Effects of transcranial direct current stimulation on surgical skills acquisition and retention.

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1) Brief abstract in English

This thesis examines how transcranial direct current stimulation (TDCS) can improve the acquisition of motor skills during surgical training. By delivering low amplitude electrical current to the scalp, TDCS modifies neuronal excitability without causing any harm to the patient. By depolarizing or hyperpolarizing neurons' resting membrane potentials, the technique can influence cortical excitability and facilitate or prevent the production of action potentials, respectively. Previous research has investigated how TDCS might improve coordination and fine motor task performance.

In this thesis we performed a systematic review, to explore the available literature on the use of TDCS to facilitate motor skill learning in the context of surgical education. We also performed a randomized, sham-controlled trial, surgical skills were evaluated by comparing the time, accuracy, and total mistakes during a surgical task in participants receiving TDCS, sham-TDCS, and a control group at time point baseline (BL), post training (PT) and retention phase (RT).

2) Brief abstract in french

Cette thèse examine comment la stimulation transcrânienne à courant continu (TDCS) peut améliorer l'acquisition des habiletés motrices pendant la formation chirurgicale. En délivrant un courant électrique de faible amplitude au cuir chevelu, la stimulation transcrânienne à courant continu (TDCS) modifie l'excitabilité neuronale sans nuire au patient. En dépolarisant ou en hyperpolarisant les potentiels de membrane au repos des neurones, la technique peut influencer l'excitabilité corticale et faciliter ou empêcher la production de potentiels d'action, respectivement. La recherche du passé a étudié comment le TDCS pourrait améliorer la coordination et la performance des tâches motrices fines.

Dans cette thèse, nous avons effectué une revue systématique afin d'explorer la littérature disponible sur l'utilisation du TDCS pour faciliter l'apprentissage des habiletés motrices dans le contexte de l'enseignement chirurgical. Nous avons également réalisé un essai randomisé contrôlé par simulation, les compétences chirurgicales ont été évaluées en comparant le temps, la précision et le nombre total d'erreurs au cours d'une tâche chirurgicale chez les participants recevant TDCS, sham-TDCS et un groupe témoin au moment de référence (BL), post-formation (PT) et phase de rétention (RT).

3) Acknowledgements

To my sister †,

to my mother,

to my father.

4) Contribution of authors

Chapter 1 - Effects Transcranial direct current stimulation on surgical skills acquisition. A systematic review.

Ahmed A. Naiem, MD: The author of this thesis wrote the protocol for the systematic review, performed the screening, selection, and qualitative analysis of the selected articles, and wrote the manuscript. **Francisco Reyna-Sepúlveda**: Performed the screening and selection of articles and was involved in the qualitative analysis of the selected articles. Review contributed to the final manuscript. Ibtisam Mahmoud MLIS: literature search. **Marie-Amélie Lukaszewski**: supervised data interpretation, review contributed to the final manuscript. **Elie Girsowicz**: conception and the design of the systematic review, supervised data interpretation and contributed to the final version of the manuscript.

Chapter 2 - Effects of transcranial direct current stimulation on surgical skills acquisition and retention.

Francisco Reyna-Sepulveda: primary role in patients' recruitment and assessment, data acquisition and interpretation and performed the statistical analyses. The author wrote the manuscript. **Ahmed Naiem**: co-supervised data acquisition and he contributed to conception and design of the manuscript. **Marie-Amelie Lukaszewski**: contributed to conception and design of the manuscript. **Alexander Thiel**: contributed to conception and design of the manuscript. **Elie Girsowicz**: recruitment, co-supervised the research project and contributed to conception and design of the manuscript.

5) **List of tables and figures**

Chapter 1

Chapter 2

6) List of Abbreviations

a. TDCS, Transcranial Direct Current Stimulation

b. COVID-19, coronavirus disease 2019

c. SBT, Simulation-based training

d. PMC, primary motor cortex

e. BL, baseline timepoint

f. PT, post training timepoint

g. RT, retention timepoint

h. SD, standard deviation

i. CI, confidence interval

j. PFC, Prefrontal cortex

k. MC, motor cortex

7) Introduction

During the next exposition I will present a comprehensive review of the literature related to TDCS and surgical education, followed by the systematic analysis and the randomized trial we performed.

a. Chapter 1 - Effects of transcranial direct current stimulation on surgical skills acquisition: a systematic review

Rationale of this study: TDCS has been hypothesized to help trainees attain skills faster. No previous systematic review on its relation to surgical skills has been explored.

Objectives of this study: We aimed to explore the available literature on the use of TDCS to facilitate motor skill learning in the context of surgical education.

b. Chapter 2 - Effect of transcranial direct current stimulation on surgical skills acquisition and retention.

Rationale of this study: TDCS with its brain-enhancing potential, in adjunct with simulation-based training may help surgical trainees attain skills faster.

Objectives of this study: Our objective is to evaluate the effect of TDCS on motor skills acquisition and retention before and after training of a surgical task in a randomized control trial, with sham-TDCS group.

8) A comprehensive review of the relevant literature

Recent challenges in Surgical Education, the impact of Covid-19.

The COVID-19 pandemic, which started in 2019 and is still ongoing, has had a significant impact on the healthcare system and surgical education[1]. The outbreak was declared a Public Health Emergency of International Concern by the World Health Organization in January 2020 and a pandemic in March 2020.[2] As of now, more than 3.3 million cases of COVID-19 have been reported in 187 countries and territories, leading to over 235,000 deaths. [3]

In addition to disrupting the lives of millions of people, COVID-19 has forced surgeons to reassess nearly every aspect of their practice. To maintain social distancing and ensure adequate hospital resources, elective surgeries have been cancelled, and clinic hours have been reduced. The contagious nature of the virus has led to the exclusion of learners from clinical teams, and inpatient care teams have downscaled to limit exposure[4]. Resident schedules have changed substantially, and educational curricula have shifted to completely online platforms.[5]

Surgical residents have faced significant challenges during the pandemic, as only urgent or emergency surgery is being performed in many countries.[6] [7] [8] [9] [10] As a result, learning opportunities have decreased, and residents are missing out on hands-on surgical training. Protocols authorizing only essential personnel in the operating room further limit training opportunities, and scarcity in personal protective equipment creates the need for further confinement of residents' opportunities to observe and assist. Additionally, staff surgeons tend to perform simpler cases that used to be delegated to senior residents to reduce operating time and the risk of COVID-19 infection.[11]

In a study published by Aziz et al[12] in 2020 they surveyed 1,102 general surgery residents who reported a significant decline in the number of cases performed during the pandemic and that educational curriculum was shifted toward off-hands didactics. Surgical trainees have been distinctively impacted by these changes. While solutions have been employed for missing in-person educational teachings and seminars, there are no substitutes in place to counterweigh for the reduction of hands-on surgical training during this period.

The Accreditation Council for Graduate Medical Education and other regulators require that residents dealing with suspected or confirmed COVID-19 have ample supervision by trained personnel. The absence of such supervision can result in rescheduled operations to maintain a safe workload.[13] [14] Furthermore, all conferences, congresses, and meetings have been canceled, further reducing opportunities for continuous education of learners.[15] [16] In the hospital floor activities are reduced, and in many attendings may be despatched to the emergency department[17].

Case discussions and departmental meetings are abandoned because of social distancing and staff availability.[18] [19] [20] The redistribution of residents in departments with greater demand in healthcare personnel may tackle crucial service needs but interrupts residency education and may cause issues with regulators and boards. [21] [22] [23]

Surgical residency training involves gaining both theoretical knowledge and necessary skills to perform surgeries safely. While operating room exposure is fundamental to skills acquisition, duty hour restrictions potentially reduce that exposure and have unclear effects on residents' ability to reach milestones. Finally, surgical educators face the challenge of ensuring their residents receive adequate training during this time. It is difficult to predict how long the pandemic will last and what its long-term impact on surgical education will be.[24] [25] [26] [27] [28]

Enhancing Surgical Education: New Technologies

The COVID-19 pandemic has brought about new challenges in surgical education, requiring innovative methods of adaptation. Online learning, virtual consults, telemedicine, simulation, and virtual reality are being incorporated into learners' curricula. However, there are few studies investigating how to enhance these new methods. Nonetheless, this crisis has created a motivation for educational innovations, which could shape the future of surgical education.[29] [30]

Home-based simulation curricula have gained increased interest, as they could ensure the stability of technical skills education during the pandemic, especially in highly technical and demanding surgical specialties. Although most simulation training programs in hospitals have been excluded as non-essential activities, they can be repurposed as rapid and effective training modalities for coronavirus readiness. Simulation-based training (SBT) provides a risk-free method of skill acquisition during surgical tuition and may reduce time to achieve skill proficiency[31].

However, SBT has limitations, including lengthy time requirements with unexceptional effect sizes and inconsistent long-term retention of skills. Therefore, defining methods to enhance SBT is essential to hasten training and improve proficiency in complex skills such as surgery, particularly in a time of decreased hands-on training.[32] One recent example of enhancing SBT is through brain stimulation, which could be electric or magnetic.

