3.1
The graph shows the performance (D`) in the three experimental groups. Performance was significantly predicted by the stimulation group (F(2,39) = 6.81, p = 0.003) and baseline performance (F(2,39) = 64.84, p < 0.0001). However, no significant interaction was observed between the two factors. Although an effect of stimulation was identified, none of these effects remained significant after the correction test for multiple comparisons using the Holm's method.

3.2.2 Reaction Time

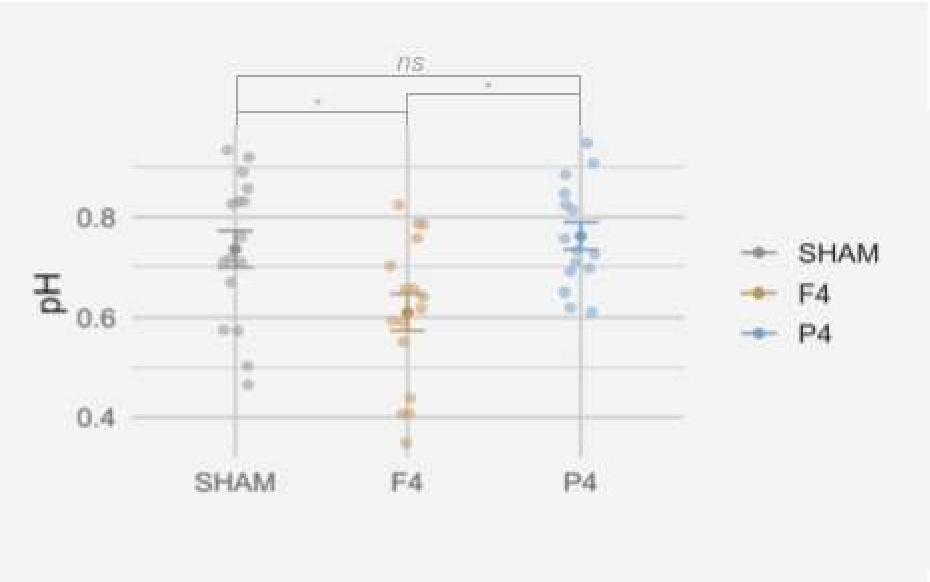
A linear mixed model analysis was conducted in accordance with the methodology described at the outset of this section, along with an examination of reaction time (see graph 3.2). However, no stimulation effect was identified *(F*(2,39) = 0.78, *p=.45) a*fter correcting for baseline performance. Age and education were not significant.



Graph 3.2
The graph represent the Reaction Time for each group, however no stimulation effect was identified (F(2,39) = 0.78, p=.45).

3.2.3 Hit rates

As pH is expressed as a percentage, we initially applied an arc-sin transformation, and then conducted a linear mixed model. The results show a significant effect of stimulation (F(2,41)=9.50, *p=.0004*), after adjusting for baseline performance. A contrast analysis revealed significant differences between the stimulation groups. The contrast between the SHAM group and the F4 group demonstrated a statistically significant difference , with an estimated effect size of 0.10 (SE = 0.042). Nevertheless, the contrast between the SHAM group and the P4 group revealed no significant difference (*t*(41) = 0.13, *p* = 0.89), with an estimate of 0.006 (SE = 0.03). Finally, the contrast between the F4 group and the P4 group demonstrated a statistically significant difference (*t*(41) = -2.43, *p* = 0.038), with an estimate of -0.11 (SE = 0.03). As can be seen in Figure 3.3, the F4 group appears to have lower hit rates than the other groups.



Graph 3.3

The subsequent post-hoc analysis suggests that the sham and p4 groups are similar (t (41) = 0.13, p = 0.89), while the other two comparisons P4-F4 and Sham-F4 are significant (i.e. (t(41) = -2.43, *p* = 0.038) and (t(41) = 2.65, p = 0.034) respectively).

3.2.4 False Alarm rates

To examine the impact of stimulation on pFA, since this value is originally a percentage, we first applied an arc-sin transformation and then we did a linear mixed model, as we did for pH. The overall results did not demonstrate a significant effect of stimulation (*F*(2/41) = 1.08, p =.35).

