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THE USE OF TRANSCRANIAL DIRECT CURRENT STIMULATION AND COMPUTER-ASSISTED TRAINING PROGRAMS IN COGNITIVE AND AFFECTIVE REHABILITATION IN POST-STROKE PATIENTS

PH.D. THESIS

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ABBREVIATIONS:

ACE: Addenbrooke's Cognitive Examination

BDI: Beck Depression Inventory

BF_{10} / BFIncl: Bayes Factor (null vs. alternative hypothesis / inclusion)

CBTT: Corsi Block Tapping Task

CCT: Computerised Cognitive Training

CE: Central Executive

CEN: Central Executive Network

CON: Cingulo-Opercular Network

CR: Cognitive Rehabilitation

DAN: Dorsal Attention Network

DLPFC: Dorsolateral Prefrontal Cortex

DSTB: Digit Span Task Backward

DSTF: Digit Span Task Forward

EF: Executive Functions

EEG: Electroencephalography

FPN: Fronto-Parietal Network

HAM-D: Hamilton Depression Rating Scale

ICC: Intra-Class Correlation

ICCT: Inhibitory Control Cognitive Training

ICH / IS: Intracerebral Hemorrhage / Ischemic Stroke

LMEM: Linear Mixed Effects Model

LST: Listening Span Task

MCID: Minimum Clinically Important Difference

MMSE: Mini-Mental State Examination

NART: National Adult Reading Test

PFC: Prefrontal Cortex

PICOS: Population, Intervention, Comparison, Outcome, Study Design

PPC: Posterior Parietal Cortex

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: International Prospective Register of Systematic Reviews

PSD: Post-Stroke Depression

PSA: Post-Stroke Anxiety

RCT: Randomised Controlled Trial **SN**: Salience Network

STAI-S: State-Trait Anxiety Inventory – State

STAI-T: State-Trait Anxiety Inventory – Trait

TMT-A/B: Trail Making Test Part A / B

tDCS: Transcranial Direct Current Stimulation

VAN: Ventral Attention Network

VSTF: Visual Span Task Forward

WM: Working Memory

WMN: Working Memory Network

WCST: Wisconsin Card Sorting Test

INTRODUCTION

This dissertation aims to investigate the applicability of transcranial direct current stimulation (tDCS) in combination with computer-assisted cognitive training (CCT) programs in the enhancement of executive function (EF) and emotion regulation in post-stroke patients. The dissertation focuses on three main areas: working memory (WM), inhibition, and mood, particularly the improvement of depressive and anxiety symptoms. The thesis also aims to highlight the need to consider a network-based approach in addition to the traditional modular approach to rehabilitation, which may allow the introduction of new, experimental therapeutic procedures.

Executive Functions after Stroke

Stroke is a neurological condition caused by a blockage (ischaemic stroke) or haemorrhage (haemorrhagic stroke) of the blood supply to the brain. The daily lives of stroke survivors are significantly affected, depending on the severity of the lesion, timing of treatment and rehabilitation (Cameron et al., 2022; Grysiewicz et al., 2008). Physical and cognitive impairments are common, and loss of mobility often alters daily functioning. Stroke is often followed by difficulty in performing daily activities, memory complaints, language dysfunction, depression, anxiety and executive dysfunction, highlighting the need to understand the neural underpinnings of these and their relevance for rehabilitation (Espuela et al., 2020; Guidetti et al., 2022; Magwood et al., 2020).

In the last decades, cognitive neuroscience has undergone a significant paradigm shift, moving from a classical modular approach to a more network-based approach. Whereas cognitive functions were previously associated with discrete brain regions, it is now widely accepted that higher-order human cognition arises from the coordinated operation of large-scale, dynamic neural networks (Bassett & Sporns, 2017). In addition, EFs and emotion regulation are integrated into a unified system of cognitive control (Dotson et al., 2020; Friedman & Robbins, 2022; Zelazo et al., 2024). According to Friedman and Robbins (2022), ‘EFs’ and ‘cognitive control’ essentially refer to the same set of basic cognitive abilities. However, the term ‘EF’ has become more widely used in clinical and rehabilitation contexts. In this work, I emphasise the characteristics of both concepts, with a particular focus on the role of cognitive control in relation to emotion regulation. In a broad sense, EFs are higher-order

processes that support goal-directed, flexible and adaptive behaviour in response to internal or external demands (Menon & D'Esposito, 2022).

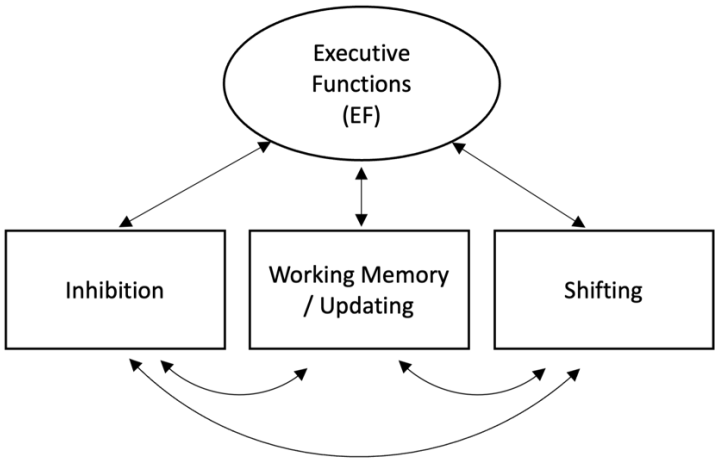


Figure 1: Miyake and Friedmann's (2000) model of executive functions, with three main components: inhibition, working memory (updating) and switching. The components form an extensive system in which the separate parts are closely interconnected (Self-Made Illustration)

Miyake and Friedman's (2000) widely accepted model divides EF into three distinct but interrelated core components: WM (updating), inhibition and shifting (Miyake et al., 2000) (Figure 1). WM refers to the ability to store and manipulate information for short periods and is essential for reasoning, learning, and understanding. Inhibitory control suppresses automatic, impulsive, or irrelevant responses, helping goal-directed behaviour. Shifting (or cognitive flexibility) involves the ability to shift attention between tasks or mental sets, to adapt to changing demands, and to consider multiple perspectives. Subsequent research by Friedman and colleagues (2022) has confirmed that these components form a common EF factor, which is the unified ability to maintain goals and manage behavior actively. Of the three basic EFs, WM and inhibitory control are intensively studied, mainly because they are easier to quantify with standardised neuropsychological tasks and are directly related to everyday cognitive performance (Best & Miller, 2010; Miyake et al., 2000). Therefore, we focused on these two components because of their close association with post-stroke cognitive impairment.

WM has a significant role in EFs as it manages the temporary storage of information and its manipulation. Its efficiency is related to cognitive control. For instance, with individuals with greater WM capacity typically performing better on tasks related to cognitive control (Engle, 2010; Redick, 2014). According to the classic model of Baddeley and Hitch (1974),

WM includes the phonological loop (storage of verbal information), the visuospatial sketch space (association of visual information), the central executive (CE), and the episodic buffer (Baddeley, 1974, 2000), which coordinates and integrates information across modalities (Figure 2).

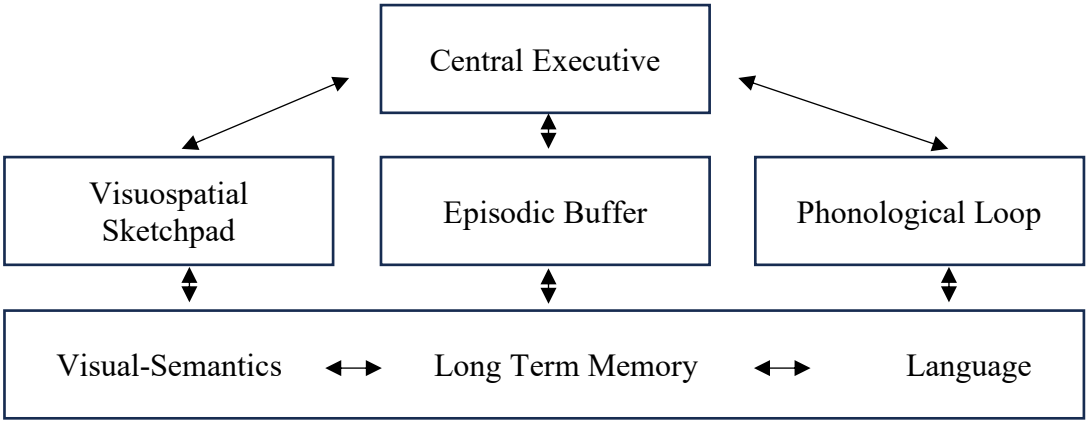


Figure 2: Baddeley's (2000) classic WM model. WM contributes to the performance of every day activities by simultaneously storing more sensory information and retaining and manipulating incoming information (Self-Made Illustration)

Inhibition plays a central role in helping individuals suppress automatic, impulsive or irrelevant responses, which is key to maintaining goal-directed behaviour (Werner et al., 2022). Post-stroke inhibition deficits can result in increased distraction, perseveration or emotional inhibition, further complicating the recovery process and reintegration into daily life (Kubis, 2016). These manifestations highlight the importance of assessing and supporting inhibition as an essential component of executive functioning. Impairment of EF is often observed after stroke and these deficits can significantly impede rehabilitation and daily functioning (Rivella & Viterbori, 2021). For example, the patient may repeat a task already performed due to poor WM or distract others due to reduced inhibitory control (Fitri et al., 2020). Understanding EFs and their neural background is essential not only for theoretical models of cognition, but also for designing and targeting effective cognitive rehabilitation strategies. For example, the prefrontal cortex - especially the dorsolateral prefrontal cortex (DLPFC) - plays a key role in EFs, its functioning depending on the integration of distributed cortical and subcortical networks (Witt et al., 2021).

Executive Functions: Frontoparietal Network

In recent years, the organizing principle of cognitive control has been further refined by network-based and differentiated psychometric interpretations of EFs. In addition, there is a growing emphasis on distinguishing between “cool” (cognitive-neutral) and “hot” (affective-motivational) dimensions of executive functioning, which allows for a more complex, transdiagnostic interpretation of control processes (Menon & D’Esposito, 2022; Tully & Niendam, 2014; Zelazo et al., 2024). This network-based approach also facilitates the design of targeted neurorehabilitation programmes that can specifically target different subsystems of the prefrontal system. From a neuroanatomical point of view, the basis of cognitive control is provided by the prefrontal cortex (PFC). According to Menon and D'Esposito (2022), the PFC does not function alone, but forms a system with at least six functionally distinct but closely cooperating larger brain networks:

1. Default Mode Network (DMN): linked to resting state, self-reflection, “mind wandering”;

2. Salience Network (SN): responsible for identifying relevant stimuli and shifting attention;

3. Dorsal Attention Network (DAN): maintains goal-directed attention;

4. Ventral Attention Network (VAN): helps process unexpected, attention-grabbing stimuli;

5. Cingulo-Opercular Network (CON): provides sustained attentional control;

6. Fronto-Parietal Network (FPN): central to cognitive control and the regulation of goal-directed behaviour.

For EFs and cognitive control, it seems reasonable to investigate the function of the FPN, in particular involving the DLPFC, the anterior cingulate cortex (ACC) and the posterior parietal regions (Menon & D’Esposito, 2022). The „DLPFC-dominated” areas are mainly engaged in rule application, goal planning and decision making, while parietal areas may play a role in maintaining (visuospatial) WM and attentional focus (Curtis, 2006). A characteristic feature of the FPN is that it changes its functional connections with other neural networks in a dynamic and flexible way, depending on the cognitive function that the person is actively using (Schimmelpfennig et al., 2023; Thompson et al., 2016).

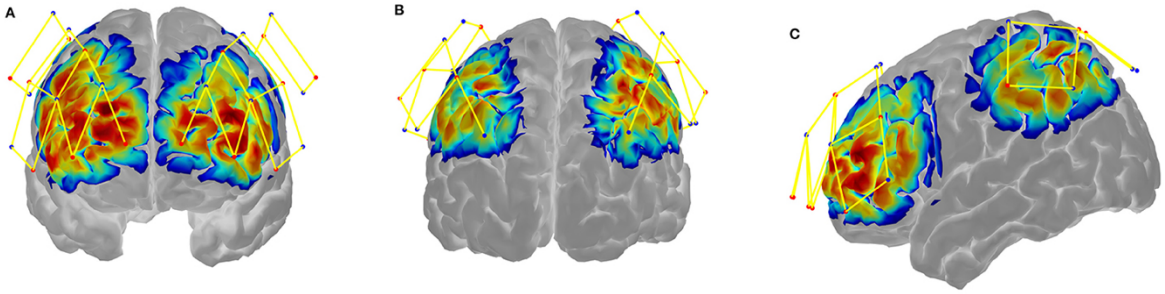


Figure 3: The Fronto-parietal Network (FPN) according to Chenot and colleagues (2021). The image shows three views of the FPN (Frontal (A), Parietal (B) and Lateral (C)), highlighting its activation in the dorsolateral prefrontal and posterior parietal cortices, which are central to cognitive control and executive functions.

This ability can be applied in cognitive rehabilitation through transfer effects, which allow the transfer of relational patterns established during skilled tasks to new tasks, facilitating learning and solving new situations (Sala et al., 2019). In addition, the FPN also plays an important role in affective regulation. In particular, the DLPFC and related structures are directly involved in the reevaluation of the cognitive content of negative affective states such as anxiety and depression (Tan et al., 2021). A number of neuropsychiatric studies have shown that underactivity of the FPN is associated with depressive symptoms, as dysfunction of the network reduces cognitive and emotional resilience, which may contribute to the long-term persistence of mood disorders (Brzezicka, 2013; Schultz et al., 2018; Tan et al., 2021). In both post-stroke depression (PSD) and anxiety (PSA), dysfunction of the integrity of the fronto-parietal network may often play a signicifant role.

It is important to note that the term Central Executive Network (CEN) and WM Network (WMN) is also frequently used in the literature to refer to the same regions and functions as FPN basically. As pointed out by Witt et al. (2021), FPN, CEN and WMN are highly overlapping, often used interchangeably, network labels that all refer to frontoparietal brain activity related to EFs and WM. Their recent meta-analysis found that the average activation maps of these networks show a correlation of more than.8 with the ‘overall executive control’ network, suggesting a strong topographic correspondence. In the present dissertation, FPN is used due to anatomical characteristics that contribute to the location of stimulation in tDCS,

during rehabilitation. This paradigm is supported by the work of Lugtmeijer and colleagues (2021), who identified the FPN as a key neural network for WM abnormalities after stroke.

Rehabilitation after Stroke

The primary goal of post-stroke rehabilitation is to improve patients' recovery and quality of life through a combination of traditional and innovative techniques (Belagaje, 2017). Conventional methods typically include speech therapy, physical therapy and occupational therapy, which focus on restoring independence of language, motor function and activities of daily living (Kelley & Borazanci, 2009). Over the past two decades, cognitive rehabilitation (CR) has developed significantly with the integration of new technologies. Non-invasive brain stimulation methods such as tDCS and transcranial magnetic stimulation (TMS) have shown promising results neuroplasticity and supporting cognitive and motor recovery after stroke (Antal & Paulus, 2012; Stinear et al., 2020; Webster et al., 2006). Likewise, CCT offers accessible and personalized programs designed to improve memory, attention and EFs (Baltaduonienė et al., 2018; Draaisma et al., 2020). These programs can be used alone or in combination with brain stimulation to increase the effectiveness of rehabilitation (Zhang et al., 2019). In clinical practice, among non-invasive brain stimulation techniques, tDCS shows promising results in post-stroke recovery by enhancing neuroplasticity and supporting cognitive and motor function (Martin et al., 2014; Webster et al., 2006). CCT has also become increasingly popular due to its accessibility, affordability and adaptability to individual needs, which also makes home rehabilitation more feasible (Van de Ven et al., 2016; Zhou et al., 2022).

Enhancing Working Memory after Stroke

Computerised Cognitive Training Programmes

CCT and tDCS have become important tools for CR after stroke. Both are non-invasive techniques aimed at supporting neural recovery, although their mechanisms and applications differ. Over the past two decades, a growing body of research evidence has shown their ability to improve a variety of cognitive domains, including EFs (Berryhill & Martin, 2018a; Zhang et al., 2019). However, results are sometimes conflicting, CCT is generally considered more reliable for targeting WM functions, for example, especially because it offers structured, adaptive training protocols tailored to individual needs (Åkerlund et al., 2013; Ohn et al., 2008).

CCT interventions are delivered via computer and aim to develop specific cognitive skills through repetitive, structured exercises. Compared to traditional tasks (e.g. paper-pencil tasks), CCT offers greater accuracy, objectivity, allowing therapists to monitor progress and adjust task difficulty to individual level of performance (Hu et al., 2021). This flexibility supports personalized rehabilitation plans and can improve motivation and compliance. Furthermore, because many CCT protocols are designed based on theoretical models, they are often aligned with the basic components of executive functioning.

In the case of WM, it is the update functions that are most often targeted (Xin et al., 2014). One of the most commonly used WM tasks is the N-back task, which requires participants to continuously monitor and update items in WM (Redick & Lindsey, 2013). Although originally designed to train updating, complex N-back tasks can involve inhibiting and switching processes, especially when distractions are introduced or task rules change. This cross-functional overlap allows for near (improvement occurs in a given function) and far transfer effects (improvement also occurs in related functions), whereby training in one domain can enhance performance in related, untrained tasks (Alloway et al., 2013; Xin et al., 2014; Zakariás et al., 2018). Within WM training, the executive components interact dynamically with each other. Studies by Scharinger et al. (2015) and Kim et al. (2017) show that updating and inhibition are closely related processes (Kim et al., 2017; Scharinger et al., 2015). Neuroimaging studies further support the idea that these effects are mediated by large-scale frontoparietal networks involving both prefrontal and parietal regions (Thompson et al., 2016).