Transcranial direct current stimulation (TDCS) in Surgical Education

TDCS has emerged as a promising tool for modulating cognitive and motor skills.[33] TDCS is a form of non-invasive brain stimulation that applies low-amplitude electrical current through the scalp to evoke neuronal excitability, primarily at the sensorimotor cortex. It exerts its effects by altering neuronal membrane potential, either through depolarization or hyperpolarization, which may improve brain function.[34] [35] [36] This excitability is believed to cause changes at the molecular in axons[37] and alter multiple intracellular inflammatory cascades in surrounding non-neuronal cells. [38] [39]

Furthermore, these effects could last long after the electrical stimulus is terminated.[40] TDCS has been applied to modulate the motor cortex, including the primary motor cortex, premotor cortex, supplementary motor areas, and basal ganglia, in motor learning. [41] It may enhance motor learning by modulating synaptic efficacy and cortical connectivity between these areas.[42] Studies have shown that simultaneous TDCS and motor training often result in a marked enhancement of skill acquisition[43], although these data are based on simple tasks rather than more complex motor skills. [44]

Recent studies have suggested that TDCS applied during complex laparoscopic[45] and neurosurgical[46] skill training can improve the rate of skill acquisition, providing initial evidence that TDCS can positively affect surgical skill training. Neuroimaging and neurophysiology findings are starting to explain the potential mechanisms behind this learning enhancement.[47]

Compared with simulators and other educational methods, the cost of TDCS devices is negligible. Maintenance and consumables are economical, and a stimulator can be used many times. TDCS can be trained through videos, guidelines, or courses. Importantly, TDCS can be applied in combination with other methods for enhanced surgical skill acquisition.

TDCS is a tool that can modulate stimulation in specific brain regions in a reversible manner. It has been used in a variety of cognitive, motor, social, and affective domains to study brain-behavior relationships.[48] In healthy populations, it has been shown to temporarily adjust behavior, improve learning, and enhance task performance. [49] In addition to its effects on the primary motor cortex (PMC), TDCS has also been investigated for its potential to improve human performance in strength, fine motor control, and coordination, with reported success. [50] [51] [52]

TDCS has been studied for its potential therapeutic uses in various medical fields. A recent consensus guideline from the International Federation of Clinical Neurophysiology has suggested its potential for modulating neuropathic pain, treating fibromyalgia, depressive disorders, and addiction disorders.[53]

TDCS generalities, electrode placement, parameters, and sham condition.

The TDCS device and consumables come with a neoprene swimming cap and straps to secure the electrodes, a programmer/stimulator connector cable, a power supply, a TDCS stimulator (with batteries inside), a TDCS stimulator parameter programmer, sponge holding bags, electrode cables (red for anodal and black for cathodal), rubber electrodes, a cable connector, conductive EEG gel, measuring equipment (washable pen and measuring tape), and saline (20 ml pouches for easy application).

The duration, intensity, and ramp up/ramp down need to be programmed after placing the electrodes, and it is essential to oversee the participant during stimulation to ensure no distress is experienced. It is also vital to check the impedance levels shown on the stimulator to ensure that stimulation is kept below 5,000 ohms.[54]

To localize the electrode placement, various methods can be used, with the most common being the 10:20 EEG system. It is essential to confirm that the electrodes stay fixed in place during stimulation, considering factors affecting the impact of its location on the task, direction of current flow, participant comfort, and safety. For motor cortex stimulation for fine motor skills, electrodes are positioned in C3 and C4.[55]

Most stimulation durations range between 5 and 30 minutes, with a current intensity between 1 and 2mA. The advisable safety threshold for human studies is 2mA, and this current has also shown to result in excitatory changes. These studies are significant as they exemplify that the outcomes of stimulation duration and intensity are not necessarily linear, and the association between these two variables needs additional investigation. [56] [57] [58]

Sham TDCS acts as a control, simulating cutaneous perceptions that are described on TDCS when started. Sham TDCS does not alter cortical excitability and is considered an efficient blinding technique, particularly for those who have never had TDCS before.[59]

TDCS tolerability and side effects

TDCS appears to be safe, well-tolerated, and relatively simple. There are no reported indications of any serious adverse effects with the use of 1-2mA TDCS. Mild transient side effects may occur, like headache, tingling (most common), fatigue, redness, trouble concentrating, mood changes, and nausea.[60] [61] [62]

9) Chapter 1 - Effects of transcranial direct current stimulation on surgical skills acquisition: a systematic review

a. Manuscript

Effects of transcranial direct current stimulation on surgical skills acquisition: a systematic review

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Abstract

Introduction: Surgical training is opportunity-based and multiple factors including exposure, time, case volume and simulation training contribute to achieving competencies. The COVID-19 pandemic and surgical residents' duty hours restrictions have decreased operative exposure and could affect their ability to attain milestones and competencies. If used as an adjunct in training, transcranial direct current stimulation (TDCS) could enhance performance in strength, fine motor and coordination skills and thus possibly help to attain surgical skills faster. In this systematic review, we aim to explore available literature on the use of TDCS in surgical education. **Methods:** We performed a systematic review of randomized trials (RCT) on Biosis, Cochrane Central, EMBASE, MEDLINE, PsycINFO databases. Studies included compared TDCS to sham in a surgical task involving trainees. Outcomes were grouped into 4 domains to overcome study outcomes' heterogeneity. These domains were: speed of skills acquisition, proficiency, i.e. ability to achieve a pre-determined score/level of proficiency, accuracy and error reduction, and lastly composite outcomes involving more than one domain. **Results:** Four RCT were identified involving 143 participants in total (61 sham, 82 TDCS). All studies utilized simulation training: three in laparoscopic training (peg transfer and pattern cutting), and one in neurosurgery training (tumor resection exercise). The mean age of the participants was 24.5±1.5 years with 58% (n=83) being females and 92% (n=131) being right hand dominant. TDCS use was associated with improved speed of skills acquisition, proficiency, accuracy and a less steep learning curve. Skills decay did not occur at 6 weeks. **Conclusion:** TDCS is a useful, safe adjunct for surgical simulation training. It is associated with improved skills acquisition in both laparoscopic and neurosurgical training tasks. Further research is needed to evaluate its use in other surgical specialties

Introduction

Mechanism of TDCS

Transcranial direct current stimulation (TDCS) is a form of noninvasive brain stimulation where low amplitude electrical current is applied to the scalp through a pair of positively (anode) and negatively charged (cathode) sponge electrodes to modulate neuronal excitability, primarily of the sensorimotor cortex. (1) At a cellular level, TDCS shifts neuronal resting membrane potential by either depolarization or hyperpolarization. (2,3) This shift facilitates or inhibits the generation of action potentials thus modulating the excitability of cortical neurons (4) and possibly altering the function of non-neuronal glia cells. (5,6) These modulatory effects, applied to a specific cortical region could improve certain targeted brain functions such gross and fine motor skills with after effects beyond the stimulation period. (3,7)

Use in medical field

The use of TDCS has been studied in various fields of medicine. A recent international Federation of Clinical Neurophysiology consensus guideline suggested potential therapeutic use in neuropathic pain modulation, fibromyalgia, depressive disorders and addiction disorders. (8) Its effect has been controversial in post stroke rehabilitations of patients with motor dysfunction. (8–11) With its effect on primary motor cortex (PMC) excitability, TDCS has been evaluated as a method to enhance motor skill learning, fine motor task performance and coordination. (12–14)

Use in surgical education

Surgical residency training is challenging as it involves gaining both theoretical knowledge and fine motor skills to perform surgeries safely. Since its inception, it has been structured as an opportunity-based training where trainees' exposure might not be standardized and subsequently their ability to attain expected competencies can vary. (15,16) In order to help trainees achieve competencies, simulation training has been utilized. (17) Moreover, recently imposed duty hour restrictions (DHR) potentially reduce that exposure and have unclear effects on ability to attain milestone and competencies. (18–22) It is also difficult to assess the impact of the current COVID-19 pandemic on attaining competencies. (23) In addition to simulation, TDCS may help trainees to attain skills faster. (24) In this systematic review, we aim to explore available literature on the use of TDCS to facilitate motor skill learning in the context of surgical education.

Materials and Methods

Data sources

We performed a systematic review by searching Biosis (via ClarivateAnalytics); The Cochrane CENTRAL Register of Controlled Trials & Cochrane Database of Systematic Reviews; Embase Classic +Embase; MEDLINE; and PsycINFO The search strategies used text words and relevant indexing to identify Clinical Trials on the effects of TDCS on the acquisition of surgical skills in trainees. The MEDLINE strategy (Appendix 1) was applied to all databases, with modifications to search terms as necessary. No language limits were applied. Search strategies were peer-reviewed by two librarians. In addition, clinical trials registries [clinicaltrials.gov], Food and Drug Administration (FDA) were searched.

Nineteen studies were identified in Web of Science and Scopus (October 20, 2020) by carrying out citation searches for the reference lists of included studies. The Medline strategy was rerun prior to submission [via Ovid 2020 August to October 27, 2020]. Ten records were found.