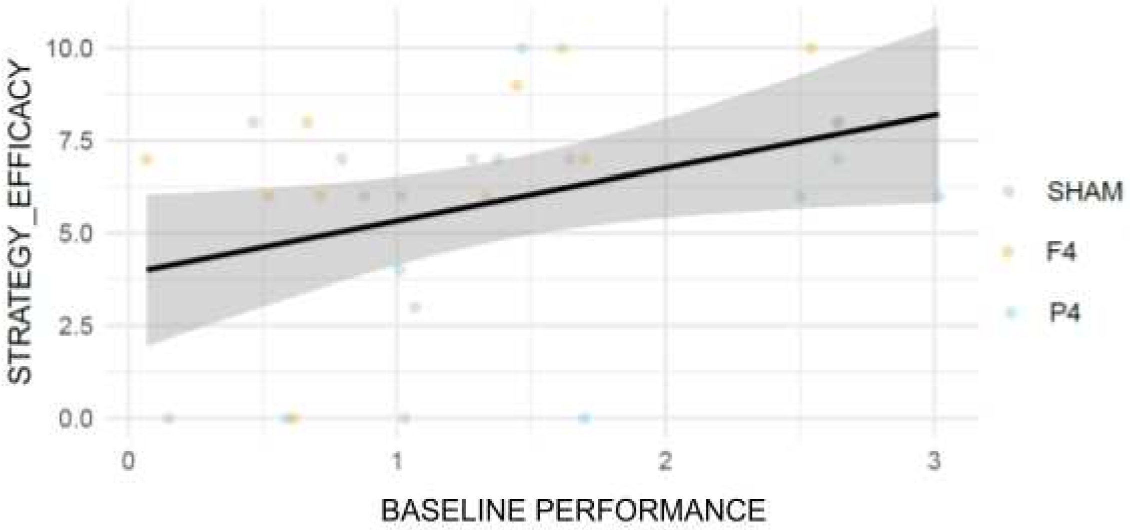
3.3 Interaction between tDCS, performance, and individual differences

The objective of this section is to examine the impact of strategy, as an individual difference, on task performance. To this end, we considered only those participants who reported using a strategy via the "strategy use" questionnaire (see chapter 2.3 Questionnaires). In particular, we employed the response to this item, "How effective was the strategy?," as a self estimated strategy efficacy measure. Thus this analysis included 35 participants in total, 13 in the P4 group, 10 in the F4 group and 16 in the sham group (see table 3.1).

3.3.1 Self perceived strategy among the groups.

An ANOVA was conducted to ascertain whether there were differences in self-perceived efficacy between the three stimulation groups. The data indicated that there were no differences between groups on perceived efficacy (F(2/24) = 1.10, p = .35).

However, data shown a relation between the perceived efficacy and the performance at the baseline (F(1/24) = 2.24, p = .007), as illustrated in chart 3.x (see also table 3.4 in the supplementary materials).



graph 3.4
the relation between the perceived strategy efficacy and the baseline performance appears to be linear and positive.

3.3.2 Strategy as a mediator of the effect of stimulation on performance

A linear mixed model was employed to predict performance (D') with strategy, stimulation, and their interaction as fixed factors, with baseline performance, age, and education as covariates. Participant ID was also included as a random factor. The results indicate a significant effect of stimulation (F(2,21)=3.68, p=0.043) , self-perceived strategy efficacy h (F(1/21) = 15.32, p = .0008), and baseline performance (F(1/21) = 11.24, p = .003). However, follow-up pairwise comparison after adjusting for the effect of baseline performance and strategy efficacy, did not reveal any significant difference between SHAM, F4, or P4 groups.

3.3.3 Percentage of Hits and strategy efficacy.

A further linear mix model was conducted between the percentage of hits and self-reported strategy efficacy in order to assess whether self-perceived efficacy moderates the relation between performance and stimulation. The results indicated a statistically significant correlation (F(1/23) = 9.14, p=.005) between pH and the reported strategy self-efficacy. Additionally, a stimulation effect (*F*(2/23)= 5.13, p=.013) and a baseline effect (F(1/23) = 6.05, p=.022) were identified.