The N-back task remains the standard for WM-focused rehabilitation and shows promising results in stroke populations (Oguh et al., 2014); however, alternative training approaches may deserve more attention. Inhibitory control, although essential for the regulation of attention, behavior, and emotional responses, has received relatively little attention in CCT research, particularly as a WM training task. Inhibition tasks such as the Flanker, Go/No-Go or Stroop tests are potential testing tools for inhibitory functions, but are rarely used systematically in clinical settings as training tasks (Kim et al., 2017; Stroop, 1935; van Geest & Engelbregt, 2022). This is an area to be explored in rehabilitation, both because its functioning as a rehabilitation tool is also poorly researched and because its effects on WM through far transfer effects are not known. Finally, the exploration of whether inhibition training can support WM subsystems - such as the phonological loop or the visuospatial sketchpad - remains an open question. Addressing this, may broaden the applicability of CCT and improve outcomes for stroke survivors with different cognitive profiles. For example, can training inhibitory functions

improve performance on WM tasks when the patient is fundamentally poor at performing N-back tasks.

In summary, CCT provides a clinically adaptable framework for enhancing cognitive functions after stroke. Although current WM protocols are primarily focused on updating, expanding research and clinical practice with a greater emphasis on inhibition could enrich the scope and impact of cognitive rehabilitation. Building on this, besides CCT, tDCS can offer a complementary neuromodulation approach - one that neurophysiologically targets the same cognitive systems and is particularly promising when combined with behavioural interventions such as CCT.

Transcranial Direct Current Stimulation

tDCS is a non-invasive neuromodulation technique that modulates synaptic activity with weak electrical currents (e.g. 2 mA), affecting neuronal excitability via sodium-calcium channels and NMDA receptors (Lefaucheur et al., 2017; Zaehle et al., 2011). Although its exact mechanisms remain partly unclear, tDCS has been shown to have potential in enhancing cognitive function by modulating excitatory or inhibitory effects depending on the stimulation parameters (Draaisma et al., 2020). Stimulation typically targets specific regions; for example, occipital areas for visual processing, and the DLPFC for WM (Berryhill & Martin, 2018). Although stimulation to WM often focuses on the DLPFC, recent evidence suggests that WM relies on broader frontoparietal areas. Studies highlight the involvement of the DLPFC and posterior parietal cortex (PPC) within the FPN (Chai et al., 2018; Kim et al., 2017). This finding may be significant in stroke, where network integrity is often disrupted, possibly reducing sensitivity to stimulation. While tDCS has improved WM in healthy populations, results in stroke patients are mixed - possibly due to the integrative nature of EFs requiring intact large-scale connectivity (Lugtmeijer et al., 2021).

Recent research suggests that network-based approaches, such as bilateral tDCS (e.g. DLPFC + PPC), may lead to more robust WM improvements (Nissim et al., 2019). However, such approaches remain rare, particularly in post-stroke populations; despite the high prevalence and importance of WM deficits for both cognitive and affective recovery. This raises the question of whether stroke-induced damage alters the plasticity or sensitivity of WM support networks. Compared to other areas, such as language (e.g. Broca's Area) or episodic memory, WM and EFs may be more dependent on intact large-scale connectivity and thus more difficult to modulate by localized stimulation alone (Lugtmeijer et al., 2021). Accordingly, it

may be worth considering the application of tDCS stimulation to the DLPFC and an extended brain structure. Such network-based approaches remain rare and, to our knowledge, only the post-stroke WM study by Otstavnon et al. (2024) has specifically targeted FPN using stimulation protocols.

Assesment of Working Memory in Clinical Practice

In order to evaluate the effectiveness of CCT and tDCS interventions targeting WM, it is essential to consider how WM is measured in experimental and clinical settings. Since WM is a complex and multidimensional construct, no single task can capture all of its features. Instead, different cognitive tasks have been developed to assess specific components of WM, such as storage, updating, inhibition and shifting. These tasks also vary in modality (e.g., verbal vs. visuospatial) and complexity. The following section briefly reviews the most widely used WM tasks in the hungarian clinical practice:

a) *Digit Span Task* is a classic WM test in the Wechsler Adult Intelligence Scale (WAIS) and other cognitive assessments. It involves reading a series of digits to the participant, who is then required to recall them in forward or backwards order immediately afterwards (Wechsler, 1944).

b) *Reading/Listening Span Task:* In this test, participants read a series of sentences and are asked to remember the final word of each sentence. The task requires reading comprehension and WM (Daneman & Carpenter, 1980).

c) *Corsi Block-Tapping Task / Visual Span Test* assesses visuospatial WM. Participants watch a sequence of blocks being tapped, and they must then reproduce the sequence by tapping the same blocks in the same order (Corsi, 1972).

d) *Trail Making Test (B)* is primarily used to assess cognitive flexibility; however, it also demands WM as participants connect alternating numbers and letters in sequence (Reitan, 1958).

These allow us to consider several aspects of WM and recognise the importance of addressing cognitive deficits, and providing the necessary support and resources to enhance recovery is essential. However, tailoring rehabilitation programs to individual needs is

challenging but can yield more effective outcomes. Comprehensive assessments are crucial for developing personalised treatment plans, and improvements in cognitive functions.

Post-Stroke Affective Disorders: Depression and Anxiety

Stroke often leads to a notable prevalence of changes in affective factors. In this population, the prevalence of PSD is approximately 30-40%, while PSA is also expected about 20% (Li et al., 2022; Schöttke & Giabbiconi, 2015). Both PSD and PSA harm the patient's quality of life and social environment, including family members and spouses. In addition, PSD and PSA have a high comorbidity rate (Franzén-Dahlin et al., 2006; Wilz & Kalytta, 2008). Over the past few decades, research suggests that rehabilitation, including psychological and psychosocial interventions, can positively influence mood-related factors post-stroke (Gyawali et al., 2023).

After stroke, cognitive enhancement can alleviate frustration and helplessness, which can positively affect mood (Narushima et al., 2003). Completing cognitive tasks can increase self-esteem and motivation, which are key components of depression, while some programs also include relaxation techniques to reduce anxiety. However, engagement with interventions such as CCT may be influenced by factors such as technological literacy and motivation (Golding et al., 2016). CCT and tDCS support mood through different mechanisms: tDCS modulates neural circuits that influence emotional processing (e.g. DLPFC, ACC), while CCT improves mood through engagement, EF training and perceived competence. A transdiagnostic perspective argues that cognitive and emotional symptoms often overlap taking into account the time factors, suggesting the need for integrated treatment protocols (Gellatly & Beck, 2016; Zheng et al., 2024). Despite their potential, few studies have examined CCT and tDCS in an integrated framework for PSA and PSD.

Transcranial Direct Current Stimulation and Computerised Cognitive Training in Modulating Affective Factors After Stroke

Research into the effectiveness of tDCS in the treatment of post-stroke mood disorders has been underway for the past decade, with existing studies reporting promising, albeit variable results. Several studies have reported that tDCS can lead to a significant reduction in depressive symptoms among stroke survivors (e.g. Li et al., 2022). However, there is a lack of randomized controlled trials (RCTs) of sufficient size that focus specifically on anxiety and depression after stroke. For example, the mechanisms underlying the antidepressant effect of tDCS are not yet

fully understood, but are thought to act through modulation of neuronal plasticity and large-scale network connectivity (Nikolin et al., 2023).

Traditionally, tDCS protocols have targeted the DLPFC to reduce depressive symptoms (Wolkenstein & Plewnia, 2013). Results from a meta-analysis by Kaiser et al. (2015) highlight reduced connectivity within the FPN and between the FPN and DAN in depression (Kaiser et al., 2015). Similar network dysfunctions have been identified in anxiety disorders suggesting that mood disorders may arise from broad frontoparietal disorders (Sylvester et al., 2012). In addition, regions involved in WM (e.g. DLPFC, posterior parietal cortex) also support emotion regulation, highlighting their transdiagnostic relevance (Chai et al., 2018). RCTs such as Valiengo and colleagues (2017) support an antidepressant effect of tDCS after stroke, although equivalent studies for anxiety are lacking (Valiengo et al., 2017). The combination of tDCS and CCT is promising but further studies are needed (Cruz Gonzalez et al., 2018).

CCTs also target functions related to the frontoparietal network. While WM updating is frequently practiced, inhibitory control - key to distraction and emotion regulation - receives less attention (Aron, 2007). The Flanker task is a classic method for measuring inhibition by requiring participants to focus on a central stimulus while ignoring conflicting stimuli (van Geest & Engelbregt, 2022). However, as the review of Geest and Engelbergt's (2022) notes, its use as CCT is rare. Although not directly targeting mood, such tasks may improve underlying cognitive processes associated with affective symptoms. In conclusion, the major affective regulation processes involve brain structures mainly associated with the FPN. At the functional level, these are significantly related to cognitive control and EFs, in which inhibitory functions and WM play a prominent role.

Assesment of Depression and Anxiety in Clinical Practice

In addition, the objective measurement of depressive and anxiety symptoms is also an essential factor in clinical work in terms of rehabilitation, as it allows the practitioner to determine the likely degree of affective discrepancy; in Hungarian practice, the following measures are the most commonly used:

a) *Beck Depression Inventory (BDI):* The BDI is a widely used self-report questionnaire that assesses the severity of depression symptoms. It consists of 21 items that measure various aspects of depression, including mood, pessimism, sense of failure, and appetite (Beck et al., 1961).

b) *Hamilton Rating Scale for Depression (HAM-D):* The HAM-D is a clinician-administered interview-based scale used to assess the severity of depressive symptoms. It covers a range of symptoms, including mood, guilt, suicidal thoughts, and weight loss (M. Hamilton, 1960).

c) *Patient Health Questionnaire-9 (PHQ-9):* The PHQ-9 is a brief self-report questionnaire often used in primary care settings. It consists of nine items that correspond to the diagnostic criteria for major depressive disorder. It is easy to administer and score (Spitzer et al., 2006).

d) *Beck Anxiety Inventory (BAI):* The BAI is a widely used self-report questionnaire that assesses the severity of anxiety symptoms. It consists of 21 items measuring various aspects of anxiety, including physical, emotional, and cognitive symptoms (Beck et al., 1988).

e) *Hamilton Anxiety Rating Scale (HAM-A):* The HAM-A is a clinician-administered interview-based scale used to assess the severity of anxiety symptoms. It covers a range of symptoms, including tension, fears, insomnia, and cognitive disturbances (Hamilton, 1959).

f) *State-Trait Anxiety Inventory (STAI):* The STAI is a self-report questionnaire that measures both state anxiety (temporary anxiety related to a specific situation) and trait anxiety (general, long-standing anxiety). It consists of separate scales for state and trait anxiety, each comprising 20 items (Spielberger et al., 1970).

g) *Generalised Anxiety Disorder 7 (GAD-7):* The GAD-7 is a brief self-report questionnaire that is often used in primary care settings. It consists of seven items that assess generalised anxiety disorder symptoms, including restlessness, fatigue, and difficulty concentrating (Spitzer et al., 2006).

SCOPE AND AIM OF THIS WORK

Current literature suggests that both cognitive and affective factors play a significant role in post-stroke rehabilitation. The success of rehabilitation interventions seems to depend on the appropriate matching of therapeutic tools with cognitive and emotional needs understood at the individual level. Several conclusions and questions emerge from the studies reviewed. These may provide a basis for the selection of alternative rehabilitation strategies and the management of cognitive and emotional impairments after stroke:

- Post-stroke cognitive and affective impairments are interconnected, with executive dysfunction, often co-occurring in rehabilitation.

- The FPN plays a signigicant role in both cognitive control and emotion regulation. Damage to this network following stroke may explain the overlap between cognitive deficits and affective disturbances.

- tDCS and CCT offer complementary pathways for rehabilitation: while tDCS modulates cortical excitability, CCT reinforces executive skills like WM. Although most training targets updating (e.g., N-back) functions; however, inhibitory training (e.g., Flanker tasks) may offer similar benefits, and could be an accessible alternative for patients with limited cognitive capacity.

- Despite their potential, both tDCS and CCT remain underutilised when explicitly targeting the FPN or explored synergistic effects between the two modalities among post-stroke patients.

These points raise the question of the effects of stimulating a large-scale cognitive network instead of the DLPFC, which is the primary focus of WM and affective regulation. Furthermore, it is also suggested that a common point for cognitive control and WM may be the enhancement of EF-related inhibitory functions by computer-assisted cognitive enhancement programs, which may offer an alternative to the more "N-back" tasks associated with updating functions. Based on the above, I have formulated the following hypotheses:

- **H1:** Based on the current literature, among the post-stroke rehabilitation tools, CCT is expected to show a more convincing rehabilitation potential compared to tDCS on WM-related measures.
- **H2:** Development of WM functions can be done by training inhibitory functions with Flanker-based inhibitory control training (ICCT).
- **H3:** Stimulation of a more extensive brain network (FPN) will show efficacy for WM and affective regulation.

- **H4:** The combined application of CCT and tDCS improves WM-related functions more effectively than the application of CCT or tDCS alone.
- **H5:** The combined application of CCT and tDCS significantly reduces post-stroke depression and anxiety symptoms compared to the application of CCT or tDCS alone.

In this thesis, I address the issues raised by the literature review on the basis of three first-authored scientific articles, an empirical study in two parts, one on the effects of tDCS and CCT on WM and mood factors, and a meta-analysis examining the rehabilitation potential of WM capacity in post-stroke patients, comparing the effectiveness of tDCS and CCT. I will first describe the methodology of the articles and then present the results, summarised in the light of the literature review presented earlier.

METHODS AND MATERIALS

(I): The objective of the meta-analysis was to examine findings from randomised controlled studies investigating the rehabilitative impacts of CCT and tDCS on WM domains in post-stroke rehabilitation. Outcome measures were selected based on clinical applicability, ensuring that all tools are widely used, easily administered, and suitable for integration into routine neurorehabilitation practice. The meta-analysis adhered to the standards outlined in the PRISMA (*Preferred Reporting of Systematic Reviews and Meta-Analyses*) guidelines with PROSPERO registration protocol (Kazinczi et al., 2024).

(II): The empirical data were collected at the Department of Neurorehabilitation, Department of Neurology, Szent-Györgyi Albert Medical Centre, University of Szeged. Participation in the study was voluntary and participants could withdraw at any time without consequences. The study protocol was approved by the local ethics committee and all procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki. Data collection and handling complied with the relevant GDPR requirements and all information was handled anonymously. The research was supervised by highly qualified professionals with training in neurology, psychiatry and psychology. Group assignment was randomised. Data collection and administration of the study protocol were carried out by experienced psychologists attached to the Neurorehabilitation Unit. The empirical results were published in two parts: one focused on

WM, while the second addressed affective factors, including depression and anxiety (Kazinczi et al., 2025b, 2025a).

Methods and Materials of Systematic Review, Meta-analysis and Meta-regression

This meta-analysis aimed to me findings from controlled studies examining the rehabilitative impacts of CCT and tDCS on WM subdomains in post-stroke rehabilitation. Adhering to PRISMA (Preferred Reporting of Systematic Reviews and Meta-Analyses) standards, the analysis followed a registered PROSPERO protocol (ID: CRD42023387182). The review protocol and analysis data can be obtained from the authors, with the PRISMA 2020.

Eligibility Criteria

The PICOS model (Population, Intervention, Comparison, Outcomes, Study Design) is a structured framework used in meta-analyses to define inclusion and exclusion criteria. In our study, we used this framework to systematically identify and select relevant studies, clearly defining the target population, the type of interventions to be tested, the comparative criteria, the outcomes of interest and the eligible studies (For PICOS see Table 1).

Outcome Measures

- **Digit Span Forward Test (DSTF)** - Assesses short-term verbal recall (phonological loop) by requiring participants to repeat number sequences in the order presented. It measures storage capacity without manipulation (Wechsler, 1944).

- **Digit Span Backward Test (DSTB)** - Evaluates WM capacity by asking participants to recall number sequences in reverse. It taps into short-term storage, manipulation, and CE processes (Wechsler, 1944).

- **Visual Span Test / Corsi Block Tapping Task (VSTF)** - Measures visuospatial WM by having participants reproduce sequences of spatial locations (e.g., blocks) in the correct order (Corsi, 1972).

PICOS	Inclusion Criteria	Exclusion Criteria
Population	Persons with average age between 40.0 and 70.0 in post-stroke condition	Persons younger than 40.0 or older than 70.0 years on group average; Persons with other/comorbid neurological conditions
Intervention(s)	CCT or tDCS with additional rehabilitation treatment	Combined application of CCT and tDCS
Comparison	Control group as conventional CR techniques or other restorative interventions or sham condition (for tDCS) or passive/waiting list control	Control group as healthy control or with neurological conditions other than stroke; tDCS control group receiving CCT/CACR; None
Outcomes	At least one outcome: Digit Span Forward/Backward Task, Visual Span Task, Corsi Block Tapping Task	None
Study designs	Studies including pre or/and post-intervention data; randomized and controlled studies, pilot studies were acceptable	Not randomized and/or controlled studies
Publication characteristics	**Inclusion Criteria**	**Exclusion Criteria**
Publication types	Primary empirical studies; Published or in-press studies; Working papers of empirical studies	Non-primary empirical studies (opinions, discussions, editorials); Reviews, meta-analyses
Years of publication	-2000	Studies before 2000
Language	English language	Non-English language

Table 1: Summary of inclusion and exclusion criteria based on the PICOS model.