Study selection and data extraction

We included all randomized trials comparing TDCS to sham in the setting of surgical training. The outcomes of interest were grouped in 4 domains in order to overcome the heterogeneity between studies' results. These domains were: Domain 1 for speed of skills acquisition, Domain 2 for proficiency, *i.e*. ability to achieve a pre-determined score/level of proficiency, Domain 3 for accuracy and error reduction, and Domain 4 for composite outcomes involving more than one domain. Abstract and full texts review for study selection was performed by two authors independently (AN and EG). Disagreement was reconciled by a third author (FRS). The same two authors extracted the data including study design, method of TDCS, participants' demographics, detailed outcomes reported.

Risk of bias was assessed using the Cochrane revised risk of bias tool for randomized trials (ROB 2) (25) by two authors (AN and FRS).

Results

Results of the systematic search are presented in figure 1. Four randomized controlled trials (RCT) involving 143 participants (61 sham, 82 TDCS) were included. (26–29) These studies compared TDCS to sham and reported outcomes within our 4 pre-defined domains (Table 1). Three additional studies were initially considered and their authors were contacted. These were not available in full text for data extraction (2 were in the process of peer review, the third was not accessible despite contacting the authors) and were not included in analysis.

Study design

The studies' protocols are summarized in table 2, including the different modalities of stimulation. All studies utilized simulation training with three in laparoscopic training (27–29), and one in neurosurgery training. (26) The most recent study by Cox et al (29) had three arms: sham, TDCS over bilateral motor area (BM1), and TDCS over the supplementary motor area (SMA). For the purpose of the data extraction and analysis the latter two groups were combined.

Risk of bias assessment

The results of the ROB-2 are presented in table 3. Three out of the 4 studies recruited solely medical or veterinary students with no clear reasoning apart from an assumption it was the studies authors judgment; the risk of bias in random sequence generation was judged as unclear in these. Moreover, all studies did not have a true control arm with no stimulation as opposed to sham. This might give rise to placebo effect and its associated bias. In addition, 3 out of the 4 studies are published from the same institute by the same first author. (26–28)

Demographics

The mean age of the participants was 24.5±1.5 years, with 58% (n=83) females and 92% (n=131) right hand dominant. One study reported previous surgical experience (Cox et al), video gaming, self-identification as athletes and/or musicians. (Detailed participants baseline characteristics in table 4)

Outcomes

Effects of TDCS on speed of skills acquisition (domain 1)

The most recent randomized trial by Cox et al (29) measured the effect of TDCS versus sham on speed by recording the time needed to complete a peg transfer (PT) laparoscopic task in addition to number of times the task is completed in a given time frame. The findings were of an improvement in speed of completion that did not reach statistical significance. [Pre-test: 135.7s (±31.3), 166.8s (±59.5), 159.2s (±93.0) for sham, BM1, and SMA respectively. Post-test: 59.5s (±18.3), 55.3s (±15.4), 54.5s (±13.1) for sham, BM1, and SMA respectively. p=0.6]

Effects of TDCS on proficiency (domain 2)

Proficiency was reported in two studies (26,27). The first study (26) reported the results of a simulated neurosurgery task involving resecting a brain tumor. It reported an improved percentage of tumor resected with TDCS (p=0.029) compared to sham (p=0.354). The second study (27) evaluated two simulated laparoscopic tasks: PT and pattern cutting (PC). It found that TDCS helped more participants achieve 90% proficiency compared to sham. For PT, it was 35% vs 5% (p=0.039). For PC, 85% vs 58% (p=0.083).

Effects of TDCS on accuracy and error reduction (domain 3)

In their neurosurgery simulation task, Ciechanski et al (26) recorded excessive forces applied on the tumor and healthy brain, considered an error. These were both reduced in participants receiving TDCS (p<0.001 for tumor tissue, p=0.003 for healthy brain tissue). Cox et al (29) described a trend towards a reduction in error in improper PT but no clear difference in pegs transferred outside the field of view.

Effects of TDCS on composite outcomes (domain 4)

All four studies reported composite outcomes evaluating more than one domain. (26–29) Ciechanski et al reported scores for both PT and PC laparoscopic tasks in their 2018 (27) and 2019 (28) studies. These were calculated using previously published scoring systems (30) and accounted for time to completion of task and errors made. PC mean scores had improved in participants receiving TDCS versus sham (208 vs 186, p=0.022) (27) in both studies but not PT. The third study in laparoscopy (29) used another scoring system and established that participant in the BM1 TDCS arm had a less steep learning curve and improved scores compared to sham.

Moreover, Ciechanski et al (26) reported both brain tumor resection effectiveness and efficiency. The former described the ratio of healthy brain tissue resected, an error, to tumor resected. There was no statistically significant difference (t= 0.600; P=0.552). Resection efficiency entailed the ratio of excessive forces on the tumor to tumor resected and described a statistically significant improvement with TDCS (t=2.897; P=0.006).

Retention of skills

Skills decay was only present in peg transfer but not pattern cutting in one laparoscopic study. (27) There was no decay in neurosurgical simulation. (26) The remaining two studies did not report the outcome. (28,29)

TDCS Safety and adverse events

Itching (18-75%) (27,28), tingling (21-64%) (27,28) and burning (11-45%) (27) were the most commonly reported side effects. Three participants had symptoms that precluded completing of the study protocol. (29) no major adverse events were reported in all four studies. (26–29) This mirrors the established safety of TDCS use in trials. (31)

Discussion

This is a systematic review and commentary on the use of TDC to facilitate motor skill acquisition in surgical training. Rigorous search of literature yielded a handful studies discussing the use of this novel technology. (26–29) Attaining new skills within a surgical residency training is usually a product of cumulative exposure to procedures and opportunities to practice under supervision.

Simulation training has expanded the opportunities to practice skills beyond the operating room and gain competence in a safe environment with no fear of morbid complications. (32,33) It is especially crucial now to maximize opportunities to learn with the shift towards controlled duty hours for trainees. (18,20–22) The rational for the use of TDCS is to exploit its modulatory effect on the motor or supplementary motor cortex to facilitate the processing of neuronal activity in sensory motor networks and thus accelerate motor skill learning and fostering skill retention by inducing synaptic plasticity. (1–3) In doing so, the ability to learn or improve upon the skill is achieved in less time. This is extrapolated from existing literature, albeit with mixed results, that suggests that TDCS improves fine motor skills learning, which similarly to surgical skills require coordination and dexterity. (34,35)

The overall results suggested a positive effect of TDCS on both neurosurgical (26) and laparoscopic (27–29) simulation training. Evidently, outcomes were heterogeneous which prevented a robust meta-analysis. We attempted to combine the various outcomes reported into 4 distinct domains that we believe are important when assessing attaining surgical skills. These were learning speed, achieving pre-specified target performance and task accuracy. The fourth domain is any combination of these domains.

Multiple inferences could be made on the effect of TDCS on surgical training. Firstly, speed of laparoscopic task completion measured directly (29) (domain 1) and indirectly as part of composite scores (27,28) (domain 4) saw an increase with TDCS. Anodal TDCS in which the dominant side motor area is stimulated improved speed in unimanual but not bimanual tasks. (27,28) In bilateral TDCS montage where the dominant and non-dominant motor cortices receive anodal and cathodal stimulation respectively, bimanual tasks were studied and there was an improvement.(29)

Bilateral motor cortical stimulation have been shown to improve learning of complex fine motor tasks via inducing cortical excitability. (35,36) Secondly, it appears that TDCS helps participants achieve predetermined levels of proficiency faster (27) as reflected by more participants achieving 80% proficiency in both PC and PT laparoscopic tasks on TDCS versus sham. This is an important consideration in modern competency-based surgical training where achieving pre-determined milestones will influence progress in training and board certification. (37) Thirdly, for a meticulous task such as brain tumor resection, TDCS improved both proficiency and accuracy of task completion.

Highly complex surgeries such as neurosurgical oncology procedures are associated with significant comorbidities, and these have increased after implementation of DHR for trainees in large scale studies. (38,39) Simulation training with TDCS would help trainees be efficient in achieving desired milestones in high stake procedures despite DHR. In addition, this improved skills retention appeared to be maintained up to 6 weeks beyond the training exercise.

There are limitations to note. All but one of the included RCT did not have a control group. The study by Ciechanski et al (26) included a group of residents that served as reference. The addition of real controls would enhance outcome comparison and eliminate placebo effect. In addition, only four studies were identified despite a rigorous search of databases and that was compounded by reported outcome heterogeneity.

Future directions

Modifications in the stimulation protocol to include cerebellar stimulation, a comparison of stimulation during task (online) versus stimulation prior to task (offline) and further utilization in other surgical specialties would enhance our understanding of this adjunct further. This could be the topic of further research.

Conclusion

TDCS seems to be a useful, safe adjunct to surgical simulation training. It is associated with improved skills acquisition in both laparoscopic and neurosurgical training tasks. Further research is needed to evaluate its use in other surgical specialties.

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Figure 1. PRISMA flow diagram showing the search algorithm.

