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Feature Article

High-definition trans cranial direct current stimulation and its effects on cognitive function: a systematic review

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High-Definition Transcranial Direct Current Stimulation (HD-tDCS) is focal and improves higher mental functions. Due to the lack of published evidence, we conducted this review on the effect of HD-tDCS on cognitive functions in healthy and diseased individuals. We performed an electronic-data and gray-literature search to obtain the relevant studies for the review. The two distinct literature searches obtained a total of 468 studies. Out of these, a total of 12 studies were conducted on higher mental functions, and of these, two were on disordered consciousness, five were on memory, two were on speech, two were on cognition, and one was on execution. We submitted nine studies with control group to methodological quality assessment using the PEDro Scale. Remaining three studies underwent quality assessment by Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group. We found that anodal HD-tDCS stimulation is significantly effective in treating disordered consciousness and improving memory, speech, cognition, and execution.

Key words: HD-tDCS; cognition; memory; consciousness; speech.

Introduction

Transcranial Direct Current Stimulation (tDCS) is a form of non-invasive brain stimulation. This method of neuromodulation has become very well known in the past two decades. The application of tDCS involves the non-invasive, non-focal stimulation of the brain by using constant direct currents. This causes the depolarization or hyperpolarization of the brain through the application of an anode and a cathode, respectively. (Lefaucheur et al. 2017). In the past decade, many studies applied tDCS to modify the motor, perceptive and cognitive process as well as treated many neurological and psychiatric disorders. (Pisoni et al. 2018). Even though the conventional tDCS effectively ensures brain modulation, the use of large electrodes and the spacing of electrodes over the scalp create unnecessary stimulation of the surrounding and interconnected structures. It is unclear whether the reported effects are due to the stimulation of targeted regions or adjacent or distal structures. Therefore, the effects of tDCS stimulation are diffuse in nature, or non-focal. (Nikolin et al. 2015) Keeping this disadvantage of traditional tDCS in mind, some researchers further refined the conventional tDCS and introduced High-Definition tDCS (HD-tDCS) with 4 X 1 small electrode (Kuo et al. 2013). The HD-tDCS is a more focal application of direct current to a distinct brain region using five one-by-one-centimeter ring electrodes. Out of these five electrodes, the central electrode is active, and the surrounding four electrodes are reference electrodes. The density of the cortical field and focal-region stimulation can be adjusted by altering the diameters of the ring electrodes (Wong et al. 2019). By using HD-tDCS, we can focally either stimulate or inhibit the brain structures using anodes or cathodes (Kuo et al. 2013). When compared to tDCS, HD-tDCS offers better long-lasting treatment effects due to its more precise cortical field and tolerability (Wong et al. 2019).

Cognitive function is an umbrella term that describes the mental procedures engaged in procuring information, manipulating knowledge, and interpreting. Cognition includes many intellectual functions and processes, such as memory, attention, perception, decision-making, learning, intelligence, judgment and evaluation, reasoning and computation, problem solving and language abilities (Zhang 2019). A prominent feature of human cognition is the performance goal-directed behavior while attending to relevant information and, at the same time, suppressing irrelevant information. These adaptive processes are collectively referred to as cognitive control. This control over cognition in the context of competing demands can be explained by the cognitive-conflict theory, which states that the anterior cingulate gyrus detects cognitive conflicts and activates the dorsolateral prefrontal cortex, which, in turn, automatically triggers the control process (Gbadeyan et al. 2016).

Two recent studies showed the fascinating effects of HD-tDCS on cognitive functions. These studies applied dorsolateral prefrontal cortex stimulation using HD-tDCS on 120 healthy adults and 36 older individuals. Both these studies proved the positive effects of HD-tDCS on the improvement of cognitive function in healthy adults and older individuals and opened a gateway to enhance cognitive functions (Gbadeyan et al. 2016; 2019). Furthermore, some researchers studied the effectiveness of HD-tDCS on memory, attention, and executive functions and showed improvements in these cognitive functions (Wagner et al. 2015; Lu et al. 2021; Wang et al. 2019; Liu et al. 2020).

Although there is some evidence that HD-tDCS can be used to change cognitive functions such as attention, memory, and executive functions, conclusive collective evidence is lacking, and individual research conclusions are ambiguous. Due to this limitation, we aimed to thoroughly review the effect of HD-tDCS on cognitive functions among normal and diseased individuals.

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Materials and methods

We registered protocol of this review on the international platform of registered systematic reviews and meta-analysis protocols (INPLASY). The registered protocol number is INPLASY 202120049 10.37766/inplasy2021.2.0049.

Eligibility criteria

Studies with randomized parallel group and cross-over design and pilot trials published from the year 2000 to 2021, studies published in English language, and full-text articles were considered for the review. Studies that focused anodal HD-tDCS and cathodal HD-tDCS as treatment interventions and studies with the primary measurements of interest were consciousness, memory, cognition, speech, and execution, which were considered as inclusion criteria for this review. On the other hand, studies with tDCS as a treatment intervention focused on measurements of aspects other than cognitive function, such as emotions, pain, and sensory-motor performance; these were considered as exclusion criteria for this review.