Search Strategy

Systematic searches were conducted by two authors in the PubMed, Scopus, Cochrane Library, and Embase databases. Additionally, studies were manually collected from December 15, 2022, to January 10, 2023. The search strategy applied an extended combination of keywords related to the PICOS, with particular focus on WM and related measures ('working memory' or 'executive functions' or 'cognition' or 'memory' or 'digit span' or 'short-term memory' or 'visual span' or 'spatial span' or 'corsi block tapping task' or 'reading span' or 'n-back') and ('tdcs' or 'transcranial direct current stimulation' or 'cognitive training' or 'computer-based cognitive training' or 'computer-assisted cognitive training' or 'cct' or 'computerised cognitive training' or 'computerised cognitive training') and ('stroke' or 'post-

stroke' or 'patients after stroke' or 'post-stroke patients'). Two authors created the database and screened titles and abstracts according to the inclusion criteria. We identified further potential studies by reviewing references related to the topic.

Study Selection

Two independent referees assessed the articles to be included. After building the databases, all references were imported into EndNote 20.3 (Clarivate) reference management software. The screening process was as follows: (1) duplicate entries were removed - first automatically and then manually; (2) titles were screened to exclude articles that contained terms that did not fit the PICOS criteria (e.g. traumatic brain injury, Parkinson's disease, transcranial magnetic stimulation); (3) abstracts were screened using the same criteria; (4) the full text of the remaining studies was assessed in detail; (5) if fewer than five relevant studies were identified for a given intervention, no meta-analysis was performed. The two assessors then compared the admission and exclusion decisions. The reference lists of the included studies were reviewed automatically and manually. Agreement between reviewers was measured using Cohen's Kappa statistics.

Risk and Bias Assessment

The methodological quality of the included studies was independently and critically assessed by two authors using the Cochrane Risk of Bias Tool (RoB2) version 2 (Cumpston et al., 2019). This tool allows for assessment in six key areas: (1) the randomisation process, (2) deviations from planned interventions, (3) missing outcomes, (4) measurement of outcomes, (5) selection of reported outcomes, and (6) overall risk of bias. Each area can be classified as either "low risk" or "high risk" or "some concern" based on predefined criteria. Each domain Studies categorised as 'high risk' were subsequently excluded from the analysis.

Data Extraction

Two authors independently extracted data, including post-intervention means, SDs, medians, and IQRs. Collected variables included author/year, sample size, mean age, sex, stroke type, time since stroke, intervention type and duration, control condition, and primary outcomes. For tDCS studies, stimulation site, dose, electrode size, and intensity were also recorded. Studies with multiple intervention groups were analysed separately per Cochrane guidelines; in cases with various controls, the active control was prioritised. Discrepancies were

resolved through discussion. In one case (Wentink et al., 2016), medians and IQRs were converted to means and SDs.

Meta-analysis with Meta-regression

The analysis was conducted using RevMan 5.4. For each study, post-intervention means and standard deviations (Mean ± SD) were extracted or estimated from medians and IQRs as needed (Wan et al., 2014). Standardised mean differences (SMD) with 95% confidence intervals (CI) were calculated using a random-effects model due to methodological variability across studies (DerSimonian & Kacker, 2007). Heterogeneity was assessed using I^2 and P-values ($P < 0.10$ or $I^2 > 50\%$ considered significant), and categorized as low (25%), moderate (50%) or high (75%) (Huedo-Medina et al., 2006). Sensitivity analyses examined the influence of individual studies on overall effect sizes (Lee, 2018); with effect size thresholds defined as small (0.2), medium (0.5), and large (0.8) (Kinney et al., 2020). Statistical significance was set at $P < 0.05$.

Methods and Materials of Empirical Study I/I. and I/II.

The focus and publication of the results of the empirical research were done in two parts. In the first part (I/I), WM functions closely related to the theoretical research were investigated. In contrast, in the second part (I/II), the effects on mood factors (depression and anxiety) were analysed. The participants, experimental design, stimulation settings, cognitive enhancement program and statistical analysis were identical in both publications, while there were differences in the output variables.

Participants

Thirty-five stroke patients (Mage = 59.6, SD = 10.9) were recruited from the Neurorehabilitation Unit at the Department of Neurology, University of Szeged. All were native Hungarian speakers, hospitalised for approximately two weeks, and received physiotherapy, speech therapy, and fine motor training. Inclusion required measurable cognitive deficits with intact reading comprehension. Exclusion criteria included dementia unrelated to stroke, cerebral atrophy, alcohol use disorder, major psychiatric illness, extensive hemorrhage, presence of metal implants, severe aphasia, or epilepsy. The mean Addenbrooke's Cognitive Examination score was 76.3 (SD = 9.89). Lesion locations included 12 right-hemispheric, 12 left-hemispheric, and 11 bilateral/subcortical. Nineteen participants received intervention

within three months post-stroke (M = 1.29 months, SD =.87), while 16 began treatment after three months (M = 41.81 months, SD = 46.21). Participants were blinded to the expected outcomes of training or tDCS and informed only of potential side effects. Sham stimulation included identical setup to active tDCS. Data collection and all procedures were conducted by trained psychologists; all materials were securely stored.

Experimental Design

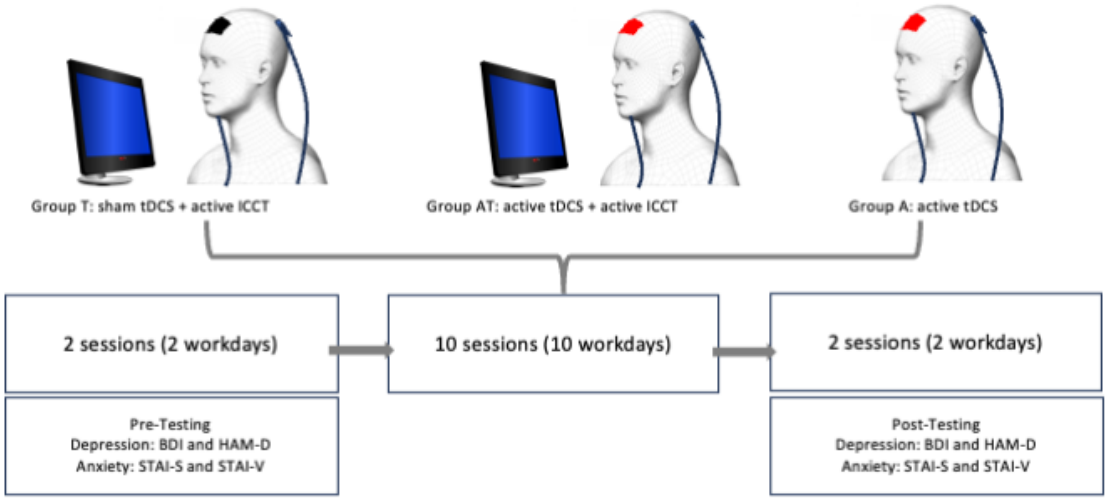


Figure 4: Experimental design. In the pre-testing phase (two sessions), we conducted a baseline evaluation using Beck's Depression Inventory (BDI), Hamilton Depression Scale (HAM-D), and Spielberger's State-Trait Anxiety Scale (STAI-S and STAI-T). In the experimental phase (10 sessions), the participants were randomly allocated into three groups: A - Active tDCS only; T - Sham tDCS with ICCT; and AT - Active tDCS with ICCT. Finally, we conducted post-testing (two sessions) using the same battery of assessments as in the baseline phase.

All participants were enlisted from the Neurorehabilitation Unit of the Department of Neurology at Albert Szent-Gyorgyi Health Centre and provided their informed consent. Rigorous criteria for inclusion and exclusion were applied to ensure a careful selection process. Participants were then randomly allocated to one of three experimental groups: Active tDCS without ICCT (Group A), Sham tDCS with ICCT (Group T), and Active tDCS with ICCT (Group AT). The participants remained unaware of the specific experimental group they were assigned during the selection process. Baseline data, including general characteristics (e.g., age, gender, type of stroke, time after stroke, education) and cognitive functions at the beginning and end of the 10-session experimental program were collected. To enhance distribution, we

divided the baseline testing into two sessions on consecutive workdays (1-2 DAYS) (*For the experimental design see Figure 4).* tDCS was administered using a NeuroConn DC Stimulator Plus device (neuroConn GmbH, Germany) at 2 mA via two 5.5 × 7.5 cm sponge electrodes.

Stimulation Parameters

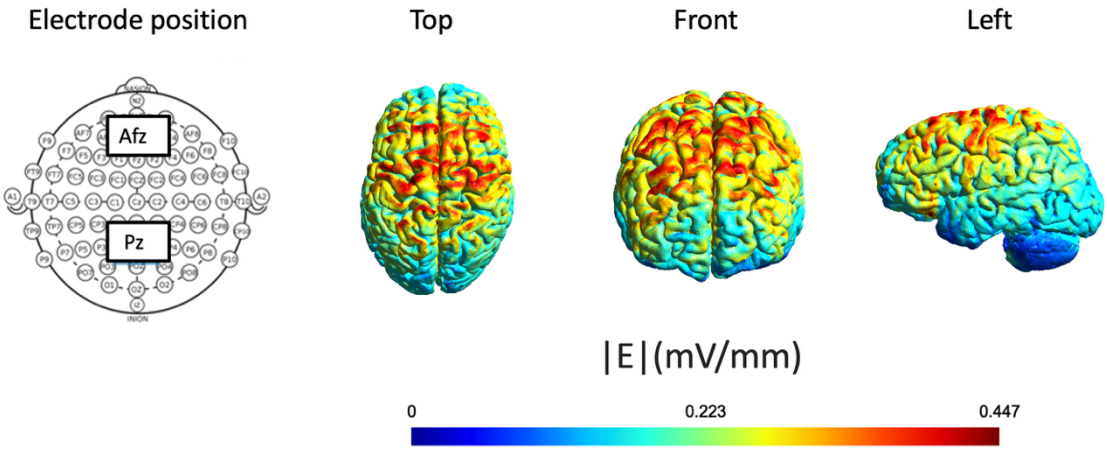


Figure 5: Stimulation Settings of Transcranial Direct Current Stimulation (tDCS). During active tDCS, specific cortical regions were stimulated, utilising an electrode current of 2 mA. The anodal electrode was positioned on the frontal regions (AFz), while the cathodal electrode was placed on the parietal regions (Pz). Using SimNibs we modelled the stimulation area with electric field strength (*E*) (*Top, Front and Left*).

The anode was placed over AFz and the cathode over Pz, following the 10-20 EEG system. Individual head measurements ensured consistent and accurate electrode placement, with scalp positions marked using dermatologically safe markers to minimise variability between sessions. Electrode positioning aimed to stimulate bilaterally across frontal to occipital regions, in line with the multiregional structure of FPN. In accordance with the internationally accepted 10-20 EEG system, electrodes were placed along the scalp midline at 10%, 20%, 20%, 20%, 20% and 10% intervals, corresponding to the landmarks Fpz, Fz, Cz, Pz and Oz. The position of AFz was determined at the midpoint between Fpz and Fz, while the position of Pz was determined according to the standard 10-20 system. SimNIBS 3.2 modelling confirmed peak stimulation in the DLPFC, parietal, and parieto-occipital cortices. Active tDCS was applied in Groups A and AT for 12 minutes per session. The AT group received cognitive training simultaneously, while the sham group (T) underwent training without stimulation. All sessions were overseen by

experienced neuropsychologists, with medical supervision from a psychiatrist and neurologist at the Neurorehabilitation Unit, University of Szeged (see Figure 5 for montage).

Computer-based Training Programme

We implemented cognitive training utilising a Flanker Task, specifically designed to improve inhibitory control, as detailed in the research conducted by Kanske and Kotz (2010) (Kanske & Kotz, 2010). The task was presented using E-prime 2.0 software (Psychology Software Tools, Pittsburgh, PA). Participants were instructed to respond to a dark computer screen 75 cm away. Throughout the task, a fixation cross preceded the appearance of the target stimulus (word) at the centre of the screen in a font size of 48. Simultaneously, the same word was displayed around the target word on the left, right, below, and above, also in font size 48 and the colour green. The target word could be either green or red. Participants were required to indicate whether the target word was displayed in red (incongruent condition; red target - green surrounding words) or green (congruent condition; green target - green surrounding words) in the middle of the screen by pressing the corresponding key. The 'A' key needed to be pressed if the target word was green when the target word was red, and the 'L' key was required on a Hungarian keyboard. The inhibitory effect was demonstrated by alternating between congruent and incongruent conditions. Participants had 5000 ms to respond to each stimulus in the initial session. If a participant completed the preceding block with an 80% success rate, the task's difficulty was adjusted by reducing the reaction time to 4000, 3000, 2000, or 1000 ms, based on each subject's previous performance. To ensure sufficient practice before each session, participants had unlimited time to familiarise themselves with the task and receive feedback. The training session comprised 4 blocks, each containing 4 sets of 45 words. The stimuli were drawn from three categories of word lists (3x15), maintaining an equal distribution of words with positive, negative, or neutral emotional valence. The words were compared in frequency, length, and syllable count, with no observed variations (*For the inhibitory control training see Figure 6*).

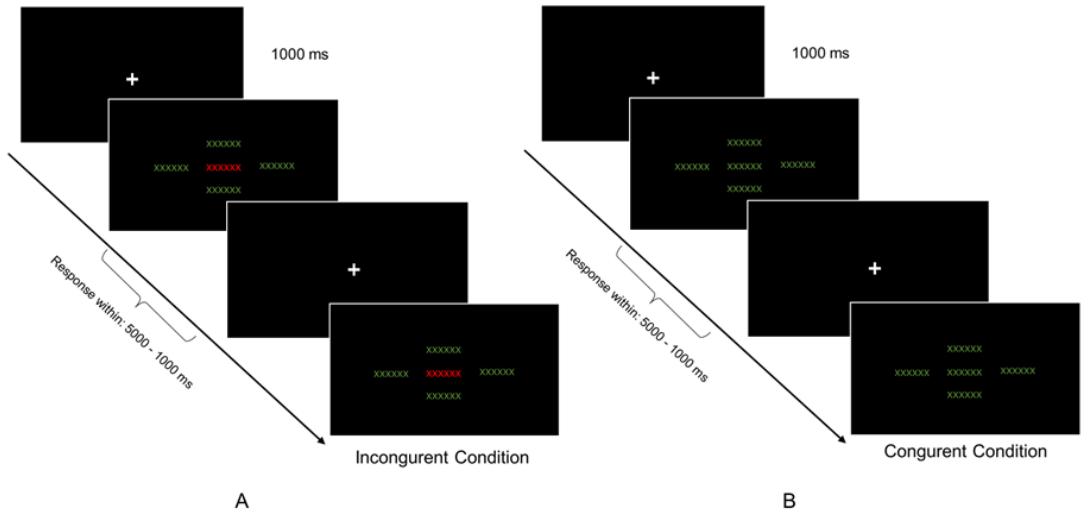


Figure 6: Inhibitory Control Training (ICCT). We employed Inhibitory Control Training to enhance inhibitory control functions. The training program involved two setups: incongruent (A) and congruent (B). In both cases, an identical word surrounding the middle word was displayed in red for the incongruent condition (A) and green for the congruent condition (B).

Clinical Psychological Testing

Empirical Study I/I.

Participants underwent an evaluation of neurocognitive and WM functions to gauge the transfer effect of CCT and the impact of tDCS stimulation. The following tests were used to examine the cognitive and affective factors:

a) *Digit Span Task (Forward and Backward) (DSTF/DSTB):* This is a classic WM test in the Wechsler Adult Intelligence Scale (WAIS) and other cognitive assessments. It involves reading a series of digits to the participant, who is then required to recall them in order immediately afterwards (Wechsler, 1944).
b) *Listening Span Task (LST):* In this test, participants listen to sentences and must remember the last word of each sentence and answer questions about the truthfulness of the sentence. The task requires listening comprehension and WM (Janacsek et al., 2009).
c) *Corsi Block-Tapping Task (CBTT)/(Visual Span Forward Test):* The task assesses visuospatial WM. Participants watch a sequence of blocks being tapped, and they must then reproduce the sequence by tapping the same blocks in the same order (Corsi, 1972).

d) *Trail Making Test, Part A/B (TMT-A/B):* This test is primarily used to assess cognitive flexibility; however, it also demands WM as participants connect alternating numbers and letters in sequence (Reitan, 1958).