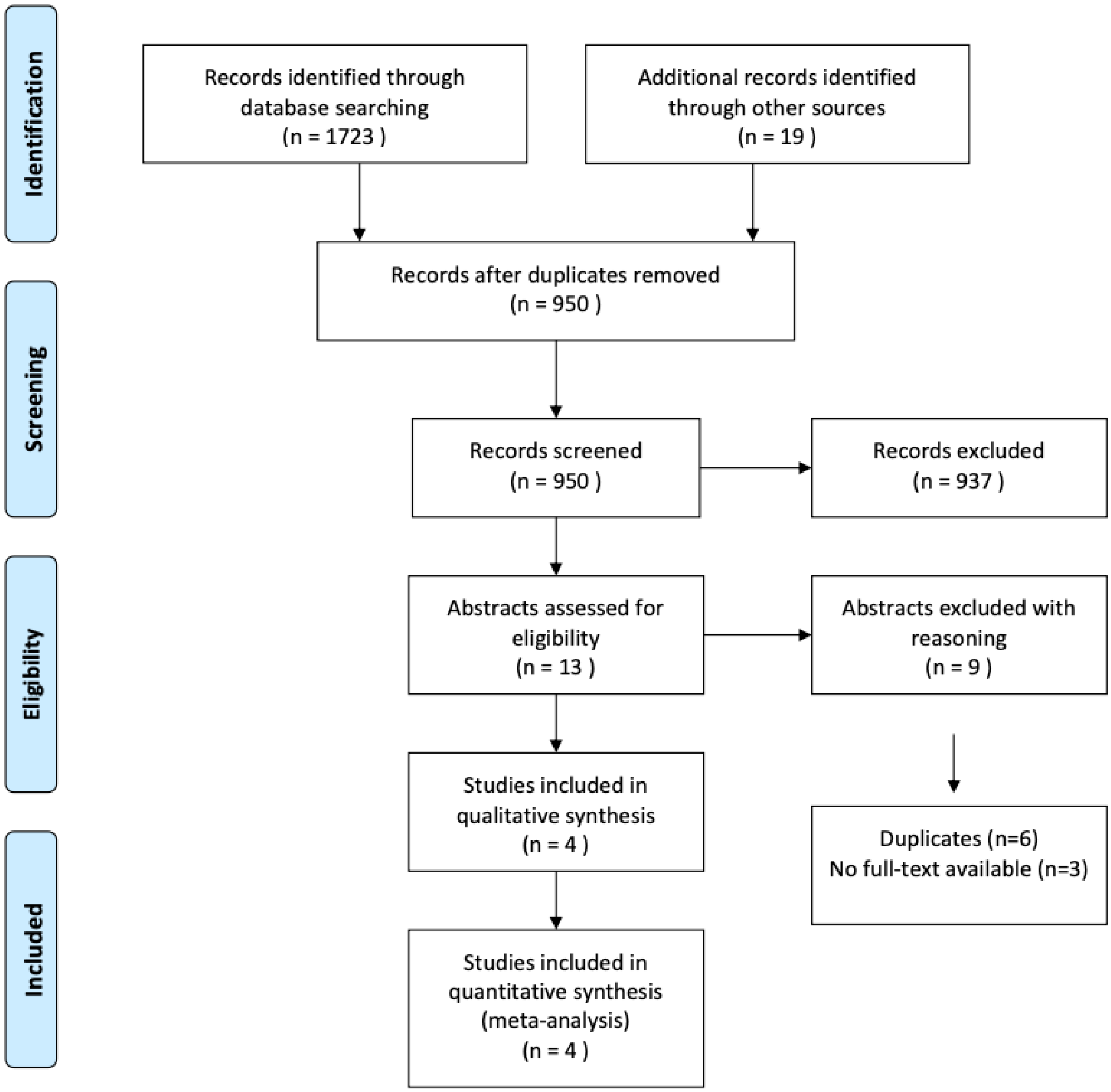

Table 1. Risk of bias assessment (RoB 2) in the included studies.

	Ciechanski et al, 2017	Ciechanski et al 2018	Ciechanski et al 2019	Cox et al 2020
Random sequence generation	**Unclear risk** Comment: Minimization vs clinician judgement	**Unclear risk** Comment: Minimization vs clinician judgement	**Unclear risk** Comment: Minimization vs clinician judgement	**Low risk**
Allocation concealment	**Low risk** Sealed envelope	**Low risk** Sealed envelope	**Low risk** Sealed envelope	**Low risk**
Blinding of participants and personnel	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Blinding of outcome assessment	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Incomplete outcome data	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Selective reporting	**Low risk**	**Low risk**	**Unclear risk** Comment: coherence and event-related potentials outcomes	**Low risk**
Other bias	**'Placebo effect'**	**'Placebo effect'**	**'Placebo effect'**	**'Placebo effect' Attrition bias as 84.5% completed protocol**

Table 2. Baseline characteristics of participants in individual studies

	Ciechanski et al, 2017		Ciechanski et al, 2018		Ciechanski et al, 2019		Cox et al 2020		
	Sham N=11	**TDCS N=11**	**Sham N=19**	**TDCS N=20**	**Sham N=11**	**TDCS N=11**	**Sham n=20**	**TDCS BM1 n=20**	**TDCS SMA n=20**
Age	24.6 (2.1)	25.8 (3.0)	24.7 (3.3)	26.3 (4.1)	25.5 (4.7)	25.9 (3.6)	22.7 (3.7)	21.9 (5.2)	23.5 (5.4)
Gender Female	73%	73%	53%	45%	27%	27%	70%	60%	80%
Ethnicity non hispanic							90%	90%	85%
Handedness right	100%	100%	89%	90%	100%	91%	90%	85%	90%
Prior open surgical							15%	5%	10%
Prior lap. experience							5%	5%	10%
Musician							40%	25%	45%
Gamer							5%	35%	5%
Athlete							55%	55%	60%

Appendix 1: Detailed methodology of the included studies

	Ciechanski et al 2017	Ciechanski et al 2018	Ciechanski et al 2019	Cox et al 2020	
Trial design	Double-blind, randomized, sham-controlled, single-center pilot trial	Double-blind, randomized, sham-controlled, single-centre trial	Parallel-design, randomized, sham-controlled, double-blind, single-center trial	Double-blinded, randomized, and sham-controlled study	
Field	Neurosurgery	FLS	FLS	FLS	
Stimulation Details					
Type	Anodal (1 anode + 1 cathode)	Anodal (1 anode + 1 cathode)	Anodal (1 anode, 4 cathodes)	Anodal (1 anode + 1 cathode)	
Electrode Holder	Head strap	Head strap	Electrode cap	Head strap	
Anode location	Dominant PMC C3 and C4	Dominant PMC C3 and C4	Dominant PMC C3 and C4	**Bilateral PMC:** 20% to the left of vertex over C3	**Supplementary motor area:** 15% anterior to vertex over Cz.
Cathode location	contralateral supraorbital area	contralateral supraorbital area	(4) on the contralateral hemisphere, surrounding F3 or F4.	20% to the right of vertex over C4	10% posterior from the nasion over Fpz
Conductive solution	normal saline	normal saline	high viscosity electrolyte-gel	normal saline	
Duration	20 minutes	20 minutes	20 minutes	20 minutes	
Voltage	1 mA	1 mA	1 mA	2 mA	
Sham Details	1 mA, 45 s ramp-up, hold for 60 s, 45 s ramp-down.	1mA, 45 s ramp-up, hold current for 60 s, 45 s ramp-down.	1mA, 30 s ramp-up, 30 s ramp-down.	30 s ramp-up, 30 s ramp-down.	
Training Details					
TDCS during Training (Online)	Yes	Yes	Yes	Yes	
Account for hand dominance	Yes	Yes	Yes	No	
Retention test	6 weeks after	6 weeks after	6 weeks after	No repetition	
Device used	DC Stimulator (neuroConn; Ilmenau, Germany)	DC Stimulator (neuroConn; Ilmenau, Germany)	Soterix 1x1 tDCS with 4x1 adaptor (Soterix Medical Inc., NY)	Soterix 1 x 1 tDCS (Soterix Medical Inc., NY)	

Table. Methodology of stimulation and training for TDCS studies in surgical education. mA: milliamperes. FLS: Fundamentals of Laparoscopic Surgery. TDCS: transcranial direct current stimulation. PMC: primary motor cortex

10) Bridge between manuscripts

During our previous exposition of the systematic review, we found out that TDCS could be a useful, safe, and promising adjunct to surgical simulation training and that it is associated with improved skills acquisition in both laparoscopic and neurosurgical training tasks. Aforementioned trials have found substantial beneficial effects in surgical performance during surgical training.

This modern initial meta-analysis reinforced the foundation of the application of TDCS in a surgical training program to improve surgical skills as TDCS was not only linked with significant progress in surgical skills but also did not cause serious adverse events when compared with the sham and control.

Based on this information, we developed a protocol to examine these discoveries, incorporating criteria that had not been explored by previous researchers. One notable addition was the inclusion of a control group, which had rarely been included in similar studies. Additionally, our study stood out by comparing this data among three distinct groups, a comparative analysis that had been infrequently conducted. Furthermore, our research distinguished itself by evaluating participants' performance in a bimanual task, which better reflects real-world situations, using a standardized simulation task of intermediate difficulty.

We designed a randomized, sham-controlled trial with a surgical task that was evaluated by comparing the time, accuracy, and total mistakes during a surgical task in participants receiving TDCS, sham-TDCS, and a control group at different time points: baseline (BL), post training (PT) and retention phase (RT).