Search strategy

For the full-text articles, we searched electronic databases such as Campbell Library, Data Base of Promoting Health Effectiveness (DoPHER), EBSCO, PEDRo, Pubmed, PROSPERO, PSycINFO, MEDLINE (Ovid), Science Direct, and SCOPUS. We used HDtDCS, cognition, memory, attention, executive functions, speech, and consciousness as the medical subject heading (MeSH) terms for the search keywords in the above databases to obtain the relevant articles. We also searched additional electronic databases, such as Google Scholar, for full-text articles. Moreover, we collected relevant articles by exploring the gray literature, such as physically checking reference lists from the retrieved full-text articles.

The reviewer team of two researchers, who were blinded to publishers, journals, and authors, made their judgment by assessing the title, year, and abstract of each relevant paper. The abstracts that lacked discrepancies after discussion were finalized and included: two members of the team again reviewed the full-text articles of included abstracts. In addition, the team included studies that focused on HD-tDCS as a treatment intervention and compared HD-tDCS with conventional tDCS or sham HD-tDCS. Studies focused on outcomes such as consciousness, memory, cognition, speech, and execution were included in the study. Studies focused on primary outcomes with secondary outcomes, such as adverse effects, were also included in the review.

Methodological quality assessment

Among the included studies, nine studies underwent an assessment of methodological quality by the two review team members using a Physiotherapy Evidence Database Scale. This scale was developed based on Delphi Consensus Technique. The total scores ranged from 0 to 10. Remaining three studies underwent quality assessment by the Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group. The total scores ranged from 0 to 12. We considered quality rating of the studies if the percentage of score < 50% as poor, 50–75% as fair, and > 75% as good quality. Disagreements between the two reviewers were solved through the opinion of a third reviewer. Remaining three studies underwent quality assessment by the Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group.

Data extraction and management

We developed a valid data-extraction form. The two reviewers extracted the data independently by using this form from the included studies. Finally, the obtained data were synthesized, and their findings are mentioned in the results section.

Results

Search results

Our search discovered a total of 468 studies; consequently, we removed 354 studies, as they were duplicates. Out of the remaining 114 studies, we further excluded 58 studies as they were irrelevant to the review. A total of 56 records were assessed for eligibility. In total, 44 articles were excluded from these 56 as they focused on the following: HD-tDCS intervention in tinnitus (four), psychiatric disorders (nine), epilepsy (two), fibromyalgia and pain (six), optokinetic nystagmus (one), and neurophysiological studies (six); the effect of HD-tDCS on sensorimotor performance (nine) and on emotions (three). In addition, four of the articles were not full text. After rejecting these 44 studies, we finally included 12 full-text articles in this review. We present the details of the included studies in Fig. 1. Out of the twelve studies on higher mental functions, two were on disordered consciousness, five were on memory, two were on speech, two were on cognition, and one was on execution.

Methodological quality assessment of included RCTs

Among the included studies that focused on the effects of HD-tDCS on memory, three were good, (Nikolin et al. 2015; Gözenman and Berryhill 2016; Nikolin et al. 2019) and one was fair (Chua et al. 2017). One study scored fair quality rating on quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group (Hill et al. 2018 as represented in Table 1a). Both studies were in the good range, showing the effect of HD-tDCS on speech; the studies that showed the effect of HD-tDCS on cognition and execution were also in the good range. The PEDro scoring of individual studies on different outcomes is represented in Table 1a. Studies that focused on consciousness one study scored fair range of quality rating, (Guo et al. 2019) another study scored good range (Wang et al. 2020) on quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group that is represented in Table 1b.

Effects of HD-tDCS on consciousness

Study design: two studies researched the effects of HD-tDCS on consciousness; both studies used the design of a pilot trial. However, one study used a within-group repeated-measures design (Wang et al. 2020).

Etiology: both studies included participants with disordered consciousness due to traumatic brain injury and hemorrhage; in one study, the etiology for disordered consciousness also included stroke and cerebral anoxia (Wang et al. 2020).

The number of participants and their characteristics: Both studies included 11 participants, each in a minimally conscious or vegetative state. The duration of the states of disordered consciousness ranged from three to eight months in the study by Guo et al. (2019), but in the study conducted by Wang et al. (2020)), the durations ranged from 40 to 320 days.