3.3.4 Hits rates, strategy efficacy and timing (considering the blocks).

The objective of this further analysis was to determine whether the strategy had an effect early on in the session, rather than on overall performance; to this purpose, a linear mixed model was employed. The results showed no interaction between blocks and perceived strategy efficacy (F(2,567)=0.53, p=0.59). However we also found an effect of stimulation (F(1,23)=8.80, p=.0014), baseline F(1,23)=29.89, p<.0001) of block (F(1,567=13.5, p=.0003), of perceived strategy efficacy (F(1,23)=36.36, p<.0001).

Table 3.3

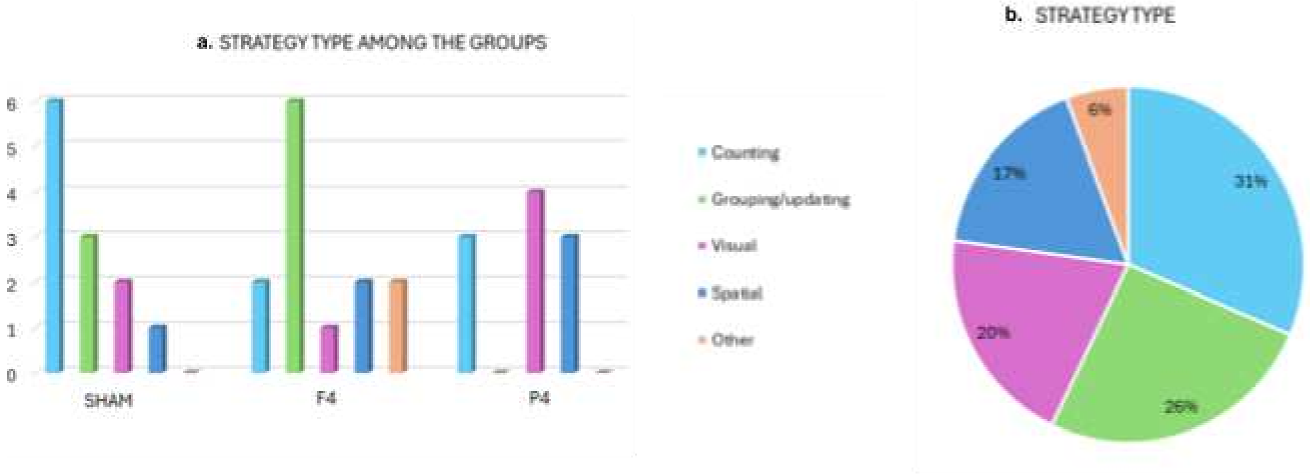
	numDF	denDF	F-value	p-value
intercept	1	567	542.44	<.0001
stimulation	2	23	8.80	0.0014
block	1	567	13.56	0.0003
Self perceived strategy efficacy	1	23	36.36	<.0001
Baseline performance	1	23	29.89	<.0001
Age	1	23	1.15	0.30
Education	1	23	1.90	0.17
Stimulation group : block	2	567	0.53	0.59

A follow-up pair-wise comparison using the Tukey method was then conducted for the stimulation groups, but no significant differences were found: between Sham and F4 (t(567) = 0.04, p = 0.10, estimate = .0008, SE = .01), between Sham and P4 (t(567) = 0.92, p = 0.62, estimate = .015, SE = .016) and finally between F4 and P4 (t(567) = 0.85, p = 0.65, estimate = .013, SE = .015).

These findings suggest that while strategy efficacy overall was significant it did not predict changes in performance over time within the session.