11) Chapter 2 - Effect of transcranial direct current stimulation on surgical skills acquisition and retention.

b. Manuscript

Effect of transcranial direct current stimulation on surgical skills acquisition and retention

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Abstract

Introduction: Decreased exposure of residents in surgical specialties have potentially impacted surgery training and had unclear effects on the ability to attain milestones and competency. Transcranial direct current stimulation (TDCS) applies a low amplitude electrical current is applied through the scalp to evoke neuronal excitability. TDCS concurrent with motor training, could have marked enhancement of surgical skills acquisition. **Materials and Methods:** A randomized, sham-controlled trial was performed. Surgical skills were evaluated by comparing the time, accuracy, and total mistakes during a surgical task in participants receiving TDCS, sham-TDCS, and a control group at time point baseline (BL), post training (PT) and retention phase (RT). **Results**: 60 participants were recruited, 59 were included. No differences were seen in TDCS vs sham TDCS or TDCS vs Control. Sham-TDCS vs control showed statistical difference ($p=0.024$) in total mistakes. When comparing the effect of the training, changes were seen at time ($p<0.001$), accuracy ($p=0.026$) and total mistakes ($p=0.004$). 4-week retention was statistically maintained in the time evaluation ($p=0.001$). **Conclusion:** No difference in surgical skills acquisition was seen between TDCS vs sham-TDCS or TDCS vs control. Outcome expectations should be considered in TDCS-based studies with a mindset that an intervention may greatly impact outcomes through placebo-like effects. We demonstrated the effectiveness of the exercise and training plan proposed for all groups. Retention wasn't symmetrical between evaluations. Without knowing the underlying mechanisms affecting TDCS, using it as an enhancement tool for surgical skills acquisition will remain challenging. **Keywords:** TDCS, surgical skills, simulation-based training, education.

Introduction

Surgical training involves gaining theoretical knowledge and the necessary skills to perform procedures safely. While operative exposure is vital to skills acquisition, duty hour restrictions potentially reduce exposure affecting their ability to attain milestones and competency (1-5).

In addition, COVID-19 pandemic brought changes to their curricula (6-7). Efforts are required to find safe environments for surgical skills learning. Simulation-based training (SBT) is an applicable, risk-free method particularly helpful for training practical and fine motor skills (8).

Enhancement techniques of motor skills are being used, one of them is transcranial direct current stimulation **(**TDCS) (9). TDCS is a form of non-invasive brain stimulation that applies a low amplitude electrical current is applied through the scalp to evoke neuronal excitability, primarily in the motor cortex (10). This current will alter the neuronal resting membrane potential with either depolarization or hyperpolarization. The surge in excitability of a stimulated region is associated with improved working memory and muscular control (11). These effects could improve brain function and last after the electrical stimulus is terminated (12). TDCS appears to be safe, well tolerated by users, and relatively simple to use (13).

When the motor cortex is stimulated by TDCS concurrent with motor training, there is often a marked enhancement of motor skill acquisition (14). It was recently described that applying TDCS simultaneous to SBT (15) in complex laparoscopic (16) and neurosurgical skill training (17) resulted in an improved skill acquisition. TDCS with its brain-enhancing potential, in adjunct with SBT may help surgical trainees attain skills faster. Our objective is to evaluate the effect of TDCS on motor skills acquisition and retention before and after training of a surgical task when compared to sham-TDCS and control group.

Materials and Methods

This randomized, sham-controlled trial for TDCS, was conducted from April to December 2021 at the Steinberg Centre for Simulation and Interactive Learning of McGill University. The study was approved by the Research Ethics Office (IRB) of the Faculty of Medicine and Health Sciences. McGill University medical students with no proper surgical training were invited to participate voluntarily via the McGill newsletter, social media, and interest groups. Consent for participation was required as per the Declaration of Helsinki. One participant was unable to be present for the planned protocol schedule and was excluded.

Description of the surgical task

The surgical task was a clock-face suturing model (CFM) (18) design stamped on 10 cm wide × 10 cm long × 0.5 mm thick expanded polytetrafluoroethylene (ePTFE) patches (W.L. Gore & Associates, Newark, DE, USA), the CFM consists of two concentric circles with diameters of 40 mm and 60 mm. These circles are crossed by six lines, which are evenly distributed circumferentially, providing 12 branches. For the suturing exercise, the patch is stretched with four clamps at a height of 4 cm (Figure 1).

Participants were asked to perform a continuous suture around the clock, starting at the 6 o'clock position, a 4-0 prolene suture with a needle holder and pick-ups were used. Participants were timed and had a max of 5 minutes to complete the exercise. All participants were introduced to the task and materials by watching the same video tutorial. They were given time to familiarize themselves with the setup (5 min). These sessions were supervised, and video recorded.

TDCS device

We used the Neuroconn DC-Stimulator Plus TDCS device (NeuroCare Group GmbH, München, Germany), which provides bilateral primary motor cortex stimulation. Electrodes were placed on primary motor cortex M1 utilizing a 10-20 electroencephalography electrode system, with two 3 x 5 cm saline-soaked sponges held in place using rubber electrodes and a rubber strap combination. M1 was identified at the middle of the length from nasium to inium. The cathodal electrode was placed 20% to the right of the vertex over C4, while the anode electrode was placed 20% to the left of the vertex over C3. The cathode was placed on the participant's self-reported hand-dominant side.

The stimulation consisted of a fade-in phase with 30 seconds of gradual ramping up of electrical current to a maximum of 2 mA, then a sustained phase of 2 mA for 20 min. For the Sham-TDCS, the fade-in and fade-out phase, was applied. No device was applied to the control group.

Study Design

Participants signed consent and were afterwards randomized into one of three groups using a computer-based software (Winpepi software, Brixton Health) with a balanced allocation of 60 subjects to groups with relative sizes of 1:1:1. The TDCS device encodes active and sham stimulation using a code, so the research team did not know what type of stimulation the participants received. The participants were assessed at three different time points: baseline (BL), post training (PT), and 4 weeks afterwards, retention assessment (RT). Between the BL and PT the training period occurred. It consisted of the repetition of the surgical task for a total of 4 times or 20 minutes (Figure 2).

General and Performance assessment variables

General demographic information, gender and age, and daily dexterity practice were collected. We used the Edinburgh handedness questionnaire (19) to determine their hand dominance. McGill University's and the Steinberg Centre for Simulation and Interactive Learning COVID-19 policies and protection measures were followed.

The evaluation included the total time, accuracy percentage, and total mistakes. Time to task completion was evaluated in seconds, with a maximum of 300 seconds (5 minutes). Accuracy was assessed as a percentage (%) of 'on-point' stitches (over the red dot in figure 1) divided by the total possible points on the exercise (24). The total mistakes score variable was defined as the addition of the total of adjustments with the hand, pickups and total needle drops during the assessments.

Data collection and statistical analysis

Data was collected using Microsoft Excel. The file was stored on the private drive of the Division of Vascular Surgery on McGill University network. We expressed continuous variables as mean and standard deviation (SD). A one-way ANOVA was used for between-group mean differences in the performance variables. Two-way ANOVA investigated the interaction of groups and assessments (BL, PT, RT) on the performance variables. Post-hoc tests were performed with the Bonferroni test. A p value < 0.05 was considered significant at a 95% confidence interval. The statistical analysis was performed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY).

Results

A total of 60 participants were recruited; one participant was excluded due to the inability to complete the study protocol timeline, leaving 59 participants (Figure 3). The TDCS group had 19 participants, 20 in sham TDCS and 20 in control. Total days (d) from BL to RT was 33.3±8.6 d for TDCS, 31.3±7.3 d for sham-TDCS, and 30.3±9.0 d for control.

Demographics and handedness

Regarding demographics (Table 1) in our three groups, the mean age in TDCS was 23.8±3.2, sham-TDCS 24.9±3.4, and control 25.3±4.6. There were 9 (47%) men in TDCS, 13 (65%) in sham TDCS, and 7 (25%) controls. Most were first-year medical students TDCS 11 (58%), sham-TDCS 9 (45%) and control 10 (50%). In respect with handedness, most were right-hand dominant TDCS 17 (89%), sham-TDCS 19 (90%) and control 19 (90%). Their interest in the surgical specialty was 15 (79%) in TDCS, 19 (95%) in sham TDCS, and 17 (85%) controls.

General and Performance Variables (Table 2)

Rate of completion (ROC) for BL for TDCS, Sham-TDCS and control was 8 (42%), 6 (30%) and 4 (20%). ROC for PT for TDCS, Sham-TDCS and control was 19 (100%), 20 (100%) and 17 (85%). ROC for RT for TDCS, Sham-TDCS and control was 17 (90%), 20 (100%) and 19 (95%).

Performance variable means were compared with a one-way ANOVA. Time to completion at BL for TDCS, Sham-TDCS and control was 291.8±17.8, 290±26.5 and 295.6 ±13.8 ($f(2)=0.3$, $p=0.740$). Time to completion at PT for TDCS, Sham-TDCS and control was 201.4±43.6, 203.8±38.4 and 230.8±45.2 ($f(2)=2.9$, $p=0.063$). Time to completion for TDCS, Sham-TDCS and control at RT was 220.5±59.2, 212.7±49.1 and 225.7±41.8 [$f(2)=0.34$, $p=0.715$].