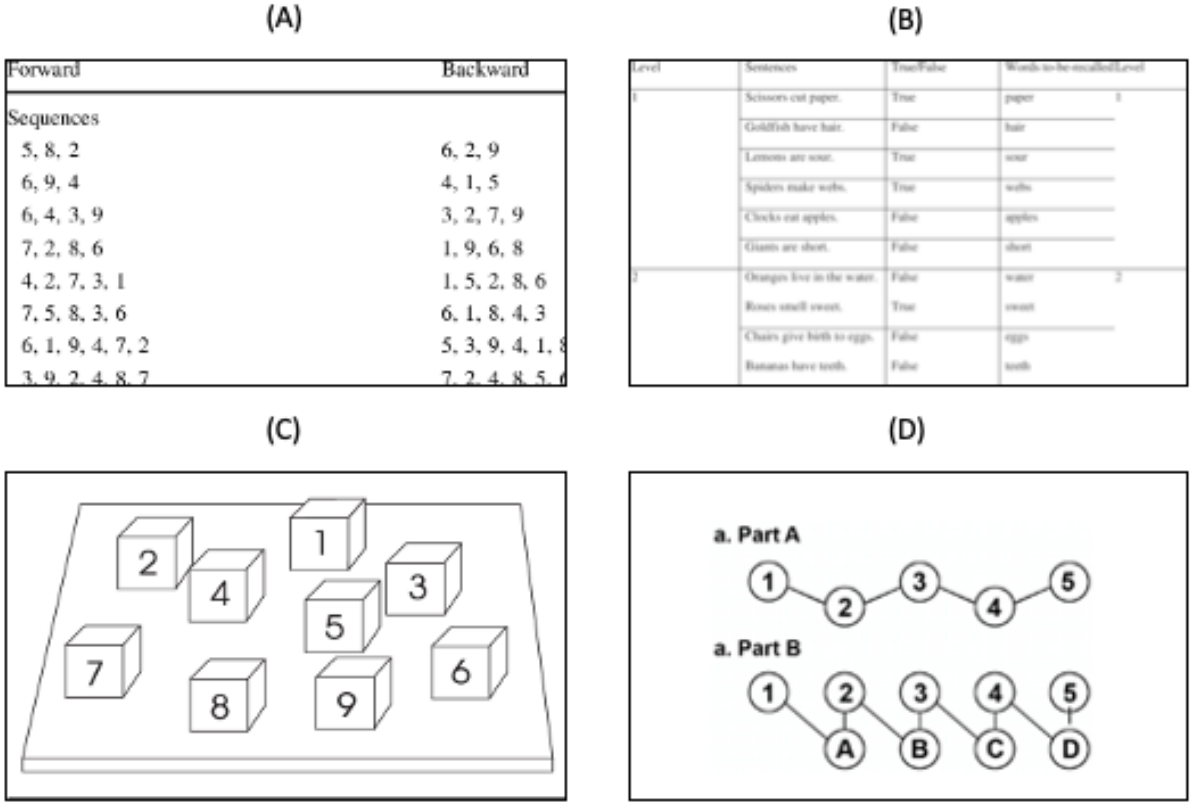


Figure 7: Applied Working Memory Assessments: During testing, the (A) Digit Span Forward and Backward, (B) Listening Span Task, (C) Corsi Block Tapping Task, and (D) Trail Making Test were administered.

Empirical Study I/II.

Patients were assessed focusing on post-stroke depression and post-stroke anxiety symptoms using the following questionnaires:

- *Beck's Depression Inventory (BDI):* The scale assesses the presence and severity of depressive symptoms in individuals. The BDI consists of 21 items, each corresponding to a specific depressive symptom. Scores above 9 indicate clinically relevant symptoms of depression (Beck et al., 1961).
- *Hamilton Depression Scale (HAM-D):* The scale is aimed to provide a standardised and systematic evaluation of the intensity and nature of depressive symptoms and consists

of 17 items, each corresponding to a specific depressive symptom or behaviour, such as mood, guilt, suicidal ideation, insomnia, and weight loss. Scores above 7 indicate clinically relevant symptoms of depression (Hamilton, 1960).

- *Spielberger's State-Trait Anxiety Inventory (State) (STAI-S):* The scale is designed to measure and evaluate a person's temporary level of anxiety. The average score is 38,4 (± 10,6) for men and 42,6 (±10,8) for women; values higher than one standard deviation in the positive range indicate clinically relevant symptoms (Spielberger et al., 1971).
- *Spielbergers's State-Trait Anxiety Inventory (Trait) (STAI-T):* The scale measures an individual's stable or enduring level of anxiety, reflecting their general tendency to experience anxiety across various situations and circumstances. The average score is 40,9 (± 7,8) for men and 45,3 (±7,9) for women; values higher than one standard deviation in the positive range indicate clinically relevant symptoms (Spielberger et al., 1971).

Additional Measurements

We also administered the following neuropsychological assessments: Addenbrooke's Cognitive Examination (ACE), which encompasses six components evaluating various cognitive abilities such as orientation, attention, memory, verbal fluency, language, and visuospatial abilities (Mathuranath et al., 2000). Flexibility and task switching were assessed using the Wisconsin Card Sorting Test (Grant & Berg, 1993). Premorbid intellectual abilities were measured with the National Adult Reading Test (NART) (Nelson & Willison, 1982).

Statistical Analysis

The SPSS package (IBM SPSS Statistics for Windows, version 25.0) was employed for data analysis, with a significance level set at $\alpha = .05$. Demographic data underwent descriptive statistical analysis, encompassing frequency, means, and standard deviations. Subsequently, the Shapiro-Wilk normality test was utilised to assess the normal distribution of data within the experimental groups. Baseline characteristics among experimental groups were scrutinised through either One-way Analysis of Variance (ANOVA) for parametric data or the Kruskal-Wallis Test for non-parametric data concerning continuous variables. Contingency tables using the $\chi 2$ test were calculated for categorical data.

Empirical Study I/I

The effects of tDCS and ICCT interventions on WM-related neuropsychological outcomes were assessed at two time points: baseline (T1) and post-intervention (T2). Data were analyzed using linear mixed effects models (LMEMs), which offer key advantages over traditional repeated measures ANOVA - such as better handling of unequal group sizes, missing data, or non-independence within subjects (Krueger & Tian, 2004). LMEMs also allow for the inclusion of random effects and continuous covariates, improving model flexibility and fit. The models included three fixed effects: Group (AT, T, A), Time (T1, T2), and their interaction (Group × Time), along with a fixed intercept. The main effect of „Time" showed overall changes across all participants, while the „Group" effect compared average scores between treatment types. The „Group × Time" interaction indicated the effect of differential improvement across groups. Statistical significance was assessed using the Satterthwaite approximation for estimating degrees of freedom and p-values. Given the variability in demographic and clinical characteristics, covariates were included in all models: age, sex, time since stroke (months), and lesion location. For each outcome, LMEM outputs included: Estimated coefficients (b) for fixed effects and covariates; Standard error (SE), t-values and p-values; Intra-class correlation (ICC) to quantify between-subject variance; Marginal R^2 (variance explained by fixed effects) and Conditional R^2 (variance explained by the full model, including random effects); Residual variance (σ^2) to assess model error. Significant interaction effects were followed by Bonferroni-corrected post hoc comparisons to pinpoint group differences. Finally, the effect sizes for Group × Time interactions were calculated to quantify the strength of treatment-related changes:

$$f_b^2 = \frac{R_{ab}^2 - R_a^2}{1 - R_{ab}^2}$$

where R_{ab}^2 represents the full model variance and R_a^2 the reduced model without the interaction term. The f^2 value corresponds to moderate ($f^2 \geq 0.15$) to large ($f^2 \geq 0.35$) effect sizes, as outlined in Cohen's (1988) guidelines (Cohen, 1988). This approach is in line with guidelines for evaluating the contribution of predictors in LMEM (Selya et al., 2012). Furthermore, Cohen's d was used to assess within-group pre-post change effect sizes:

$$d = \frac{M_{post} - M_{pre}}{SD_{pooled}} \; ; \; SD_{pooled} = \sqrt{\frac{SD_{pre}^2 + SD_{post}^2}{2}} ; SD = SE \; x \sqrt{n}$$

According to Cohen (1988), effect sizes can be interpreted as small (d = 0.2-0.5), medium (d = 0.5-0.8), and large (d ≥ 0.8). Based on this classification, an a priori power analysis was performed using GPower software (Faul et al., 2009), with parameters set at α =.05, power (1-β) =.90, and an effect size of f = 0.35. The analysis indicated that a minimum of 30 participants in total would be required to achieve adequate statistical power (0.91).

Empirical Study I/II

Frequentist statistical analysis

The analysis was performed using the JAMOVI project (version 2.3) and significance was set at the .05 level. A 2 × 2 mixed ANOVA model was used to examine the effect of treatment and experimental conditions. The baseline and post-test scores of the psychological assessments after the ten experimental sessions were defined as [PRE-POST], while the experimental conditions were defined as [CONDITION]. For statistically significant results, differences were tested using Tukey-corrected post-hoc tests. In terms of effect size, ηp2 values are interpreted as follows: values less than 0.01 indicate a negligible effect, 0.01-0.06 a small effect, 0.06-0.14 a medium effect, and values above 0.14 a large effect. Furthermore, Pearson correlation analysis was performed to examine the correlation between pre- and post-intervention scores.

Bayesian Statistical Analysis

Bayesian statistics were used to address potential baseline differences and sample size imbalances by providing a probabilistic approach that takes prior information into account. All Bayesian analyses were conducted using the Jamovi statistical software. Bayesian mixed-model ANOVA was used to evaluate treatment effects over time. Results were interpreted using Bayes Factors (BF_{10}), which indicate how much more likely the observed data are under the alternative hypothesis (H_1) compared to the null hypothesis (H_0). Specifically, values of $BF_{10} > 1$ suggest evidence in favor of H_1 (i.e., an effect), whereas $BF_{10} < 1$ supports H_0 (i.e., no effect). The strength of evidence is typically categorized as follows: $BF_{10} < 0.1$: strong evidence for H_0, 0.1-

0.33: moderate evidence for H_0, 0.33-1: weak evidence for H_0, 1-3: weak evidence for H_1, 3-10: moderate evidence for H_1, >10: strong evidence for H_1. In addition to BF_{10}, Bayes Factors for inclusion (BFIncl) were calculated to assess the relevance of each predictor in the model. BFIncl quantifies the change in evidence when a factor is included versus excluded, using the same thresholds of interpretation as BF_{10}. Together, these indices provide a nuanced understanding of the data, especially in complex models where traditional frequentist approaches may fall short.

Minimum Clinically Important Difference

Following Masson and Tejani (2013), the minimum clinically importand difference (MCID) for the Beck Depression Inventory (BDI) was calculated using a hybrid method combining anchor- and distribution-based approaches (Masson & Tejani, 2013). Clinically relevant improvement was defined by three criteria: (1) improvement in score direction, (2) a minimum 5-point reduction, and (3) a ≥29.64% decrease from baseline. Two classifications were applied: (I) both absolute and relative change thresholds met, and (II) ≥29.64% relative change regardless of absolute score. Chi-squared tests were used to compare group differences in the proportion of participants achieving MCID.

RESULTS

Results of Systematic Review, Meta-analysis and Meta-regression

Search Results

4,142 records were identified (PubMed: 609, Scopus: 1,036, Embase: 929, Cochrane Library: 1,544; plus 24 from manual search). After removing duplicates and applying eligibility criteria, 53 studies were screened in full. Of these, 44 were excluded due to language, population, study design, missing outcomes, or combined interventions. Ultimately, nine studies using CCT alone met inclusion criteria (Bo et al., 2019; Cho et al., 2015; De Luca et al., 2018; Ho et al., 2022; Tarantino et al., 2021; Van De Ven, Murre, et al., 2017; Wentink et al., 2016; Westerberg et al., 2007; Yoo et al., 2015). For the initial search, the Cohen's Kappa was 0.71, indicating significant agreement. Considering the specificity of the neuropsychological tests and interventions included, which might be expected to result in rare events relative to the overall population, we also calculated the prevalence- and bias-adjusted Kappa (PABAK) to provide another measure of agreement (Chen et al., 2009). For abstract screening, the Cohen's

Kappa was 0.75 and the PABAK was 0.79. For the full-text filtering, the Cohen's Kappa was 0.77 and the PABAK was 0.82 - reflecting good agreement in both phases. Any disagreements were resolved by discussion. The process of study selection is illustrated in the PRISMA flowchart (see Figure 1).

Study Characteristics

The nine studies (2007-2022) included 461 participants (234 intervention, 227 control). The studies were from different countries, including China (1), Italy (2), Korea (2), the Netherlands (2), Sweden (1) and Taiwan (1). Sample sizes ranged from 9 to 57 (mean: \~25 per group), with participants aged 43.9-67.5 years (mean: 59.0) and a male-to-female ratio of 1.31:1. The average time since stroke was 13.8 months. Control conditions varied: other restorative interventions (4), traditional cognitive rehab (2), combined methods (1), wait-list (1), and passive control (1). Five studies focused on improving overall cognitive function.

Results of Risk and Bias Assessment

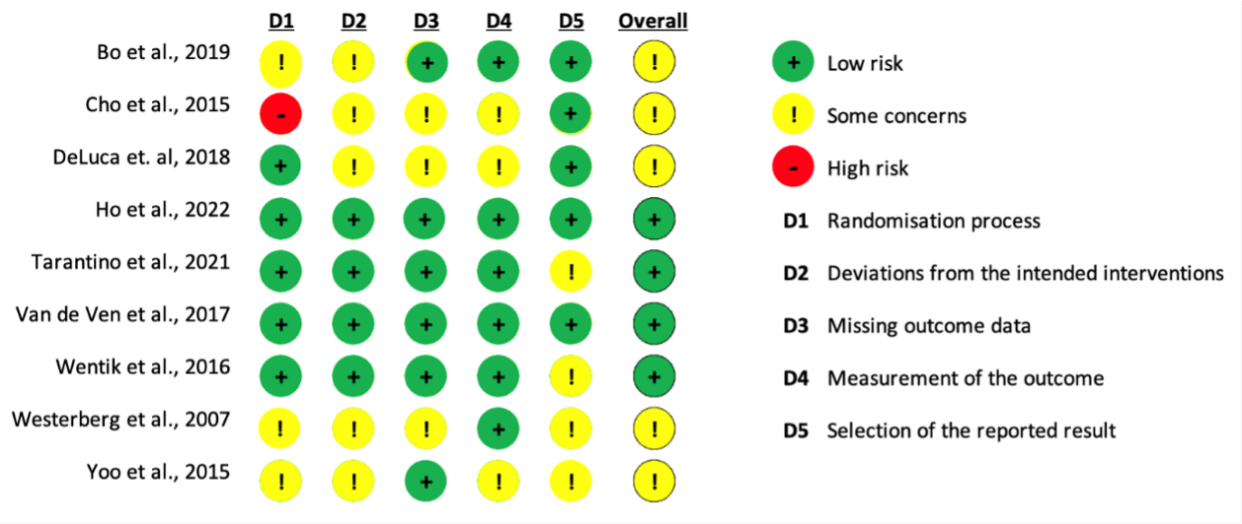


Figure 8: Results of risk and bias assessment

Of the nine studies selected, four were classified as ‘low risk’, five as ‘of some concern’ and none as ‘high risk’. Regarding randomisation and allocation procedures, one study did not provide sufficient information for a full assessment. In four cases, some aspects of the randomisation or allocation procedures raised questions, while the remaining studies met the expected standards in this area. In addition, in three studies the rationale for the choice of

measurement tools was unclear or missing. Although several of the included studies focused on global cognitive outcomes, no clear sources of bias were identified for the WM-specific measures used in the meta-analysis. A summary of the methodological quality assessments is shown in Figure 8.

Intervention Characteristics

Six different CCT programs were identified: Cogpack, RehaCom, Erica, Lumosity, RoboMemo and BrainGymmer. One study used an unspecified program. These tools were used alone or in conjunction with traditional rehabilitation, typically for 10-58, 20-60 minute sessions. Lumosity and RehaCom were the most commonly used, both offering ~30 modules targeting areas such as memory, attention and EF. Cogpack offers 64 customisable tasks for different cognitive skills, making it suitable for clinical use. RehaCom is often used in stroke rehabilitation with adaptive difficulty settings. Erica provides flexible training in five cognitive domains. RoboMemo targets visuospatial and auditory WM, while BrainGymmer includes varied tasks for attention, inhibition, flexibility and WM.

Outcomes of Meta-analysis and Meta-regression

Short-term memory performance, as measured by the **Digit Span Forward Task (DSTF),** was analysed in eight studies, 384 in total. Results indicated moderate heterogeneity ($P = 0.05$; $I^2 = 50\%$) and no significant improvement compared to control conditions ($Z = 1.95$; $P = 0.05$; SMD = 0.30, 95% CI = 0.06-0.46). Funnel plot analysis showed asymmetry and sensitivity analysis identified two studies (Bo et al., 2019; Westerberg, 2007) as contributing factors to the observed heterogeneity. After exclusion of these studies, heterogeneity was reduced to zero ($I^2 = 0\%$; $P = 0.54$), but the result was still not significant ($Z = 0.70$; $P = 0.49$; SMD = 0.08, 95% CI = -0.15-0.32).

WM performance, measured by the **Digit Span Backward Task (DSTB),** was assessed in four studies involving a total of 193 participants. Meta-analysis showed a statistically significant improvement in WM performance compared to controls ($Z = 2.65$; $P = 0.008$). The analysis revealed negligible heterogeneity ($P = 0.93$; $I^2 = 0\%$) and the observed effect size was moderate (SMD = 0.39, 95% CI = 0.10-0.67).