3.3.5 Type of strategy.

In the strategy questionnaire, participants were asked to provide a description of the strategy they used, if any. Of the 47 subjects, 35 claimed to have used a strategy, representing 76.1% of the sample. Conversely, 11 participants claimed to not have used a strategy, representing 23.8% of the sample. This information is presented in Table 3.4 in the supplementary material. The categorization proposed by Laine (see section on strategies 1.4) was adapted to align with the experimental context (Laine et al., 2018). The 11 categories proposed by Laine were reduced and modified to reflect the strategies observed in the data. This was done because some strategies appeared more frequently than others and some did not appear at all. This occurred because the n-back task used by Laine was verbal, while the task used in the current study was visuospatial. Consequently, the strategies reported by the participants were categorized into five distinct types: counting, grouping/updating, visual, spatial, and other. The "counting" strategy entailed responses such as "I counted" or "I mentally counted." Responses such as "I attempted to visualize the sequence of the three cloves and modified it as the new clove was introduced to facilitate comparison" or "I memorized the cloves in groups of three, comparing each group of three with the next" were classified as "grouping/updating." Responses such as "I constructed a visual image of the three blocks" were included in the "visual" category. Responses such as "I attempted to recall the triangles by quadrants, so that the number was four, not eight, and then proceeded to the specific eighth" and "I maintained a count and attempted to visualize the positions as a spinning wheel, disregarding those that had not illuminated" were categorized as "spatial." All responses that could not be attributed to one of the previously defined categories were classified as "other." This included responses such as "I tried ignoring irrelevant stimuli from time to time, and relying on sensory memory, trying to see the whole circle to detect changes and not focusing on triangles." As illustrated in Image 3.x, the most frequently utilized strategy was "counting", representing 31% of the total.



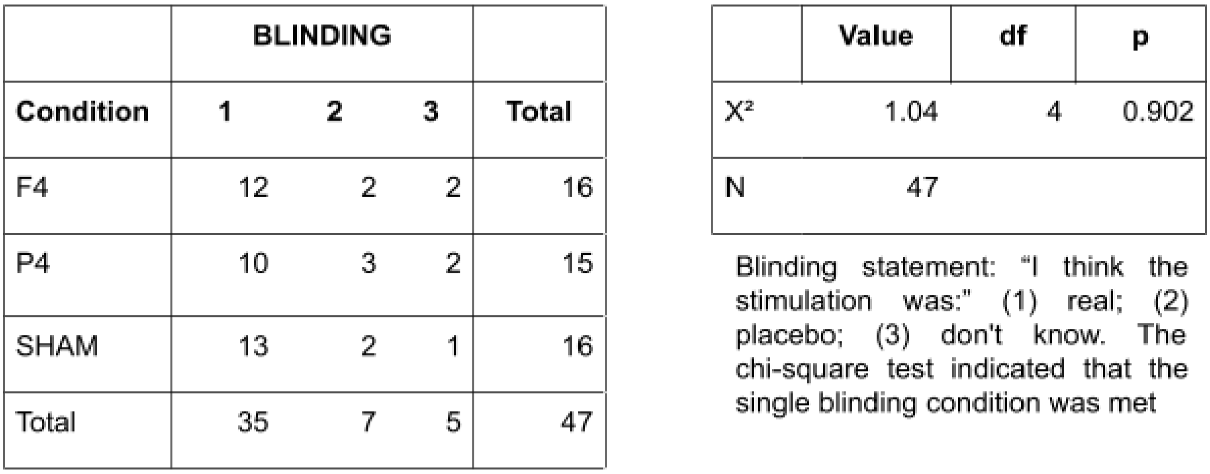
graph 3.5
panel a shows the distribution of strategy types among the sham, p4, or f4 conditions. Panel b represents the distribution of strategy types across all stimulation groups.

3.4. Feedback on tDCS

3.4.1 Blinding condition

To ensure that the single-blinding condition was met, we asked in the sensation questionnaire which protocol (active or sham) they had been exposed to. The answer could be "real", "placebo", or "don't know". Chi-square analysis indicated that the condition was met (X^2 (4) = 1.04, p = 0.902), (see table 3.3).