Accuracy at BL for TDCS, Sham-TDCS and control was 53.5±24.2, 50.8±21.1 and 47.3±17.3 [f(2)=0.43, p=0.652]. Accuracy at PT for TDCS, Sham-TDCS and control was 59.2±23.0, 63.5±19.2, 57.5±16.4 [f(2)=0.5, p=0.611]. Accuracy at RT for TDCS, Sham-TDCS and control was 55±20.3, 61.9±17.6, and 60.2±17.3, [f(2)=0.72, p=0.491]

Total mistakes at BL for TDCS, Sham-TDCS and control was 4.1±2.2, 3.7±2.2 and 4.2±1.4 [f(2)=0.4, p=0.670]. Total mistakes at PT for TDCS, Sham-TDCS and control was 2.8±2.2, 1.8±1.2 and 3.3±1.6 [f(2)=3.8, p=0.027]. Total mistakes at RT for TDCS, Sham-TDCS and control was 3.6±2.7, 2.7±1.7 and 4.5±3.5 [f(2)=2, p=0.145]

Post-hoc analysis for total mistakes in PT was performed (Table 3). Difference between TDCS – Sham TDCS had a mean of 1.042 [confidence interval (CI): -0.34, 2.43, p=1.0]. TDCS vs Control had a mean difference of -0.458(CI: -1.81, 0.89, p=0.695). Sham TDCS vs Control had a mean difference of -1.5(CI: -2.83, -0.17, p=0.024).

Effect of training and retention capabilities of participants

Training and retention effect was compared with a two-way ANOVA (Table 4). For time at BL, PT and RT a mean of 292.7±19.7, 212.1±43.5 and 219.6±49.3 [f(2)=74.2, p<0.001] was seen. For accuracy at BL, PT and RT a mean of 50.49±20.62, 60±19.3 and 59.1±18.2 [f(2)=4.26, p=0.015] was seen. For total mistakes at BL, PT and RT a mean of 3.9±1.9, 2.6±1.8 and 3.5±2.7 [f(2)=5.65, p=0.004] was seen.

When comparing BL, PT and RT in respect of our performance variables in the post-hoc analysis (Table 5). A mean difference between PT-BL for time was -80.55 (CI: -63.2,-7.8, p<0.001), for accuracy was 9.6 (CI: 18.1,1.05), p=0.026, and total mistakes of -1.32 (CI: -0.36, -2.28, p=0.004). A mean difference between RT-PT for time was 7.44 (CI: 24.7,-9.8, p=0.931), for accuracy was -0.98

(CI: 7.5,-9.5, p=0.1), total mistakes 0.94 (CI: 1.9, -0.009, p=0.06). A mean difference between RT-BL for time was -73.11 (CI: -55.8,-90.3, p<0.001), for accuracy was 8.6 (CI: 17,0.06, p=0.055), total mistakes 0.37 (CI: 0.58,1.3, p=1).

Discussion

This randomized trial represents the first use of TDCS for acquiring fine motor surgical skills in a study involving a treatment group, sham group, and control group within the context of TDCS and surgical education research. As anticipated, participants with right-handed brain dominance were in the majority and interestingly numerous students engaged in daily dexterity practice.

To strengthen the validity of our study, only a small number of individuals who underwent a surgical clerkship rotation. Additionally, the duration between baseline and retention assessments was carefully controlled to align with the duration of TDCS effects. Previous research has indicated that the effectiveness of TDCS begins to diminish after four weeks (32). Notably, our study did not observe any adverse effects, which aligns with existing literature reporting the absence of serious adverse effects associated with TDCS at 1–2 mA (33).

A systematic review (34) and previous studies suggested a positive effect of TDCS on both neurosurgical (17) and laparoscopic (15,16) simulation training. Our statistical analysis comparing the study groups revealed no significant differences in terms of time and accuracy variables. However, a significant difference was observed in total mistakes during post-training assessment. The post-hoc test indicated a statistical difference between the Sham-TDCS group and the control group, with the control group exhibiting a notably higher rate of total mistakes. These findings indicate the presence of a placebo or sham effect in TDCS-enhanced surgical education. Some researchers propose that this placebo effect stems from outcome expectations bias, emphasizing the need to consider it in TDCS-based experimental studies and clinical trials (25).

The mindset surrounding interventions like TDCS can have a substantial impact on outcomes (26) as anticipation and expectations play a significant role in TDCS adoption and adherence. Factors such as electrode placement (28), current strength (29), and stimulation schedule (30) may contribute as well to the variability in outcomes but do not fully explain it. Additionally, significant inter-individual differences in responsiveness to TDCS have been observed (28).

To optimize TDCS enhanced learning, it is necessary to refine stimulation parameters and target locations. A meta-analysis (20) provides evidence suggesting that individuals who receive TDCS to the motor cortex during motor skill practice demonstrate better performance compared to those who receive sham TDCS. Contrary to our motor cortex stimulation setup, Ashcroft et al. (23) demonstrated improved early-phase surgical skill acquisition by applying prefrontal cortex (PFC) TDCS, leading to reduced physiological parameters such as stress, which has been demonstrated by other researchers as well (24). These findings suggest that surgeons who can sustain PFC activation under stressful conditions are able to maintain their performance.

Our analysis of the surgical skills training exercise revealed significant statistical differences between all testing sessions, indicating notable improvements on time. Post-hoc tests further confirmed significant differences in performance variables from baseline to post-training, demonstrating the effectiveness of our training method. Moreover, the study had a remarkably high completion rate, which enhances its relevance for potential utilization in future TDCS studies.

There were no significant differences observed between the post-training and retention assessments, indicating that the skills acquired during the exercise were retained across all study groups. However, the training effect was statistically significant for the time variable when comparing baseline to retention. In contrast, accuracy and total mistakes did not show significant improvement from baseline to retention. This discrepancy could be attributed to the modulatory effect of TDCS on cognitive and motor skills (31). The time variable appears to be more closely associated with cognitive learning, while motor skills (accuracy and total mistakes) were influenced differently.

Limitations of this study include being a single-center study with a low study population.

Conclusions

No difference in surgical skills acquisition was seen between TDCS vs sham-TDCS or TDCS vs control. We provide a useful and proven training method for future TDCS-related surgical skills studies. Without considering the underlying mechanisms of TDCS, using it as an enhancement tool for surgical skills acquisition will remain challenging.

Tables

Table 1. Demographic Characteristics and Edinburgh Handedness Questionnaire result of included Participants. n (%). SD: Standard Deviation

Characteristic	TDCS (n = 19)	Sham-TDCS (n = 20)	Control (n = 20)
Age, mean (SD), y	23.8 (±3.2)	24.9 (±3.4)	25.3 (±4.6)
Sex			
Men	9 (47)	13 (65)	7 (35)
Woman	10 (53)	7 (35)	13 (65)
McGill University undergraduate medical year			
First	11 (58)	9 (45)	10 (50)
Second	3 (16)	5 (25)	5 (25)
Third	3 (16)	3 (15)	3 (15)
Fourth	2 (11)	3 (15)	2 (10)
Dominant hand			
Left	2 (11)	1 (5)	1 (5)
Right	17 (89)	19 (95)	19 (95)
Daily dexterity practice	13 (68)	16 (80)	15 (75)
Interest in surgical specialty	15 (79)	19 (95)	17 (85)
Plays video games	9 (47)	11 (55)	11 (55)
Plays musical instrument	6 (32)	7 (35)	6 (30)
Prior surgical clerkship rotation	1 (5)	2 (10)	1 (5)

Table 2. Performance variables results in (%) and mean ± standard dev. of rate of completion, time, accuracy, and total errors at the three different evaluation time points BL, PT, and RT.

Variable	**TDCS (n = 19)**	**Sham TDCS (n = 20)**	**Control (n = 20)**	
Rate of completion				
Baseline	8 (42%)	6 (30%)	4 (20%)	
Post training	19 (100%)	20 (100%)	17 (85%)	
Retention	17 (90%)	20 (100%)	19 (95%)	
Days from Baseline to Retention	33.3 (±8.6)	31.3 (±7.3)	30.3 (±9.0)	
Performance Variables				**One-way ANOVA**
Time to completion (seconds)				**(f-value, sig)**
Baseline	291.8 (±17.8)	290.9 (±26.5)	295.6 (±13.8)	f(2)=0.3, p=0.740
Post training	201.4 (±43.6)	203.8 (±38.4)	230.8 (±45.2)	f(2)=2.9, p=0.063
Retention	220.5 (±59.2)	212.7 (±49.1)	225.7 (±41.8)	f(2)=0.34, p=0.715
Accuracy percentage				
Baseline	53.5 (±24.2)	50.8 (±21.1)	47.3 (±17.3)	f(2)=0.43, p=0.652
Post training	59.2 (±23.0)	63.5 (±19.2)	57.5 (±16.4)	f(2)=0.5, p=0.611
Retention	55 (±20.3)	61.9 (±17.6)	60.2 (±17.3)	f(2)=0.72, p=0.491
Total mistakes				
Baseline	4.1 (±2.2)	3.7 (±2.2)	4.2 (±1.4)	f(2)=0.4, p=0.670
Post training	2.8 (±2.2)	1.8 (±1.2)	3.3 (±1.6)	**f(2)=3.8, p=0.027**
Retention	3.6 (±2.7)	2.7 (±1.7)	4.5 (±3.5)	f(2)=2, p=0.145

Statistical analysis to compare means with a one-way ANOVA. Statistical significance was reached when p=<0.05.