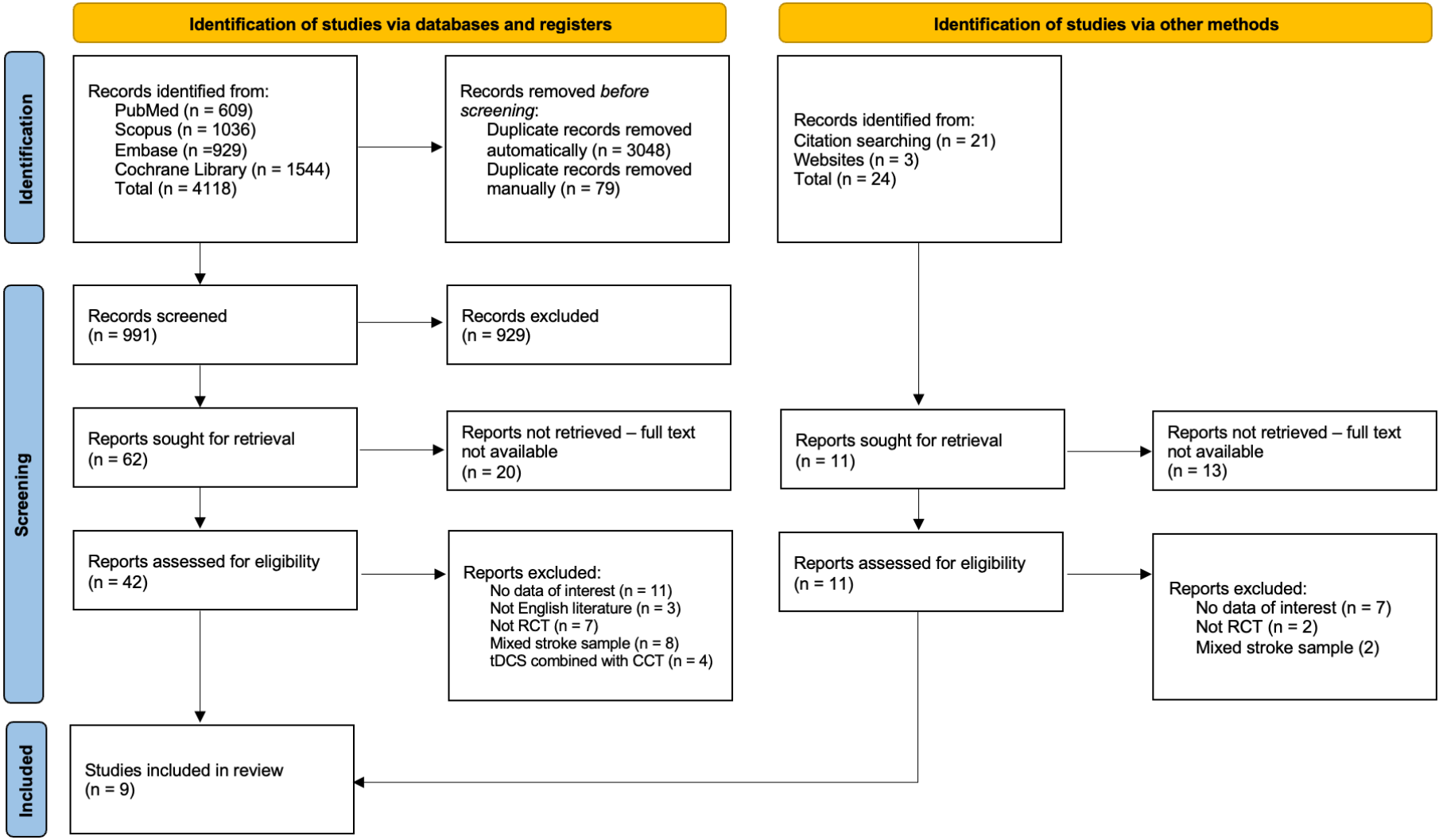


Figure 7: Identification and selection flowchart according to PRISMA

Table 2. Characteristics of CCT and tDCS studies

Author/ Year	Sample size (Intervention/Control)	Mean Age (years)	Sex (M/F)	Stroke Type	Time after stroke (avg. months)	Additional treatment to CCT	Type	Duration (Mins/Sessions)	Control	Aim/primary outcomes
Bo et al., 2019	45/47	67.50	21/24	VCI	< 6.0	Physical exercise	COGPACK	60 mins/ 36 sessions	Other restorative intervention	Cognitive functions / DSTF, TMT-B, Stroop, Mental Rotation
Cho et al., 2015	12/13	60.00	7/5	N/A	5.3	Other restorative intervention	RehaCom	30 mins/ 24 sessions	Other restorative intervention	Memory and attention / DSTF, DSTB, VSTF, VCPT, ACCPT
De Luca et al., 2017	20/15	43.90	11/9	IS/ICH	3.0	Conventional CR	Erica	45 mins/ 24 sessions	Conventional CR	Cognitive functions / DSTF, BNT, MMSE, PVF, RAV, RAVL-I/R, SVF, TT
Ho et al., 2022	19/20	63.60	12/7	IS/ICH	19.9	Conventional CR	Lumosity	20 mins/ 24 sessions	Conventional CR	Cognitive functions / DSTF, DSTB, VSTF, MMSE, SDMT
Tarantino et al., 2021	18/19	64.60	12/6	IS/ICH	3.1	Conventional CR and other restorative intervention	Pilot with E-prime	60 mins/10 sessions	Conventional CR and Other restorative intervention	Executive functions / DSTF, DSTB, VSTF, TMT-A, PVF, SVF, WCST, Stroop
Van de Ven et al., 2017	38/24	60.90	19/16	N/A	28.3	Conventional CR and other restorative intervention	BrainGymmer	30 mins/ 58 sessions	Waiting list control	Cognitive flexibility / VSTF, TMT-A/B, DSTF, RAVL, N-back, Raven PM
Wentink et al., 2016	50/57	59.00	34/19	IS/ICH	26.0	No	Lumosity	20 mins/ 40 sessions	Other restorative intervention	Cognitive functions / DSTF, DSTB, TMT-A/B, Flanker Task, Raven PM
Westerberg et al., 2007	9/9	55.00	8/1	IS/ICH	20.8	No	RoboMemo	40 mins/ 23 sessions	Passive control	Working memory / DSTF, VSTF, Stroop, Raven, PASAT, Ruff 2x7
Yoo et al., 2015	23/23	56.30	9/14	N/A	11.8	Other restorative intervention	RehaCom	30 mins/ 25 sessions	Other restorative intervention	Cognitive function / DSTF, VSTF, VeLT, ViLT, ACCPT, VCPT, TMT-A

Table 2: Characteristics of the sample. Abbreviations: Trail-Making Test (TMT), Stroop Test, Mental Rotation, Visual Continuous Performance Test (VCPT); Auditory Controlled Continuous Performance Test (ACCPT), Boston Naming Test (BNT), Mini-Mental State Examination (MMSE), Phonemic Verbal Fluency (PVF); Raven's Coloured Progressive Matrices (RAV); Rey Auditory Verbal Learning Test Immediate (RAVLI); Rey Auditory Verbal Learning Test Late (RAVLL); Semantic Verbal Fluency (SVF); Token Test (TT); Symbol Digit Modalities Test (SDMT), Wisconsin Card Sorting Test (WCST), Paced Auditory Serial Addition Test (PASAT), Verbal Learning Test (VeLT), Visual Learning Test (ViLT), Digit Span Forward Test (DSTF), Digit Span Backward Test (DSTB), Visual Span Forward Test (VSTF)

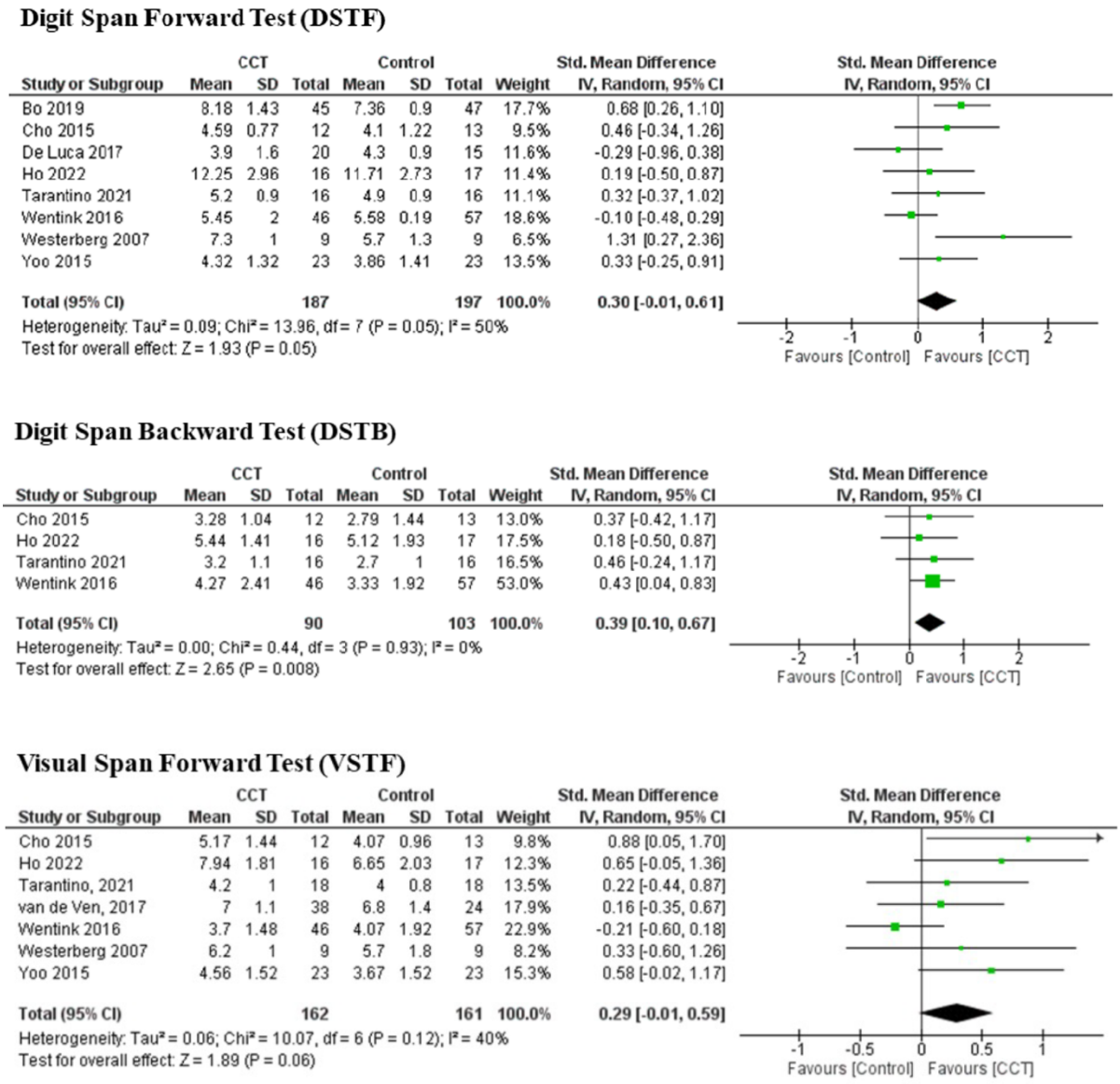


Figure 9: Effects of Computerised Cognitive Training (CCT) on working memory performance compared to control conditions. Improvements were assessed across three domains: short-term verbal recall (Digit Span Forward Test - DSTF), verbal working memory (Digit Span Backward Test - DSTB), and visuospatial working memory (Visual Span Forward Test - VSTF)

For visuospatial span, measured using the **Visual Span Task (VSTF),** data from seven CCT trials (n = 323) were analysed. Initial analysis revealed no statistically significant effect (SMD = 0.22, 95% CI = -0.01-0.44; Z = 1.90; P = 0.06), with moderate heterogeneity (I^2 = 40%; P = 0.12). Funnel plot analysis suggested that a single study (Wentink, 2016) contributed disproportionately to heterogeneity. When this study was removed, heterogeneity was eliminated (I^2 = 0%) and the revised analysis showed a significant effect in favour of CCT (SMD = 0.43, 95% CI = 0.16-0.69; Z = 3.14; P = 0.002).

In the meta-regression analysis, potential sources of variability in the effectiveness of CCT and tDCS interventions—namely participant age, session duration (in minutes), and the number of intervention sessions—were examined as moderating variables. The results indicated that none of these factors had a statistically significant moderating effect on neuropsychological test outcomes ((Figure 9 and Supplementary Table 1-2).

Results of Empirical Study I/I. and I/II.

The mean age of participants was 59.68 years (SD = 11.10), and there were no significant differences between groups in age or education (M = 12.03 years, SD = 3.40). Demographic variables (education, age, lesion location and time since stroke) also did not differ significantly between groups. Gender distribution was balanced (22 males, 13 females), and stroke location and time since stroke (≤ or > 3 months) were similarly distributed. Baseline cognitive function as measured by NART and ACE did not differ significantly between groups. According to LMEM, no significant baseline differences were found in primary cognitive outcome measures (DSTF, DSTB, LST, CBTT, TMT-A/B). Shapiro-Wilk tests indicated a non-normal distribution for these variables at baseline. No significant baseline differences were found between the experimental groups in the primary outcome measures (BDI, STAI-S, STAI-T), except for HAM-D, where the active tDCS group showed significantly lower scores. Overall cognitive performance assessed by ACE showed no group differences, with an overall mean score of 76.3 (SD = 9.89). The Shapiro-Wilk test showed that the baseline distributions of STAI-T and HAM-D deviated from normality. At baseline, the BDI and HAM-D scores were above the clinical threshold, while the STAI-S and STAI-T scores were within the normal limits. Correlation analyses revealed strong associations between pre- and post-treatment measures of affective symptoms. The strongest correlation was observed between post-treatment STAI-T and BDI scores ($r = .79$, $p < .001$). Pre-treatment BDI was also strongly correlated with post-treatment BDI ($r = .75$, $p < .001$). A moderate correlation was found between pre-treatment STAI-T and post-treatment BDI scores ($r = .43$, $p = .010$). Baseline HAM-D scores were significantly correlated with both post-treatment HAM-D ($r = .68$, $p < .001$) and BDI scores ($r = .58$, $p < .001$). In addition, pre- and post-treatment STAI-T scores showed a significant correlation ($r = .65$, $p < .001$) (Supplementary Table 3-6).

Digit Span Forward (DSTF): No significant main effects found. However, a significant *time* × *group* interaction ($p = 0.028$) indicated greater improvement in the AT group. Random effects showed high individual variance (ICC = 0.65), with a strong overall model fit (R^2 conditional = 0.72).

Digit Span Backward (DSTB): No significant effects or interactions observed. Moderate individual variability (ICC = 0.37). Fixed effects explained little variance (R^2 marginal = 0.14), full model moderate (R^2 conditional = 0.45). For detailed results see Supplementary Table 6-8.

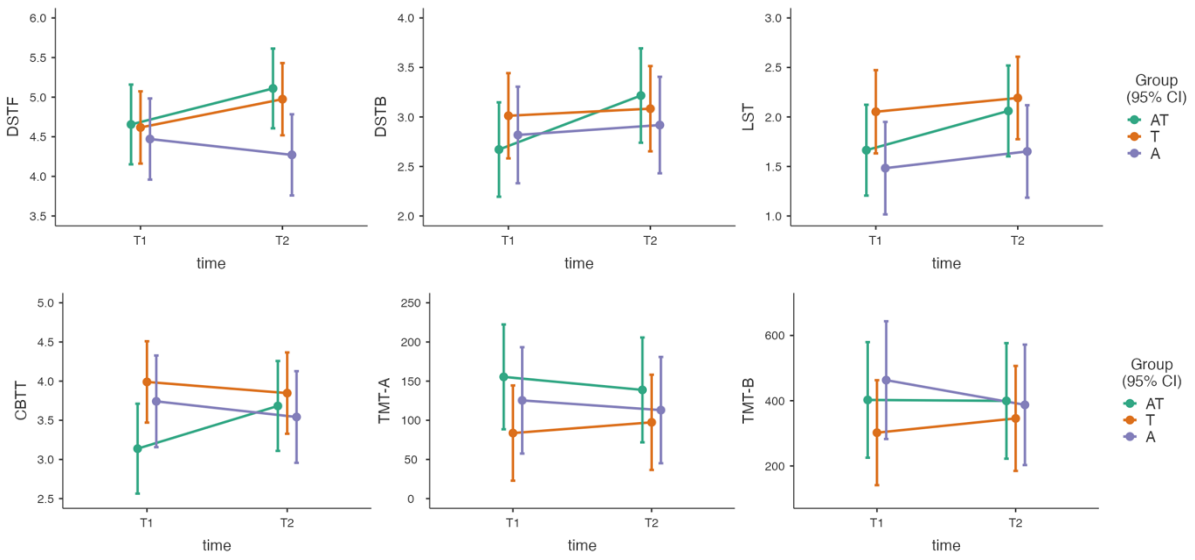


Figure 10: The results between the three experimental groups (AT, T, A) at T1 and T2 for the neuropsychological tests: DSTF=Digit Span Task; DSTB=Backward Digit Span Task; LST=Listening, Span Task; CBTT=Corsi Block Tapping Task; TMT = Trail Making Test.

Listening Span Test (LST): A significant main effect of *time* ($p = 0.006$) indicated improvement post-intervention. No group differences or interaction effects. High individual variance (ICC = 0.78), model fit strong (R^2 conditional = 0.84).

Corsi Block Tapping Task: No significant fixed effects or interactions. Moderate individual variability (ICC = 0.53). R^2 marginal = 0.26, conditional = 0.65.

Trail Making Test A (TMT-A): No significant effects. Very high individual differences (ICC = 0.90), suggesting strong participant-level variance. R^2 marginal = 0.10, conditional = 0.91.