Table 3.5



	BLINDING			
Condition	**1**	**2**	**3**	**Total**
F4	12	2	2	16
P4	10	3	2	15
SHAM	13	2	1	16
Total	35	7	5	47

	Value	df	p
X^2	1.04	4	0.902
N	47		

Blinding statement: “I think the stimulation was:” (1) real; (2) placebo; (3) don't know. The chi-square test indicated that the single blinding condition was met

3.4.2 Sensation and side effects.

At the end of each session, participants were asked to fill out a survey form called **stimulation-related sensation detection module (TES).** This questionnaire is used to monitor sensation and potential side effects elicited by the stimulation. It was completed after the stimulation and after the TLX questionnaire. The primary objective of the questionnaire was to ascertain whether the participants experienced sensations such as warmth, tingling, pain, burning, itchy, metallic taste, or fatigue. Additionally, we sought to record the duration of these sensations and their onset. Furthermore, we inquired about the impact of these sensations on performance. In the final session, participants were asked whether they had noticed the placebo session, allowing us to ascertain whether the blinding condition had been maintained.The following table presents the principal findings. In addition to those below, one participant in the sham group reported "clouded mind", and two participants, one in the F4 condition and the other in the P4 condition reported headaches..

Table 3.6

		ITCHING					PAIN				
Group		**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
F4	Count	7	4	4	1	0	8	6	1	0	1
	%	43.7 %	25 %	25 %	6.25%	0%	50 %	37.5%	6.25 %	0 %	6.25 %
P4	Count	6	8	1	0	0	9	4	1	1	0
	%	40 %	53.2 %	6.67 %	0 %	0%	60%	26.7 %	6.67 %	6.67 %	0 %
SHAM	Count	7	6	1	0	0	12	2	0	0	0
	%	50 %	42.8 %	7.13 %	0 %	0%	85.7 %	14.3 %	0 %	0 %	0 %
Total	Count	20	18	6	1	0	29	12	2	1	1
	%	44.3%	40 %	13.2 %	2.21 %	0%	64.3 %	26.7 %	4.43 %	2.21 %	2.21 %

		FATIGUE					BURNING				
Group		1	2	3	4	5	**1**	**2**	**3**	**4**	**5**
F4	Count	12	4	0	0	0	3	8	4	1	0
	%	75 %	25 %	0 %	0 %	0 %	18.7%	50%	25%	6.25%	%0
P4	Count	11	3	1	0	0	7	4	0	3	1
	%	73.2%	20%	6.67%	0 %	0 %	46.7%	26.7%	0%	20%	6.67%
SHAM	Count	7	6	1	0	0	6	5	0	3	0
	%	50%	42.9%	7.13 %	0 %	0 %	42.9%	35.7%	0%	21.4%	0%
Total	Count	30	13	2	0	0	16	17	4	7	1
	%	66.7%	28.9%	4.43 %	0 %	0 %	35.6%	37.8%	8.89%	15.6%	2.21%

		METALLIC FLAVOUR					TINGLING				
Group		1	2	3	4	5	1	2	3	4	5
F4	Count	15	1	0	0	0	1	7	5	3	0
	%	95.7%	6.25%	0%	0%	0%	6.25%	43.7%	31.2%	18.7%	0%
P4	Count	15	0	0	0	0	5	4	3	3	0
	%	100%	0%	0%	0%	0%	33.2%	26.67%	20%	20%	0%
SHAM	Count	14	0	0	0	0	5	5	4	0	0
	%	100%	0%	0%	0%	0%	35.6%	35.6%	28.6%	0%	0%
Total	Count	44	1	0	0	0	11	16	12	6	0
	%	97.8%	2.1%	0%	0%	0%	24.3%	35.6%	26.7%	13.2%	0%

		HEAT				
Group		**1**	**2**	**3**	**4**	**5**
F4	Count	8	5	2	1	0
	%	50%	31.2%	12.5%	6.25%	0%
P4	Count	7	7	1	0	0
	%	46.7%	46.7%	6.67%	0%	0%
SHAM	Count	4	7	1	1	1
	%	28.6%	50%	7.13%	7.13%	7.13%
Total	Count	19	19	4	2	1
	%	42.1%	42.1%	8.89%	4.43%	2.21%

The contingency table presented is a summary of the participants' reports of sensations. Based on the following scale, participants were asked to rate the intensity of their feelings:

1= none
2= slight
3= moderate
4= fairly
5= very

4. Discussion

The objective of this thesis was to examine the impact of non-invasive stimulation in two distinct protocols and individual differences, such as strategy, on a working memory task, and their interaction with the brain region targeted by the stimulation. The study involved three tDCS stimulation protocols: placebo, when no stimulation was administered, F4, targeting the right dorso-lateral prefrontal cortex, and P4, targeting the right posterior parietal cortex. Individual differences, such as strategy, were recorded through questionnaires, as they could potentially interact with the tDCS protocol and modulate performance.