Table 3. Difference between statistically significant assessments**.** Statistical analysis to compare means with a one-way ANOVA.

Difference between groups.	**Mean dif, CI, sig.**
Total Errors - Post training	
TDCS - Sham TDCS	1.042 (-0.34, 2.43), p=1.0
TDCS - Control	-0.458 (-1.81, 0.89), p=0.695
Sham TDCS - control	-1.5 (-2.83, -0.17), **p=0.024**

Mean dif, mean difference; CI, Confidence interval; sig, significance. Statistical significance was reached when p=<0.05. Post-hoc tests were performed with Bonferroni correction.

Table 4. Two-way ANOVA between assessments (BL, PT and RT) and performance variables.

Effect of training and retention capabilities of performance variables				
	Baseline	**Post training**	**Retention**	**f-value, p**
Time	292.7±19.7	212.1±43.5	219.6±49.3	f(2)=74.2, **p<0.001**
Accuracy	50.49±20.62	60±19.3	59.1±18.2	f(2)=4.26, **p=0.015**
Total Mistakes	3.9±1.9	2.6±1.8	3.5±2.7	f(2)=5.65, **p=0.004**

Statistical analysis to compare results with a two-way ANOVA. Statistical significance was reached when p=<0.05.

Table 5. Two-way ANOVA post-hoc between assessments (BL, PT and RT) and performance variables.

Difference between:	Time (Mean dif, CI)	sig.	Accuracy (Mean dif, CI)	sig.	Total Mistakes (Mean dif, CI)	sig.
PT - BL	-80.55 (-63.2,-7.8)	**<0.001**	9.6 (18.1,1.05)	**0.026**	-1.32 (-0.36, -2.28)	**0.004**
RT - PT	7.44 (24.7,-9.8)	0.931	-0.98 (7.5,-9.5)	0.1	0.94 (1.9, -0.009)	0.06
RT - BL	-73.11 (-55.8,-90.3)	**<0.001**	8.6 (17,0.06)	0.055	0.37 (0.58,1.3)	1

Mean dif: mean difference, CI: Confidence Interval, BL: Baseline, PT: Post training, RT: Retention, TDCS: Transcranial Direct Current Stimulation. Statistical analysis to compare results with a two-way ANOVA. Post-hoc with Bonferrroni test. Statistical significance was reached when p=<0.05

Figures

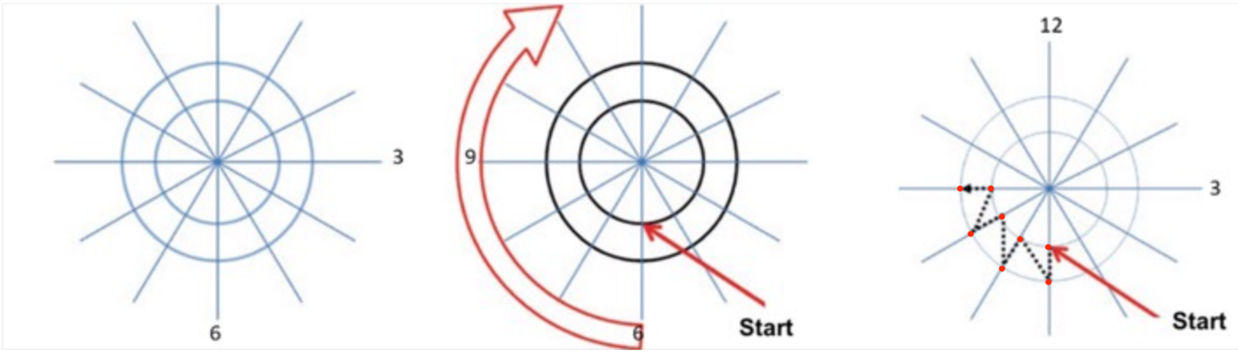

Figure 1. Clock-face model suturing task. A continuous suture starts at 6 o'clock position in a clockwise fashion. Red dots represent the "on point" stitch used during evaluation. From Mitchell E.L., Sheahan M.G., Schwiesow M. (2019) Simulation in Vascular Surgery. In: Stefanidis D., Korndorffer Jr. J., Sweet R. (eds) Comprehensive Healthcare Simulation: Surgery and Surgical Subspecialties. Comprehensive Healthcare Simulation. Springer, Cham.

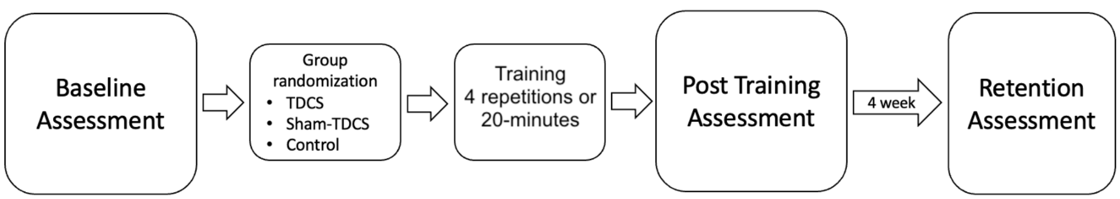

Figure 2. Study Protocol TDCS: Transcranial Direct Current Stimulation.

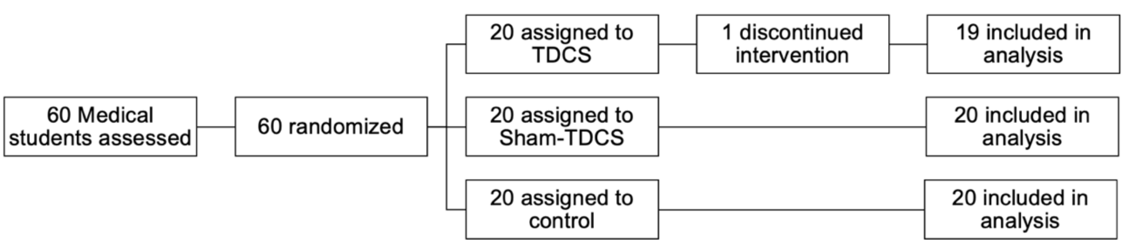

Figure 3. Participant recruitment flowchart.

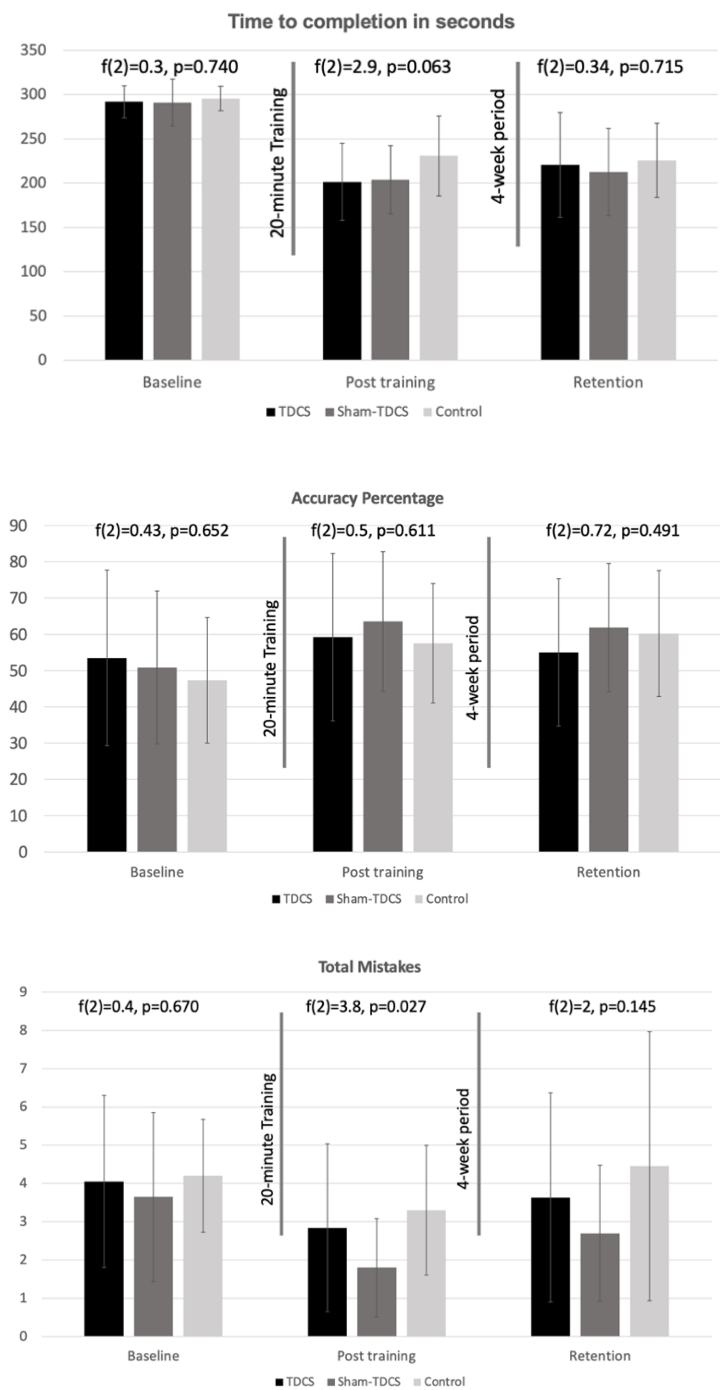

Figure 4. Bar charts with mean and standard deviation for time, accuracy, and total errors variables for TDCS, sham-TDCS and control in the three different evaluations (Baseline, Post Training, and Retention). TDCS: transcranial direct current stimulation.