Trail Making Test B (TMT-B): No significant fixed effects. High individual variance (ICC = 0.75). Minimal variance explained by fixed predictors (R^2 marginal = 0.09), full model better (R^2 conditional = 0.75).

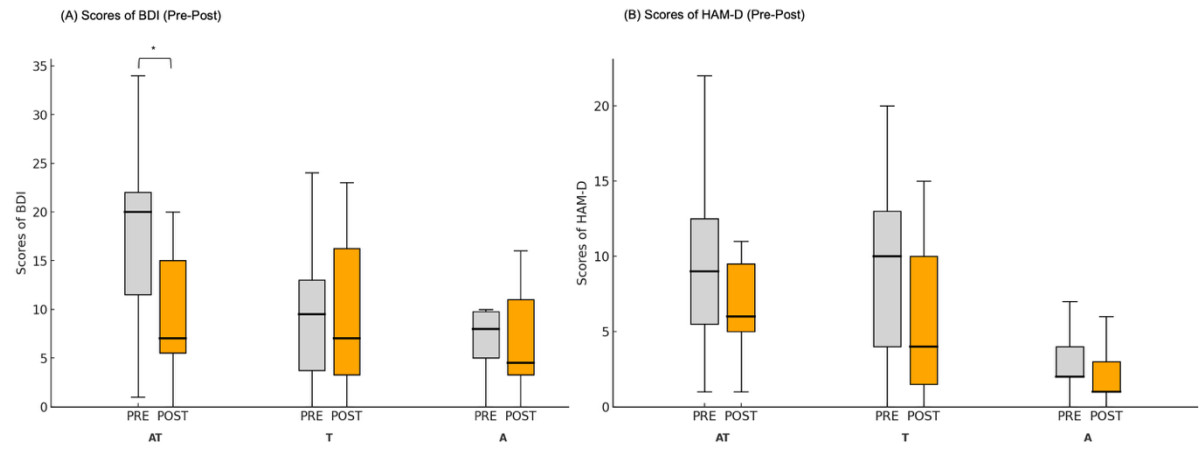
Empirical Study I/II.

Beck Depression Inventory (BDI): *Frequentist analysis:* A significant main effect of time was observed ($p < .001$, $\eta p^2 = 0.30$), as well as a significant time × group interaction ($p < .001$, $\eta p^2 = 0.40$), indicating that depressive symptoms improved over time, especially in the AT (active tDCS + CCT) group. There was no significant main effect of condition alone. Post hoc comparisons revealed a statistically significant pre-post improvement only in the AT group. *Bayesian analysis:* The Pre-Post + Condition model showed the strongest support, confirming that both time and treatment group independently influenced depression scores. The interaction term received weaker support. Post hoc findings suggested that the AT group benefited most, consistent with the frequentist results (Supplementary Table 9).

Hamilton Depression Rating Scale (HAM-D): *Frequentist analysis:* A significant main effect of time ($p = .004$, $\eta p^2 = 0.23$) and a main effect of condition ($p = .012$, $\eta p^2 = 0.25$) were observed, but the time × condition interaction was not significant ($p = .385$). This indicates that depressive symptoms improved overall and differed between groups, but the rate of change was similar. *Bayesian analysis:* The model including both time and condition showed the highest support, while the interaction term showed only moderate evidence. A small group difference was found between AT and A groups, but not between T and A groups. This suggests the combined intervention had the strongest, though not exclusively time-dependent, effect (Supplementary Table 9).

Spielberger State Anxiety Inventory (STAI-S): *Frequentist analysis:* No significant changes were detected in state anxiety scores. The main effect of time approached significance ($p = .063$), but the condition and interaction effects were not significant. *Bayesian analysis:* All models showed weak evidence. The Pre-Post model had slightly more support, but overall, no meaningful time or group effects were found (Supplementary Table 10).

(A)



(B)

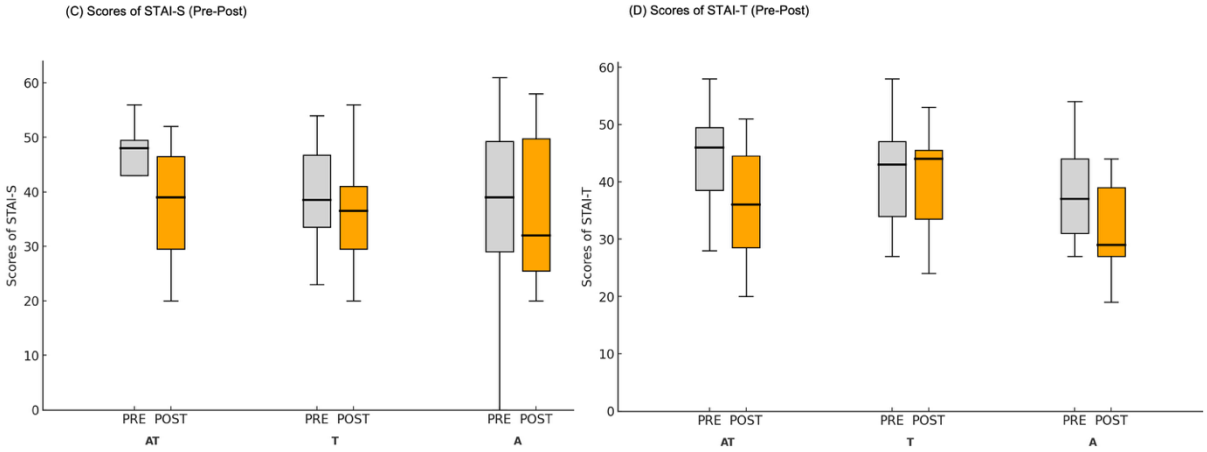


Figure 11: Pre- and post-intervention results of affective symptom scores among the three experimental groups: A - Active tDCS only; T - Sham tDCS with ICCT; AT - Active tDCS with ICCT. (A) Depression-related outcomes showed significant improvement in the AT group on the Beck Depression Inventory (BDI), while the Hamilton Depression Rating Scale (HAM-D) indicated a global treatment effect, despite no significant condition-specific changes. For anxiety measures (B), Spielberger's State-Trait Anxiety Inventory - State (STAI-S) showed no significant changes, whereas STAI-Trait (STAI-T) revealed a global improvement over time, but without significant group differences. (*p < .05)

Spielberger Trait Anxiety Inventory (STAI-T): *Frequentist analysis:* A significant main effect of time (p = .015, ηp^2 = 0.18) indicated a general reduction in trait anxiety across all groups. Neither the condition nor interaction effects reached significance. *Bayesian analysis:* The model including both time and condition received the strongest support,

though only the time effect had substantial evidence. A small, non-significant trend suggested greater improvement in the AT group (Supplementary Table 10).

Minimum Clinically Important Differences (MCID): Both MCID criteria confirmed that significantly more participants in the AT group reached clinically meaningful improvement compared to the A and T groups ($\chi^2 = 10.14$, p = .006; $\chi^2 = 8.43$, $p = .015$). These findings reinforce the superior clinical effectiveness of the combined tDCS and CCT intervention (Supplementary Table 11).

DISCUSSION

The aim of this dissertation was to investigate the effects of two widely used neurorehabilitation techniques, tDCS and CCT, on WM and affective regulation in post-stroke patients. Building on a theoretical framework that emphasizes the role of the FPN in both executive and affective function, the empirical study investigated whether inhibition-focused CCT and large-scale tDCS stimulation targeting the FPN could produce measurable improvements. The novelty of our research lies in the fact that instead of the traditionally used N-back (updating) tasks, we use an inhibition-based cognitive training program targeting both executive and affective processing, combined with frontoparietal tDCS in a transdiagnostic framework. A further strength of our methodological approach is that we selected the measurement tools with clinical applicability. These instruments are easy to use, widely accepted in neuropsychological practice, and provide practical utility in the everyday rehabilitation setting.

The results of the experiment and subsequent analyses showed that although no general improvement was found across all WM measures, there were specific effects. Specifically, the AT group (active tDCS combined with CCT) showed improvements in short-term verbal span and affective aspects of depression-related symptoms (BDI), suggesting a possible synergistic effect of the combination of neurostimulation and targeted cognitive training. However, other neuropsychological test results showed no significant changes, and anxiety-related variables showed only weak or non-specific effects. These suggest that although both interventions appear promising, their effectiveness is likely to be domain-dependent and influenced by individual variability. Importantly, applied inhibitory training alone may not reliably produce the expected transfer effects attributed to conventional WM training, such as the N-back task. To complement the empirical results, we conducted a systematic review and meta-analysis

focusing on WM outcomes in tDCS and CCT studies. The results of the meta-analysis showed a significant effect of CCT on complex and visuospatial WM subscales, whereas for tDCS there was insufficient evidence to perform a meta-analysis. These results support the growing consensus that CCT may improve specific WM functions, although the effect may not be uniform across all WM components.

In summary, these are the main findings of our investigations:

Empirical Study

- **Digit Span Forward Test (short-term phonological recall):** Significant time × group interaction, with greater improvement in the AT group.
- **Listening Span Test (complex working memory):** Significant main effect of time indicating overall improvement across groups.
- **BDI (depression):** Significant main effect of time and time × group interaction; depressive symptoms improved significantly only in the AT group.
- **HAM-D (depression):** Significant main effect of time and group, with no difference in interaction
- **STAI-T (anxiety):** Significant main effect of time, showing a global reduction in trait anxiety across groups.

Meta-analysis outcomes

- **Digit Span Backward Test (WM capacity):** Significant improvement over controls
- **Visual Span Forward Test (Visuospatial WM):** Significant improvement over controls

Taken together, the results partially confirm the original hypotheses:

- **H1** was partially supported, as meta-analysis provided evidence for the effectiveness of CCT in improving specific areas of WM (e.g., visuospatial and complex WM), while evidence for tDCS remained limited. However, the effects were not uniform across all WM measures.
- **H2** was unsupported: ICCT did not result in a significant transfer effect on WM performance.

- **H3** was unsupported: stimulation of FPN with tDCS did not meet the expectations. No consistent benefit was observed.
- **H4** was not supported; overall, no main WM effect was observed, although a significant difference emerged between the A and AT groups in the DSTF.
- **H5** was partially supported, the combination of CCT and tDCS resulted in a significant reduction in depressive symptoms compared to the standalone applications; however, no clear effect was found in the anxiety measures.

I discuss the results in detail in the light of research and theoretical considerations:

Systematic Review and Meta-analysis

This study investigated the effectiveness of CCT on post-stroke WM performance using the DSTF, DSTB and the VSTF. Although the tDCS would have been initially considered, it was excluded from the final meta-analysis due to a lack of adequate studies focusing on WM outcomes. Therefore, our results primarily reflect the effects of CCT. Our meta-analysis showed a significant positive effect of CCT on WM, especially on verbal WM measured by DSTB and visuospatial WM measured by VSTF. These results are in line with previous reviews supporting the efficacy of CCT in cognitive rehabilitation, especially for EF. For instance, Van de Ven and colleagues (2016) reported that CCT produced moderate to large improvements in EF domains such as WM (Van de Ven et al., 2016). However, we did not register significant improvements for DSTF, which may reflect the separation of short-term memory from executive processes. This interpretation aligns with Lugtmeijer and colleagues (2021), who classified forward span tasks as low-load, reflecting primarily short-term memory capacity, while backward span tasks were classified as high-load, requiring manipulation and thus taking up the CE of WM. The data also suggest that CCT can be particularly effective in improving complex WM processes that rely on CE, while simpler storage-based tasks (such as DSTF) are less responsive. This observation contributes to the ongoing debate on the different trainability of WM subcomponents and reinforces the need to consider that it may be more worthwhile to target slightly more effortful CE-specific mechanisms in post-stroke rehabilitation. Our results also support the notion that online, active engagement generated by CCT may be preferable to passive, offline stimulation methods (such as tDCS) although the latter remains speculative as there is currently insufficient tDCS data in this area.

A strength of this work is the targeted study of WM and its subcomponents, an area that is often either underrepresented in stroke rehabilitation research or grouped together with general cognitive function. However, methodological variation in studies remains a major challenge, particularly in terms of intervention content, intensity and outcome evaluation. CCT programs can vary widely in structure, from general cognitive platforms to more targeted WM modules, and few are designed specifically to train WM. Nevertheless, the observed improvements indicate that improvements in WM can occur in the absence of task-specific training, possibly through transfer effects from broader EF engagement, which is a distinctly positive outcome in this regard. This is in line with findings by Shipstead and colleagues (2012), who highlighted that WM improvements often stem from generalised EF training rather than narrow task-specific gains Mező, (Shipstead et al., 2012). Another important aspect concerns the measurement practice. Many studies in the WM literature rely on N-back tasks to evaluate WM capacity, while in our analysis we used DSTB and VSTF and DSTF tasks. These tasks involve different cognitive operations (e.g. manipulation versus continuous updating), which may explain some of the differences in the effects found. As Jaeggi and colleagues (2010) emphasised that while N-back tasks primarily engage continuous updating mechanisms, span tasks rely more on active retrieval and sequencing Mező, (Jaeggi et al., 2010).

From a clinical perspective, the results support the practical value of CCT in post-stroke rehabilitation. CCT programmes are widely available and can be adapted to the individual needs of patients. Their digital nature allows for remote implementation through web browsers or mobile applications, which is particularly beneficial for patients with limited mobility or limited access to face-to-face therapy. Furthermore, many CCT platforms have automatic difficulty level setting, real-time feedback and game elements that can enhance motivation and adherence to treatment. These benefits make CCT a cost-effective and flexible tool that can complement traditional rehabilitation approaches. Given the demonstrated improvement in WM, particularly in complex and visuospatial subdomains, integrating targeted CCT modules into multidisciplinary stroke recovery protocols may optimize functional outcomes and also facilitate transferability towards activities of daily living.

A limiting factor is that our study included only English-language publications, which may have resulted in linguistic and cultural bias. In addition, we found significant differences in the profile of participants, including age, time since stroke, and type of stroke (ischemic vs. hemorrhagic). Although subgroup analyses could not be performed due to data limitations,

these differences likely contribute to the variability in response and should be addressed in future studies. Finally, standardised CCT interventions may not sufficiently capture individual differences in cognitive profiles, motivation or rehabilitation needs - factors that may significantly moderate treatment effects. In light of these findings, we argue for the further development and use of structured, site-specific CCT programs in WM rehabilitation, and for more controlled research designs that include comparable active and passive control conditions. Future studies should also investigate whether CCT should be used in the early or chronic phase after stroke and how it can be integrated into multidisciplinary rehabilitation frameworks. The development of standardised WM outcome measures for stroke populations would also greatly facilitate the development of the field.

Empirical Results

Building on an integrative theoretical framework of EF, WM and affective regulation, the aim of our empirical study was to assess the potential rehabilitation benefits of tDCS and CCT; considering new options: tDCS was targeted to a broad frontoparietal area instead of classical stimulation targeting the DLPFC, and WM was targeted with inhibitory control cognitive training as part of EF rather than with updating function. According to recent findings that training inhibitory functions can induce a near transfer effect, we hypothesized that targeting inhibition would lead to improvements in several WM regions and affective outcomes. Our results showed no statistically significant improvement in overall WM capacity or affective symptoms. These results are in line with those of Jo and colleagues (2009), who also found no significant improvement in WM performance following tDCS intervention in stroke patients, suggesting possible limitations in efficacy or protocol design (Jo et al., 2009). However, we did observe subtle positive trends in short-term phonological storage, which may suggest a limited transfer effect. Remarkably, participants receiving ICCT outperformed members of the group receiving active tDCS alone, although these differences did not reach statistical significance, nevertheless the most considerable directional improvement was measured overall in the combined group, despite the lack of statistical significance. Martin and colleagues (2014) similarly reported that the combination of CCT and concurrent tDCS results in increased, albeit often only sub-threshold, improvements in cognitive tasks, suggesting synergistic but variable, less pronounced effects (Martin et al., 2014). These results point to the potential limitations of both the scope of stimulation and the generalizability of inhibitory training as a tool for WM

development in stroke rehabilitation. In the following, several interpretations of the results are explored.

Applying Large-scale Stimulation to Enhance Working Memory

Starting with tDCS, our study indicates that multiregional stimulation did not improve WM-related cognitive functions. Active tDCS without a training task showed limited benefits across all neurocognitive assessments. This could be attributed to inadequate localisation or intensity of the direct current, as suggested by Utz and colleagues (2010), who proposed placing tDCS electrodes over the specific brain region associated with the cognitive function under investigation (Utz et al., 2010). However, conflicting evidence exists, with studies such as Datta and colleagues (2011) indicating that ensuring a precise localisation of current flow may not be guaranteed even with accurate electrode placement (Datta et al., 2011). In the realm of WM research, there is a consensus that anodal electrode placement over DLPFC and surrounding areas (e.g., F3, F4, AFz) is a suitable choice. However, the placement of cathodal electrodes varies considerably depending on the specific goals of the study, as noted in research by Thair and colleagues (2017) (Thair et al., 2017).

In our model, the stimulation also targeted the DLPFC, extending the stimulation area to potentially cover the FPN. The variability in methodologies across studies could account for the inconsistent findings regarding the use of tDCS. This variability encompasses differences in samples, treatment frequency, duration, current intensity, electrode size, and localisation. As the results of meta-analyses show, research in this field involves stimulation durations ranging from 5 to 30 minutes, with intensities typically falling between 1 and 3 mA. The recommended safety threshold is 2 mA, and electrodes between 25 cm2 and 35 cm2 appear to be a suitable choice for cognitive rehabilitation, as suggested by various studies.