The results of the study indicate that stimulation alone had no significant effect on performance, in line with previous research (for a review see Horvath et al., 2015; Jantz et al., 2016; Narmashiri & Akbari, 2023). However, it was observed that the group stimulated on the right frontal cortex (F4) obtained a significantly lower percentage of hits. This result remained consistent even after accounting for individual differences in performance at the beginning of the experiment, by including baseline performance as a covariate. Given that no significant differences were observed in other performance measures, such as reaction time or D', further experiments are required to elucidate this result.

When taking into account individual differences, operationalised as strategy use, we found a significant correlation between the effectiveness of the self-reported strategy and performance in terms of D' and hit rate. This indicates that those who employed a strategy and reported high levels of effectiveness also demonstrated high levels of performance in recognizing the target.

Moreover, no interaction was observed between self-perceived strategy, timing in terms of blocks, and hit rates. This indicates that, despite the overall significance of self-perceived strategy, it did not predict performance changes over time (within the session). One potential explanation for this result is that a better performance in the task may have driven participants to be more confident in reporting their strategy as successful, even in the absence of feedback during the task or after.

Furthermore, while strategy efficacy did predict performance, it did not moderate the effect of stimulation on performance, meaning that one type of stimulation was not more likely than other to support efficient strategy use. It is possible that this is related to the age of the population considered (young adults). As previously stated in the introduction, the most significant effects of strategies and tDCS on performance were observed in older adults with low capacity (Assecondi et al., 2022). It appears that these two components may provide a compensatory effect on performance, as they tend to experience greater difficulty in employing strategies (Dunlosky & Kane, 2007). In this case, given that the sample consisted of young people, it is possible that they were already proficient at employing the adopted strategies, thus negating the compensatory effect of stimulation. We did not observe the magnification effects that were reported by Lövdén (2012), as the session was single and this effect is observable in multi-session studies.

Collectively, these findings suggest that individual differences should be considered when conducting working memory studies, with the potential to benefit individuals in performance on WM tasks such as n-back. With regard to stimulation, the results of this analysis indicate that there is no clear benefit to one stimulation protocol over another. This is in line with the findings of Martin (2023), but further investigation is necessary, especially in populations where brain activity is more distributed across the brain, such as older adults.

One potential limitation of this thesis is the administration of the strategy questionnaire at a later time, after the third session, although they were asked to answer on specific sessions. However, based on the results found by Bailey (2011), it can be assumed that the use of the strategy commenced from the first blocks of the experiment. The absence of a discernible impact on performance in response to tDCS aligns with the disparate outcomes observed in the extant literature. One contributing factor to this variability is the high degree of heterogeneity among protocols in terms of current intensity, duration of stimulation, position and size of electrodes, and so forth (Narmashiri & Akbari, 2023). Our study aimed to further explore these parameters.

Furthermore, a potential explanation for the lack of results for the frontal configuration could be found in the single-session design that was employed. In fact, some studies (e.g. Richmond et al., 2014) had found significant effects of tDCS on performance, but their experimental designs involved multiple session training. These could suggest that tDCS may require more than one session to enhance performance.

One interesting finding that emerged from the data was the predictive effect observed at baseline on performance. This may provide an explanation for the lack of significant effects, despite the absence of significant differences between the groups with regard to individual variables. While we accounted for performance and baseline, it is possible that other baseline characteristics have an effect on tDCS effectiveness: these include, for example, individual cortical excitability, which has not been measured in this study. Based on these considerations, we can hypothesize that there may be other individual variables, which we have not yet identified or examined, that could have predicted and influenced the performance.Further analysis is necessary to substantiate this hypothesis.