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12) Comprehensive scholarly discussion of all the findings

During Chapter 1 we concluded that our review reveals hopeful results on the use of TDCS in surgical skills training. The foremost discovery of this chapter was that TDCS was associated with meaningful improvement in surgical skills than the sham control which would propose that the application of TDCS would be related with not only by a placebo effect but also probable favorable result in the surgical skill acquirement. We found some evidence to conduct our Chapter 2 study while analyzing the limitations other studies had.

During Chapter 2 we couldn't find a clear advantage of TDCS. And we found a beneficial effect from sham-TDCS like the TDCS group, which was translated as an expectations of outcomes effect. Participants who were assigned to have TDCS or Sham-TDCS had high expectations of outcomes, they performed the tasks motivated by the possibility of skills enhancement, questioning the efficacy of TDCS[63]. We highlight the need for further investigations of such stimulation methods as well as factors which may influence results.

When we encompass the finding from Chapter 1 and Chapter 2, we observe that although previous authors have published findings in respect of the utility of TDCS in surgical education, there has been some research investigating the use of TDCS as a tool for enhancing surgical education and training. Differences between our study and other authors include parameters of stimulation. TDCS settings can differ extensively, and numerous aspects need to be well-defined. Including electrode dimension and positioning, length of stimulation, number of sessions per day, and rest amid sessions. [64]

To address this, we found one study found that TDCS applied to the PFC during laparoscopic training improved task performance and reduced the time to complete the task[65], TDCS applied to the PMC during VR laparoscopic training improved performance and reduced the number of errors made by surgical residents[66].

Diverse levels of electric current can be applied, thus making miscellaneous physiological and adverse effects. Total applied TDCS is defined by amperes, duration, and montage. However, the amperes that efficiently influences neuronal tissue depends on other inconvenient issues. These include skin and head resistance, resistance of head structures and brain tissue, base cortical excitability varies depending on medication of your study subject[67]. Such discrete influences are a source of inconsistency and, if significant enough, may result in negative findings as shown on Chapter 2.

In respect of protection and latent probability of a positive or negative effect over the undesired cortex, the anode/cathode conductors were substantial to result in a non-focal electric field, which was probable to span to the neighboring cortical or subcortical areas, making the TDCS effect unpredictable. Another problem being that TDCS devices are not identical.

The use of TDCS over the unilateral motor cortex was found to be beneficial in unimanual tasks, although this may not fully reflect the complexity of real-life surgical scenarios. Bilateral TDCS has been shown to improve bimanual coordination in simple motor training.[68] Studies have also demonstrated that TDCS over the bilateral motor cortex can decrease the time required to achieve a satisfactory level of skill, particularly in complex motor training such as surgical skills.

In our study in Chapter 2, we applied TDCS to both motor cortices. We also mentioned that adjustments in the protocol to include different brain areas or different moment (offline vs online) of the stimulation and task performed could be matters for further research.

The positive effect of TDCS on cognitive performance may not be solely explained by the polarity or targeted cortex, and future research should investigate the effectiveness of TDCS on surgical skill acquisition across different targeted cortices. A wide range of surgical tasks and various assessment scales for measuring surgical skills have been reviewed, including pattern-cutting, tumor resection volume, knot tensile strength, and overall performance scores.

Our meta-analysis supports the safety of the use of TDCS in simulation-based training. There were no serious adverse effects in our study. The most regularly reported were mild itching and burning sensation[69]. In our case it became one of the most important factors that were analyzed during Chapter 2.

In respect of our study design, we had another difference with other authors, the most relevant one is that we are the only study that included a control group and sham, most studies don't include the 3 study groups. Exactly how TDCS demonstrates as surgical skills improvements remains a topic of enduring deliberation and it would be better questioned linking TDCS with neuroimaging.

To understand the importance of TDCS, It is expected that it would be best harmonized as a teaching adjunct, on surgical skills courses to those participants who might select to use it. It would important that beginners preserve full independence on using TDCS, at the same time as also being accepted by supervisory organizations. Nevertheless, qualitative records[70] suggests a general acceptance for its use.

It's vital to mention that the use of TDCS in surgical education is still in initial research and is not yet generally used. More research is needed to fully recognize the potential benefits and risks of TDCS for surgical education and training. It's also important to note that TDCS is not a substitute for traditional surgical training like hands-on experience and practice. It is remarkable to believe how a technology such as TDCS could be merged into surgical skills training together with the potential ethical effects of doing this.

13) Conclusion and summary

During Chapter 1 we provided a comprehensive systematic review of TDCS that pointed towards it being a useful, safe adjunct to surgical simulation training. It was previously associated with improved skills acquisition in both laparoscopic and neurosurgical training tasks. We mentioned that further research is needed to evaluate its use in other surgical specialties.

During Chapter 2 we follow-up for the first time with a study in the vascular surgery field with 3 arms, stimulation, sham, and control as no previous study had done. Inversely to some literature we found no difference in surgical skills acquisition was seen between TDCS vs sham-TDCS or TDCS vs control.

We provide a useful and proven training method for future TDCS-related surgical skills studies. Without considering the underlying mechanisms of TDCS, specifically toward the expectations of outcomes effect, using it as an enhancement tool for surgical skills acquisition will remain challenging.

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15) Appendices

Chapter 1 Publication

Surgical Simulation

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REVIEW ARTICLE

Effects of transcranial direct current stimulation on surgical skills acquisition: a systematic review

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Abstract

Background: Surgical training is opportunity based, and multiple factors including exposure time, case volume and simulation training contribute to achieving competencies. We aimed to evaluate the effects of transcranial direct current stimulation (TDCS) as an adjunct to attain surgical skills faster. **Methods:** A registered systematic review (PROSPERO number CRD42020211985) of randomized trials (RCTs) on Biosis, Cochrane Central, EMBASE, MEDLINE, PsycINFO databases was carried out. Studies included compared active TDCS to sham stimulation in a surgical task involving trainees. Outcomes were grouped into four domains to overcome the heterogeneity of study outcomes: speed of skills acquisition; proficiency, i.e. ability to achieve a pre-determined score/level of proficiency; accuracy and error reduction; and composite outcomes involving more than one domain. **Results:** Four RCTs were identified involving 143 participants in total (61 sham, 82 TDCS). All studies utilized simulation training: three in laparoscopic training (peg transfer and pattern cutting), and one in neurosurgery training (tumour resection exercise). The mean age of the participants was 24.5±1.5 years, 58% (n=83) were female and 92% (n=131) were right hand dominant. Use of TDCS was associated with improved speed of skills acquisition, proficiency, accuracy and a less steep learning curve. This performance advantage was sustained for at least 6 weeks. **Conclusions:** TDCS may be a useful, safe adjunct for surgical simulation training. It is associated with improved skills acquisition in both laparoscopic and neurosurgical training tasks. Further research is needed to evaluate its use in other surgical specialties.

Keywords: *transcranial direct current stimulation; surgical education; simulation training; motor skill learning*

Introduction

Mechanism of TDCS

Transcranial direct current stimulation (TDCS) is a form of non-invasive brain stimulation whereby low amplitude electrical current is applied to the scalp through a pair of positively (anode) and negatively charged (cathode) sponge electrodes to modulate neuronal excitability, primarily of the sensorimotor cortex.[1] At a cellular level, TDCS shifts the neuronal resting membrane potential by either depolarization or hyperpolarization.[2,3] This shift facilitates or inhibits the generation of action potentials, thus modulating the excitability of cortical neurons[4] and possibly altering the function of non-neuronal glia cells.[5,6] These modulations, applied to a specific cortical region could improve certain targeted brain functions such as gross and fine motor skills with after effects beyond the stimulation period.[3,7]

Use in the medical field

The use of TDCS has been studied in various fields of medicine. A recent International Federation of Clinical Neurophysiology consensus guideline suggested potential therapeutic use in neuropathic pain modulation, fibromyalgia, depressive disorders and addiction disorders.[8] Its effect has been controversial in post-stroke rehabilitation of patients with motor dysfunction.[8–11] As a result of its effect on primary motor cortex (M1) excitability, TDCS has been evaluated as a method to enhance motor skill learning, fine motor task performance and coordination.[12–14]

Use in surgical education

Surgical residency training is challenging because it involves acquiring both theoretical knowledge and fine motor skills

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