Based on recommendations from existing literature, we followed the prescribed methodology, deviating only from the selection of cathodal electrode placement to ensure a broader stimulation area. As a result, it can be deduced that the specific positioning of the cathode electrode employed in this experiment may be less conducive to eliciting positive changes in executive functions. It is crucial to note, however, that our model revealed a peak current flow intensity/electric field (~0.39 V/m), almost equivalent to that of a 1 mA anodal stimulation (~0.49 V/m), as calculated by Esmaeilpour and colleagues (2018) (Esmaeilpour et al., 2018). The expanded stimulation area could account for this similarity. Our results support the notion that targeted and higher-intensity tDCS may be imperative for rehabilitation purposes

to instigate meaningful behavioural changes. Conversely, previous studies have documented objectively measurable electrophysiological alterations associated with WM function (Kanske & Kotz, 2010; Scharinger et al., 2015).

Our observations are in contrast to recent results by Otstavnov and colleagues (2024), who reported significant improvements in WM accuracy and recall speed using high-definition tDCS (HD-tDCS) targeting the FPN during a complex span task in healthy young adults. Although their sample is significantly different from ours, their results further support the possibility of stimulating the FPN. Parietal areas are known to facilitate stimulus processing and temporal storage, while frontal regions are critically involved in higher-order processes (Otstavnov et al., 2024). The discrepancy between our results and the positive results reported by Otstavnov et al. may be due to several factors, including differences in stimulation accuracy (conventional tDCS vs. HD-tDCS), task sensitivity or the neurobiological profile of the populations studied. Importantly, heterogeneity, impaired cortico-cortical connectivity and reduced neuroplasticity are common in stroke patients. All these may weaken the effectiveness of otherwise effective neuromodulation approaches in healthy samples. Therefore, future research should explore the use of optimised stimulation protocols (e.g. HD-tDCS) coupled with targeted cognitive tasks and consider the use of pattern stratification or neuroimaging-based modelling.

Finally, in the AT group, we applied online tDCS (stimulation combined with training) but did not observe significant differences from the ICCT combined with sham tDCS. The absence of an evident effect from the tDCS treatment complicates the determination of whether online tDCS stimulation was more beneficial than offline stimulation within the current experimental design. However, this does not imply that no benefits can be anticipated from offline stimulation, as Hill and colleagues (2016) demonstrated, who identified a positive impact of offline anodal tDCS stimulation on WM among healthy individuals (Hill et al., 2016). Notably, the existing literature tends to have some limitations in addressing less favourable effects of tDCS, given that adverse or null impact are less likely to be published in this field. This aspect may shape our assumptions regarding the effectiveness of non-invasive brain stimulation techniques on cognitive functions (Kekic et al., 2016). Together, these considerations raise the uncertainty about the efficacy of tDCS in post-stroke cognitive rehabilitation and also highlight the need to explore alternative cognitive interventions.

Using Inhibitory Control Training to Enhance Working Memory

In our research, we did not detect a significant time or group interaction as a main effect when examining the overall treatment effect. This raises questions about the actual transfer effect from ICCT to WM. Further clarification is needed to understand why we did not detect a significant transfer effect in tasks requiring more complex EF. Building on the insights of Miyake et al. (2000), one plausible explanation may be that ICCT does not have an overall effect on EFs as a whole, despite being described as a complex system (Miyake et al., 2000).

Another point to consider is the possible lack of a reciprocal relationship between updating and inhibition, or the idea that the relationship between updating and inhibition functions differently in healthy individuals than in stroke patients. In addition, we cannot ignore the possibility that prolonged training of inhibitory control functions may exhaust CE processes, as suggested by Hedden and Park (2001). This possible depletion could explain the lack of improvement observed in complex WM measures (Hedden & Park, 2001).

However, there is also the question of whether, in clinical practice and in everyday life, instrumental electrophysiological measurements or neuropsychological tests should be considered as indicators of a successful rehabilitation method. It is important to point out that the majority of studies on cognitive training tasks do not show any improvement in trained functions anyway (Melby-Lervåg et al., 2016). Moreover, some studies have documented positive changes in untrained domains and in targeted cognitive skills, just as we found in our meta-analysis (Payne & Stine-Morrow, 2017). That is, presumably the detection of an effect depends largely on the setting of the experiments as well as on the characteristics of the population under study. Finally, the observed improvement trend in verbal short-term memory (DSTF) may also suggest that our ICCT training put more load on EF fu and complex WM, while putting less load on pure storage tasks. This may explain why only phonological memory improved, while complex WM or visual short-term memory showed no improvement. The lack of the latter may be partly explained by the electrode placement of the tDCS: the cathode electrode was placed over the parietal areas, which are close to the areas involved in visuospatial processing, and thus may have had an inhibitory effect. This points to the key role of appropriate electrode placement in the combination of cognitive training and neuromodulation. Future research would benefit from separating training-specific effects from possible stimulation interference in different cognitive domains.

Using Large-scale Stimulation and Cognitive Training to Enhance Affective Control

In terms of affective regulation, our results showed clinically significant improvements in BDI scores, especially in the combined tDCS (AT) group. In addition, we observed positive trends in the HAM-D scale, but no trend-like effect was seen in the anxiety tests (STAI-S, STAI-T). However, these effects were not consistent, so their clinical significance requires cautious interpretation. Although our original hypothesis expected that combined active tDCS would alleviate mood symptoms, this was only partially confirmed. Similarly, our additional hypothesis - that ICCT would enhance the effect of tDCS - was only partially confirmed. These findings are similar to previous findings that depressive symptoms (PSD) are more modifiable than anxiety symptoms (PSA). The changes in BDI scores in the AT group is consistent with studies by Li and colleagues (2022), while the more modest changes in PSA are consistent with previous findings by Kulshresthaa and colleagues (2022) (Kulshresthaa et al., 2022). Notably, these studies highlight stronger effects when CCT is combined with tDCS. However, despite the significant reduction in BDI scores observed in the AT group, it is important to note that baseline depression scores were higher in this group, which may have provided a more contrasting measure of improvement, but were also significant in practical clinical comparisons.

We also hypothesised that affective symptoms may be influenced not only by the DLPFC, but also by a wider cortical network involving frontoparietal structures. However, our stimulation protocol targeting this area did not result in a reduction in test scores. This suggests that focal stimulation of the DLPFC may be more effective in mood regulation than stimulation of the broader frontoparietal network. While Li and colleagues (2022) reported on the overall efficacy of tDCS, our results, as well as those of Garcia (2020) and Stein and colleagues (2020), suggest that the location of stimulation may be critical (Garcia et al., 2020; Stein et al., 2020). In terms of PSA, our results and previous research suggest that tDCS alone is unlikely to lead to a strong improvement. Even in non-stroke patient populations with anxiety, anxiety-related outcomes appear to be less responsive to tDCS unless combined with medication or cognitive-behavioral therapy (Stein et al., 2020). This underscores the limited and understudied utility of tDCS in the treatment of PSA.

It should also be noted that CCT has received less attention in affective rehabilitation than tDCS. However, its potential accessibility and its benefits in cognitive factors may make it a promising tool for this purpose. Although the mechanism of action of CCT in mood regulation is still less clearly defined, several studies suggest that cognitive enhancement may

indirectly improve mood and quality of life (Nie et al., 2022; Van de Ven et al., 2016) reason for this may be an improvement in the quality of information processing. CCTs are available in a variety of formats - including memory, attention and language-based modules - and thus may influence mood through improving cognitive processes. As it has been pointed out before, this may reflect the limits of CCT in neurologically affected populations. Cognitive control deficits are core features of stroke-related dysfunction, and CCT may be more effective in populations without such impairments. Future research should investigate which types of CCTs are best suited for affective modulation in clinical populations.

Overall, our findings suggest that neither tDCS nor CCT alone produces strong, clinically meaningful effects on mood in post-stroke patients. Although some improvement in depressive symptoms was seen; the absence of anxiety modulation and the non-significant effects of CCT point to the need for further research.

Limitations

Our studies have several limitations. First, the sample size in our empirical study was relatively small, potentially limiting statistical power and the ability to detect subtle treatment effects. The heterogeneity of stroke patients - in terms of lesion location, chronic condition and cognitive profile - may also have influenced the variables. The lack of follow-up evaluations also limits conclusions on the sustainability of observed changes. In the meta-analysis, although we were able to include a broader sample base (e.g. DSTF (n = 384), DSTB (n = 193) and VSTF (n = 323)), some WM sub-domains were under-represented in the tDCS studies. Most of the included studies were short-term and lacked long-term follow-up, making it difficult to assess lasting changes. Possible publication bias and language restrictions (only English-language RCTs were included from different countries) may also have affected the results. Together, these limitations suggest that although promising results were obtained, especially for CCT, the results should be interpreted with caution and future research should use larger, more homogeneous clinical samples with well-controlled protocols and longer follow-up.

CONCLUSION

This work investigated the effects of tDCS and CCT on WM and affective symptoms in post-stroke patients, through a systematic review with meta-analysis and empirical studies. The novelty of our research lies in its exploration of a relatively understudied area using a combined intervention approach with an alternative stimulation protocol and inhibitory control-based

cognitive training. Although the empirical interventions did not result in significant improvements in overall WM parameters or mood symptoms, positive statistically significant changes were observed, particularly in short-term memory tasks (DSTF) and in the reduction of depressive symptoms (as measured by the BDI) in the combined (tDCS + CCT) group. Furthermore, our meta-analysis provided additional support for the effectiveness of CCT, especially in improving visuospatial (VSTF) and complex WM subcomponents (DSTB). In contrast, the evidence for tDCS as a stand-alone intervention remained inconclusive, largely due to methodological differences and limited available data. Taken together, our findings suggest that CCT appears to be a preferable intervention compared to tDCS solely. However, our empirical results also indicate that the combination of tDCS and CCT led to the most pronounced changes across cognitive and affective parameters, supporting the potential benefit of integrating these methods.

Importantly, the stimulation montage used in our empirical protocol - targeting midline frontal and parietal regions (AFz–Pz) - did not showed robust effects, suggesting that this specific electrode configuration may not have been optimal for the studied population. This outcome highlights the need for refining stimulation protocols and individualizing interventions based on network connectivity and lesion characteristics. Due to the small sample size, heterogeneity of participants, and lack of long-term follow-up, the results should be interpreted with caution. Nonetheless, this thesis contributes valuable empirical and meta-analytic evidence to the field of cognitive rehabilitation and underscores the importance of future research with larger, homogeneous samples, long-term assessments, and optimally designed combined intervention protocols to clarify the synergistic potential of tDCS and CCT in post-stroke recovery.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1.: Results of Sensitivity Analysis

Outcome	Int.	SDM	95% IC	Z/P (Effect)	I^2	No. S.	Removed studies.
Before analysis							
DSTF	CCT	0.30	[-0.01, 0.61]	1.93/0.05	50%	8	Bo (2019), Westerberg (2017)
VSTF	CCT	0.29	[-0.01, 0.59]	1.89/0.06	40%	7	Wentink (2016)
After analysis							
DSTF	CCT	0.08	[-0.15, 0.32]	0.70/0.47	0%	6	
VSTF	CCT	0.42	[0.15, 0.69]	3.05/0.002	0%	6	

Results of sensitivity analyses for the Digit Span Forward Test (DSTF) and Visual Span Forward Test (VSTF) in CCT interventions, showing standardized mean differences (SMD), 95% confidence intervals, Z- and p-values, heterogeneity (I^2), number of studies included, and studies removed to reduce heterogeneity. Results are presented before and after the exclusion of outlier studies.

Supplementary Table 2: Results of meta-regression in the case of CCT

Moderator	No of comparisons (k)	Z	p	Risk ratio estimate (95% CI)	Tau^2/Q
CCT					
Digit Span Test Forward (DSTF)					
Age	8				0.043/9.911
Intercept		1.24	0.217	-1.441 (3.728 to 0.845)	
Moderator		1.49	0.135	0.029 (0.009 to 0.067)	
Duration	8				0.040/9.692
Intercept		0.40	0.692	-0.129 (-0.767 to 0.509)	
Moderator		1.40	0.161	0.011 (-0.004 to 0.027)	
No of sessions	8				0.109/13.907
Intercept		0.82	0.413	0.436 (-0.609 to 1.483)	
Moderator		0.26	0.796	0.005 (-0.040 to 0.031)	
Digit Span Backward Test (DSTB)					
Age	4				0/0.364
Intercept		0.37	0.707	1.418 (-5.968 to 8.804)	
Moderator		0.27	0.748	-0.017 (-0.138 to 0.104)	
Duration	4				0/0.387
Intercept		1.03	0.302	0.323 (-0.291 to 0.938)	
Moderator		0.23	0.819	0.002 (-0.017 to 0.022)	
No of sessions	4				0/0.424
Intercept		0.78	0.434	0.336 (-0.506 to 1.178)	
Moderator		0.13	0.900	0.001 (-0.024 to 0.027)	
Visual Span Forward Test (VSTF)					
Age	7				0.092/10.082
Intercept		0.04	0.970	0.127 (6.373 to 6.626)	
Moderator		0.05	0.957	0.002 (0.105 to 0.111)	
Duration	7				0.093/9.601
Intercept		0.55	0.580	0.247 (-0.629 to 1.123)	
Moderator		0.14	0.888	0.002 (-0.024 to 0.028)	
No of sessions	7				0.070/8.315
Intercept		1.59	0.111	0.599 (-0.137 to 1.337)	
Moderator		0.89	0.373	0.009 (-0.030 to 0.011)	

Results of meta-regression analyses for CCT interventions on the Digit Span Forward Test (DSTF), Digit Span Backward Test (DSTB), and Visual Span Forward Test (VSTF). The table presents the number of comparisons (k), Z- and p-values, risk ratio estimates with 95% confidence intervals, and heterogeneity statistics (Tau^2/Q) for each potential moderator (participant age, session duration, number of sessions). None of the moderators showed a statistically significant effect on outcomes.

Supplementary Table 3: Baseline characteristics of the empirical sample

	Sample	AT group	A group	T group	
	Mean SD (±)	Mean SD (±)	Mean SD (±)	Mean SD (±)	Between Group Significance (*p*)
Age	59.68 11.10	54.27 12.97	63.20 9.63	61.54 9.36	.135
Education (years)	12.03 3.40	11.36 3.10	11.60 3.13	12.92 3.88	.493
ACE	76.31 9.89	75.45 9.88	71.50 8.37	79.92 10.00	.084
Gender (male/female)	22/13	6/5	5/5	11/3	.341
Stroke localization (left/right/both or subcortical)	12/12/11	5/2/4	3/5/2	4/5/5	.626
Elapsed time after stroke (within three months/after three months)	19/16	6/5	7/3	6/8	.435

The table summarises the demographic and clinical baseline data for the total sample and the three experimental groups (AT, A and T). Variables include age, education (years), ACE scores, sex, stroke location and time since stroke. Data are presented as mean ± SD for continuous variables and as numbers for categorical variables, with *p*-values indicating no significant difference between groups. Abbreviations: Active tDCS treatment (A), sham tDCS treatment with ICCT (T), active tDCS treatment with ICCT (AT).

Supplementary Table 4: Baseline and post-testing data of the sample

	Baseline (±SD)					Post-testing (±SD)			
Measure	Sample	AT group (n=11)	T group (n=14)	A group (n=10)	Baseline Difference (*p*)	Sample	AT group (n=11)	T group (n=14)	A group (n=10)
BDI	11.80 (8.63)	17.36 (8.95)	9.21 (6.53)	9.30 (8.69)	.056	7.00 (7.51)	9.45 (6.88)	9.86 (8.11)	7.70 (7.90)
HAM-D	7.29 (5.92)	9.45 (6.49)	8.50 (5.84)	2.78 (2.17)	.002*	4.86 (4.25)	6.82 (3.28)	5.00 (5.16)	2.50 (2.64)
STAI - S	40.30 (12.70)	44.50 (10.00)	39.30 (9.86)	37.20 (18.02)	.362	36.60 (11.60)	37.90 (11.38)	35.30 (9.78)	37.10 (4.67)
STAI-T	43.00 (12.10)	46.20 (10.74)	39.40 (7.08)	36.90 (16.92)	.075	36.80 (9.55)	37.90 (9.43)	38.10 (10.22)	33.80 (8.99)

The table presents the baseline and post-test scores for the full sample and the three experimental groups (AT, A and T) for the four outcome measures: the Beck's Depression Inventory (BDI), the Hamilton Assessment of Depression Scale (HAM-D), the State Anxiety Inventory (STAI-S) and the Trait Anxiety Inventory (STAI-T). Mean scores and standard deviations (SD) are given for each group. Baseline differences between groups are analysed, with p-values given to indicate statistical significance. For HAM-D, a significant baseline difference was observed (p =.002). Post-test results show between-group variation, reflecting the effect of interventions on these scores. Abbreviations: Active tDCS treatment (A), sham tDCS treatment with ICCT (T), active tDCS treatment with ICCT (AT).