Working memory is more than a mere repository of sensory information; it is an essential cognitive function for everyday life. The thesis aimed to explore potential support for this special type of memory. It can be concluded that individual differences may assist participants in the task, and therefore warrant further investigation, while the two protocols tested do not demonstrate any particular benefits compared to placebo.

4.1 Further Directions

Given the importance of working memory, further analysis and studies are needed.

Further investigation is required into the role of strategy in helping subjects during performance and whether there are other individual differences that may facilitate the working memory task. It would also be interesting to investigate the older adults population and compare this population with the young. Indeed, as previously stated, older adults could potentially benefit more from the strategic use and implementation of techniques that would result in a compensatory effect, thereby achieving similar performance to that achieved by the younger population. Older adults could also find one electrode configuration more beneficial than the other, given the changes in brain activity distribution with age. Additionally, individual differences could be leveraged to enhance the effectiveness of cognitive training. In fact, based on the ATI model, designing these treatments by tailoring them to the individual could lead to enhanced performance. One potential approach is to enhance motivation for the training, encouraging participants to become more engaged and purposeful in their treatment (e.g. Mohammed et al., 2017). This could indirectly enhance the effectiveness of the training, for instance by reducing dropout rates.

Another important aspect to consider is to make these working memory tasks more ecologically valid. Although the objective of this study is to investigate working memory without the influence of artifacts, the proposed stimuli are challenging to find in everyday life. Therefore, it is necessary to consider a task that can utilize items and paradigms similar to those encountered in everyday life. One potential avenue for exploration is the "gamification" of n-back. In such instances, the n-back item could be presented as an everyday object, and the game could represent a real-life situation in which working memory is employed (for an example see Christian Scharinger et al., 2023).

Finally, further studies are required to identify the most effective tDCS protocols, which may involve a review of the existing literature.

4.2 Limitation Of The Study

As previously stated, a potential limitation of this thesis is the administration of the strategy questionnaire at a later time, after the third session. However, respondents were asked to indicate whether the strategy had been employed from the first, second, or last session. Moreover, the absence of a pre- and post-treatment measure precluded the measurement of any transfer effects.

Another aspect to consider is the absence of a measure or task that investigated participants' performance before treatment. Such a measure would have been important to determine the baseline performance of each participant.

Moreover, young adults are likely to have limited potential for improvement. This can be attributed to the fact that higher performers, often young adults, already possess a proficiency level that makes additional gains from interventions less significant.

Studies have indicated that compensation strategies tend to reduce the performance gap between high and low performers, especially in tasks where higher performers are already adept (e.g. Tagliabue et al., 2022). Consequently, young adults, who are typically higher performers, may not exhibit substantial improvement with training since they are near the peak of their cognitive capabilities.

In addition, young adults experience less pronounced shifts in cognitive functions compared to older adults. Cognitive functions, such as working memory, tend to be more stable in younger populations. Research has demonstrated that reaction times and accuracy in working memory tasks decline earlier in older adults, beginning around age 35 for reaction times and age 60 for accuracy (Zarantonello et al., 2020). Furthermore, older adults face more significant challenges in employing effective strategies for cognitive tasks, which may result in greater variability and potential for improvement with interventions. Conversely, young adults are more likely to develop spontaneous strategies, which limits the scope for noticeable improvement during cognitive training.

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6. Supplemental Material

Table 3.4

STRATEGY USE

stimulation		Yes	No	Total
F4	Count	13	3	16
	%	81.25%	18.75%	100.00%
P4	Count	10	4	14
	%	71.43%	28.57%	100.00%
SHAM	Count	12	4	16
	%	75.00%	25.00%	100.00%
Total	Count	35	11	46
	%	76.09%	23.91%	100.00%

Table 3.2

	df	Sum Sq	Mean Sq	F -VALUE	Pr(>F)
Group of stimulation	2	16.37	8.17	1.10	0.350227
Baseline performance	1	61.83	61.88	8.28	0.008242**
Age	1	16.70	16.67	2.24	0.147776
Education	1	2.62	2.62	0.34	0.558720
Residual	24	179.12	7.45		

Significant codes: “**” = 0.01

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