Supplementary Table 5: Correlation Matrix for Pre- and Post-Treatment Measures Across Depression and Anxiety Scales

		Pre BDI	Pre STAI-S	Pre STAI-T	Pre HAM-D	Post BDI	Post STAI-S	Post STAI-T	Post HAM-D
Pre BDI	r								
	df								
	p-value								
Pre STAI-S	r	0.60							
	df	33							
	p-value	< .001							
Pre STAI-T	r	0.57	0.86						
	df	32	32						
	p-value	< .001	< .001						
Pre HAM-D	r	0.58	0.50	0.35					
	df	32	32	31					
	p-value	< .001	0.003	0.043					
Post BDI	r	0.75	0.55	0.43	0.58				
	df	33	33	32	32				
	p-value	< .001	< .001	0.010	< .001				
Post STAI-S	r	0.45	0.61	0.54	0.39	0.56			
	df	33	33	32	32	33			
	p-value	0.007	< .001	0.001	0.021	< .001			
Post STAI-T	r	0.68	0.75	0.65	0.71	0.79	0.64		
	df	33	33	32	32	33	33		
	p-value	< .001	< .001	< .001	< .001	< .001	< .001		
Post HAM-D	r	0.54	0.47	0.28	0.68	0.60	0.35	0.58	
	df	33	33	32	32	33	33	33	
	p-value	< .001	0.004	0.106	< .001	< .001	0.040	< .001	

The table presents the Pearson correlation coefficients and p-values for relationships between pre-and post-treatment measures of depression and anxiety scales, including the Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI-S and STAI-T), and Hamilton Depression Rating Scale (HAM-D). Strong correlations were observed across several measures, particularly between Post STAI-T and Post BDI (r=.79,p<.001) and between Pre BDI and Post BDI (r=.75,p<.001). These findings highlight consistent relationships between depressive and anxiety-related outcomes before and after treatment.

Supplementary Table 6: Linear Mixed-effects Model statistics for neuropsychological tests related to working memory in the experimental groups - Intercepts and slopes

			DSTF	DSTB	CBTT	LST	TMT-A (sec)	TMT-B (sec)
Intercepts	AT	T1 scores	4.66	2.67	3.14	1.66	155.43	402.39
		SE	0.25	0.24	0.28	0.23	32.75	87.12
		95% CI	[4.15, 5.16]	[2.19, 3.15]	[2.56, 3.71]	[1.21, 2.12]	[88.49, 222.36]	[225.25, 579.53]
	A	T1 scores	4.47	2.82	3.74	1.48	125.40	463.05
		SE	0.25	0.24	0.29	0.23	33.22	88.79
		95% CI	[3.96, 4.98]	[2.33, 3.31]	[3.16, 4.33]	[1.02, 1,95]	[57.51, 193.29]	[282.60, 643.50]
	T	T1 scores	4.62	3.01	3.99	2.05	88.67	302.00
		SE	0.22	0.21	0.26	0.21	29.74	79.10
		95% CI	[4.15, 5.16]	[2.58, 3.44]	[3.47, 4.51]	[1.63, 2.47]	[22.87, 144.48]	[141.12, 462.88]
Slopes	AT	T2 scores	5.11	3.22	3.68	2.06	138.79	399.39
		95% CI	[4.61, 5.61]	[2.74, 3.69]	[3.11, 4.26]	[1.60, 2.52]	[71.85, 205.73]	[222.25, 576.53]
		SE	0.25	0.24	0.28	0.23	32.75	87.12
		MD	0.45	0.55	0.54	0.40	-16.64	-3.00
		Cohen's d (Pre-post)	0.54	0.69	0.58	0.52	0.15	0.01
	A	T2 scores	4.27	2.92	3.54	1.65	113.00	387.31
		95% CI	[3.76, 4.78]	[2.43, 3.41]	[2.96, 4.13]	[1.18, 2.12]	[45.11, 180.89]	[202.74, 571.87]
		SE	0.25	0.24	0.29	0.23	33.22	91.06
		MD	-0.20	0.10	-0.20	0.16	-12,40	-75.74
		Cohen's d (Pre-post)	0.25	0.13	0.21	0.23	0.12	0.26
	T	T2 scores	4.97	3.08	3.85	2.19	97.39	345.72
		95% CI	[4.52, 5.43]	[2.65, 3.51]	[3.33, 4.37]	[1.78, 2.61]	[36.58, 158.19]	[184.83, 506.60]
		SE	0.25	0.21	0.26	0.20	29.74	79.10
		MD	0.35	0.07	-0.14	0.14	8.72	43.72
		Cohen's d (Pre-post)	0.39	0.08	0.14	0.18	0.07	0.14

The table presents the intercept (baseline (T1) scores) and slope values (indicating the rate of change over time (T2)) across the groups. Mean differences (MD) reflect the average difference between baseline and post measurements. Cohen's d (Pre-post): represents the effect size for the change within each group from pre- to post-intervention. Abbreviations: DSTF=Forward Digit Span Task; DSTB=Backward Digit Span Task; LST=Listening Span Task; CBTT=Corsi Block Tapping Task; TMT = Trail Making Test; T1=Pre-measurement (Baseline); T2=Post-measurement; SE=Standard Error; CI=Condifence Interval; A=Active tDCS without ICCT; T=Sham tDCS with ICCT; AT=Active tDCS with ICCT.

Supplementary Table 7: Linear Mixed-effects Model statistics for neuropsychological tests related to working memory in the experimental groups - Main effects and interactions

			DSTF	DSTB	CBTT	LST	TMT-A (sec)	TMT-B (sec)
Main effects and Interactions	**Time**	*b*	0.20	0.24	0.07	0.23	-5.11	-11.68
	T1/T2	*SE*	0.12	0.14	0.15	0.08	7.68	33.28
		t-value	1.84	1.67	0.46	2.96	-0.67	-0.35
		p	0.076	0.105	0.651	**0.006***	0.511	0.728
	Group							
	T/AT	*b*	-0.09	0.10	0.51	0.26	-56.58	-77.03
		SE	0.31	0.27	0.34	0.29	43.39	111.53
		t-value	-0.28	0.38	1.49	0.89	-1.30	-0.69
		p	0.781	0.704	0.149	0.381	0.203	0.496
	A/AT	*b*	-0.51	-0.08	0.23	-0.30	-27.91	24.29
		SE	0.34	0.30	0.37	0.32	47.49	122.53
		t-value	-1.51	-0.25	0.62	-0.93	-0.59	0.20
		p	0.142	0.801	0.541	0.362	0.562	0.844
	Group x Time							
	T/AT	*b*	-0.10	-0.47	-0.69	-0.26	30.35	46.71
		SE	0.26	0.34	0.35	0.19	18.12	77.09
		t-value	-0.37	-1.40	-1.97	-1.37	1.67	0.61
		p	0.713	0.171	0.057	0.182	0.104	0.549
	A/AT	*b*	-0.65	-0.45	-0.75	-0.23	4.24	-72.74
		SE	0.28	0.37	0.38	0.20	19.65	85.74
		t-value	-2.30	-1.21	-1.97	-1.13	0.22	0.85
		p	**0.028***	0.234	0.058	0.267	0.831	0.403
	Effect size of interaction	f^2	0.143	0.018	0.000	0.086	0.000	0.000

The table summarizes main effects and interactions for WM tests across groups, showing time effects (T1 vs. T2), group comparisons (A vs. T vs. AT), and effect sizes, with significant results ($p < 0.05$) marked by *. Estimate (b) values represent the predicted changes in test scores, reflecting how factors influence the measured scores across conditions. T-values, and p-values represent model parameters, while f^2 represent the effect size of interaction. Abbreviations: SE=Standard Error, DSTF=Forward Digit Span Task; DSTB=Backward Digit Span Task; LST=Listening Span Task; CBTT=Corsi Block Tapping Task; TMT = Trail Making Test; T1=Pre-measurement (Baseline); T2=Post-measurement; A=Active tDCS without ICCT; T=Sham tDCS with ICCT; AT=Active tDCS with ICCT.

Supplementary Table 8: Linear Mixed-effects Model statistics for neuropsychological tests related to working memory in the experimental groups - Demographic and clinical factors

		DSTF	DSTB	CBTT	LST	TMT-A (sec)	TMT-B (sec)
Age	*b*	0.01	-0.00	-0.02	-0.01	2.12	6.74
	SE	0.01	0.01	0.01	0.01	1.85	4.75
	t-value	0.76	-0.26	-1.33	-1.20	1.14	1.42
	p			0.195	0.242	0.262	0.168
Time since stroke (m)	*b*	-0.01	-0.00	-0.00	-0.00	-0.36	-0.16
	SE	0.00	0.00	0.00	0.00	0.59	1.51
	t-value	-1.56	-1.13	-0.64	-0.62	-0.51	-0.11
	p	0.129	0.269	0.528	0.543	0.544	0.916
Location of lesion							
Right/Left	*b*	-0.18	-0.28	-0.03	-0.25	4.21	60.19
	SE	0.32	0.28	0.35	0.30	44.54	114.46
	t-value	-0.55	-0.99	-0.09	-0.83	0.09	0.53
	p	0.585	0.332	0.931	0.414	0.925	0.603
Both sides or subcortical/Left	*b*	-0.20	-0.31	-0.26	-0.30	37.31	87.75
	SE	0.31	0.27	0.34	0.29	43.44	112.17
	t-value	-0.64	-1.15	-0.76	-1.03	0.86	0.78
	p	0.528	0.262	0.451	0.310	0.398	0.441
Gender (F/M)	*b*	-0.08	-0.03	-0.68	-0.21	-27.64	-19.96
	SE	0.30	0.26	0.33	0.28	41.86	107.80
	t-value	-0.27	-0.13	-2.05	-0.75	-0.66	-0.19
	p	0.789	0.897	0.050	0.458	0.515	0.854

The table presents the model statistics for WM-related neuropsychological tests, assessing the impact of demographic and clinical factors, including age, time since stroke, lesion location, and gender. Estimate values show how each factor affects the test scores. T-values, and p-values represent model parameters. Abbreviations: SE=Standard Error, DSTF=Forward Digit Span Task; DSTB=Backward Digit Span Task; LST=Listening Span Task; CBTT=Corsi Block Tapping Task; TMT = Trail Making Test.

Supplementary Table 9: Results of Bayesian Repeated Measures ANOVA for PSD

Beck's Depression Inventory (BDI)										
Model Comparison					**Post Hoc Comparison**					
Models	**P(M|data)**	**P(Incl|data)**	**BF10**	**BFIncl**	**Levels**		**Prior Odds**	**Posterior Odds**	**$BF_{10,U}$**	**Error %**
Null model	0.00		1.00		**Pre-Post Factor**					
Pre-Post Factor	0.02	.99	4.28	101.47	Level 1	Level 2	1.00	4.18	4.18	.00
Condition	0.00	.98	0.63	30.82	**Condition**					
Pre-Post Factor + Condition	0.01	.97	2.60	113.17	AT	T	.59	.55	.93	.01
Pre-Post Factor + Condition + Pre-Post Factor * Condition	0.97		240.69			A	.59	.71	1.20	.01
					T	A	.59	.19	.32	.01
Hamilton Depression Rating Scale (HAM-D)										
Null model	.01		1.00		**Pre-Post Factor**					
Pre-Post Factor	.10	.97	16.44	20.03	Level 1	Level 2	1.00	18.35	18.35	.00
Condition	.03	.90	4.42	5.76	**Condition**					
Pre-Post Factor + Condition	.69	.18	115.86	.89	AT	T	.59	.23	.39	.01
Pre-Post Factor + Condition + Pre-Post Factor * Condition	.18		30.50			A	.59	171.61	292.16	.00
					T	A	.59	7.65	13.02	.00

The Hamilton Depression Rating Scale (HAM-D) and Beck's Depression Inventory (BDI) outcomes of the Bayesian Repeated Measures ANOVA are summarized in the table. The models assess the effects of Pre-Post Factor, Condition, and their interaction on scores, reporting posterior probabilities P(M|data), inclusion probabilities P(Incl|data), Bayes factors (BF10), and inclusion Bayes factors (BFIncl). For BDI, the most robust model includes the Pre-Post Factor and Condition interaction (BF10=240.69), while the Pre-Post Factor model for HAM-D shows significant effects (BF10=115.86). Post-hoc comparisons reveal pairwise group differences using adjusted posterior odds and Bayes factors. These findings highlight the influence of treatment conditions and pre-post changes on depressive symptoms. Abbreviations: Active tDCS treatment (A), sham tDCS treatment with ICCT (T), active tDCS treatment with ICCT (AT).

Supplementary Table 10: Results of Bayesian Repeated Measures ANOVA for PSA

Spielberger's State Anxiety Inventory (STAI-S)										
Model Comparison					**Post Hoc Comparison**					
Models	**P(M|data)**	**P(Incl|data)**	**BF10**	**BFIncl**	**Levels**		**Prior Odds**	**Posterior Odds**	**$BF_{10,U}$**	**Error %**
Null model	.31		1.00		**Pre-Post Factor**					
Pre-Post Factor	.39	.58	1.26	.93	Level 1	Level 2	1.00	1.11	1.11	.02
Condition	.11	.31	.36	.30	**Condition**					
Pre-Post Factor + Condition	.15	.05	.48	.22	AT	T	.59	.34	.58	.01
Pre-Post Factor + Condition + Pre-Post Factor * Condition	.05		.17			A	.59	.26	0.44	.01
					T	A	.59	.17	.29	.01
Spielberger's State Anxiety Inventory (STAI-T)										
Null model	.16		1.00		**Pre-Post Factor**					
Pre-Post Factor	.37	.75	2.33	2.03	Level 1	Level 2	1.00	2.13	2.13	.00
Condition	.09	.47	.55	.58	**Condition**					
Pre-Post Factor + Condition	.21	.17	1.28	.84	AT	T	.59	.26	.45	.01
Pre-Post Factor + Condition + Pre-Post Factor * Condition	.17		1.09			A	.59	.64	1.09	.01
					T	A	.59	.30	.51	.01

The Spielberger's State and Trait Anxiety Inventory (STAI-S and STAI-T) outcomes from Bayesian Repeated Measures ANOVA are summarized in the table. For STAI-S, the Pre-Post Factor model showed moderate support (BF10=1.26), while for STAI-T, more robust support was observed (BF10= 2.33), indicating pre-post changes were notable for trait anxiety. No significant interaction effects or group-level differences were detected, suggesting that changes were primarily associated with time rather than treatment conditions. Abbreviations: Active tDCS treatment (A), sham tDCS treatment with ICCT (T), active tDCS treatment with ICCT (AT).

Supplementary Table 11: Proportion of Participants Meeting MCID Criteria Across Groups for BDI

Subject	Group	Pre-Post Change	Absolute value of change	BDI change >5	BDI change > 29.64%	Direction	MCID Criterion I.	MCID Criterion II.
1.00	T	-1.00	1.00	no	0.04	improved	no	no
2.00	T	1.00	1.00	no	0.50	deteriorated	no	no
3.00	T	0.00	0.00	no	0.00	unaltered	no	no
4.00	T	4.00	4.00	no	0.50	deteriorated	no	no
5.00	T	-3.00	3.00	no	0.43	improved	no	yes
6.00	T	10.00	10.00	yes	0.77	deteriorated	no	no
7.00	T	-4.00	4.00	no	0.36	improved	no	yes
8.00	T	-6.00	6.00	yes	0.46	improved	yes	yes
9.00	T	2.00	2.00	no	0.13	deteriorated	no	no
10.00	T	0.00	0.00	no	0.00	deteriorated	no	no
11.00	T	8.00	8.00	yes	0.73	deteriorated	no	no
12.00	T	-2.00	2.00	no	1.00	improved	no	yes
13.00	T	0.00	0.00	no	0.00	unaltered	no	no
14.00	T	0.00	0.00	no	1.00	unaltered	no	no
15.00	A	-3.00	3.00	no	0.11	improved	no	no
16.00	A	5.00	5.00	no	0.71	deteriorated	no	no
17.00	A	-6.00	6.00	yes	0.60	improved	yes	yes
18.00	A	-5.00	5.00	no	1.00	improved	no	yes
19.00	A	-6.00	6.00	yes	0.67	improved	yes	yes
20.00	A	0.00	0.00	no	1.00	unaltered	no	no
21.00	A	0.00	0.00	no	0.00	unaltered	no	no
22.00	A	4.00	4.00	no	1.00	deteriorated	no	no
23.00	A	-1.00	1.00	no	0.11	improved	no	no
24.00	A	-4.00	4.00	no	0.20	improved	no	no
25.00	AT	-5.00	5.00	no	0.24	improved	no	no
26.00	AT	-1.00	1.00	no	1.00	improved	no	yes
27.00	AT	-11.00	11.00	yes	0.46	improved	yes	yes
28.00	AT	-8.00	8.00	yes	0.53	improved	yes	yes
29.00	AT	-8.00	8.00	yes	0.36	improved	yes	yes
30.00	AT	-9.00	9.00	yes	1.00	improved	yes	yes
31.00	AT	0.00	0.00	no	0.00	unaltered	no	no
32.00	AT	-17.00	17.00	yes	0.50	improved	yes	yes
33.00	AT	-7.00	7.00	yes	0.54	improved	yes	yes
34.00	AT	-4.00	4.00	no	0.40	improved	no	yes
35.00	AT	-17.00	17.00	yes	0.77	improved	yes	yes

Table of criteria used to define the minimum clinically important difference (MCID). It includes thresholds for the direction of improvement, absolute change in score, and percentage of baseline score. as well as data for each participant used to assess whether these criteria were met. Active tDCS treatment (A), sham tDCS treatment with ICCT (T), active tDCS treatment with ICCT (AT); Beck's Depression Inventory (BDI), MCID Criterion I.: Assesses meaningful improvement by considering both BDI change >5 and BDI change > 29.64% in participants' scores; MCID Criterion II.: Assesses meaningful improvement by considering only BDI change > 29.64% in participants' scores