Electrode placement: Both studies involved the placement of an anode over the precuneus area and cathodes in the radius of

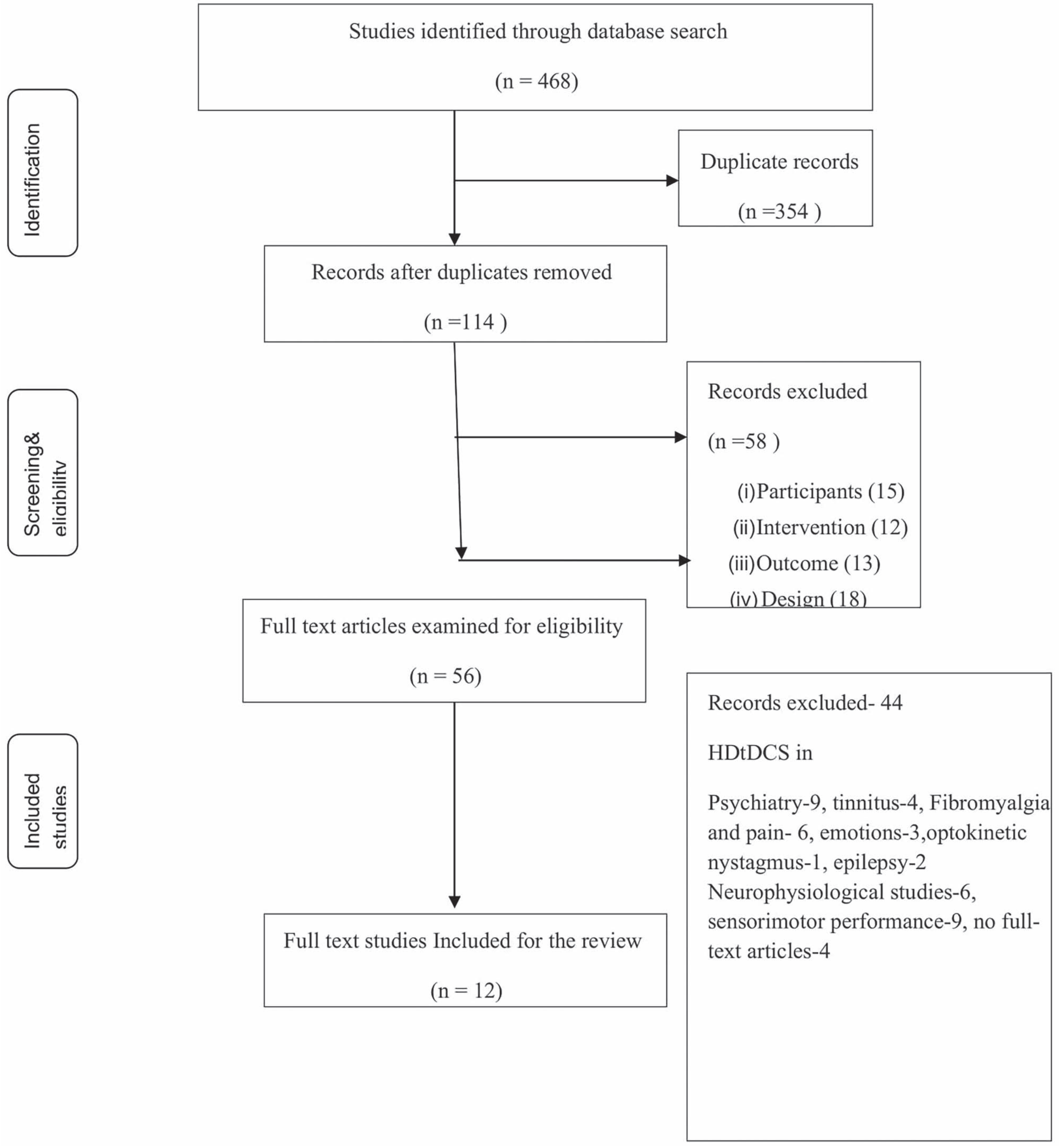

Fig. 1. Flow diagram of search strategy, screening and included studies.

3.5 cm around the anode according to the 10–20 International EEG (Electroencephalograph) system (JN. Acharya et al. 2016).

Stimulation parameters and duration of treatment: both studies applied HD-tDCS stimulation with two mA of current for 20 min, for two sessions per day, on 14 consecutive days. Both studies reported positive results: a statistically significant effect of HD-tDCS on consciousness in terms of behavior measured by the coma-recovery revised scale after 7 and 14 days of treatment. Guo Y et al. reported a statistically significant change in the delta band coherence in the EEG only after 7 and 14 days. However, experiments by Wang et al. (2020) reported a positive effect that was electro-physiologically measured by mismatch negativity after a single session, seven days, and 14 days of treatment in subjects with disordered consciousness.

Summary: the evidence from these two pilot trials suggests the long-lasting effects of HD-tDCS treatment on improvements in consciousness. However, the evidence is very weak, as these trials did not include a control group, used small samples, and lacked randomization and a balance between diagnosis and etiology. Therefore, future studies should feature randomized clinical trials with large sample sizes, and studies should be conducted separately on minimally conscious and vegetative subjects to examine the long-term effects. In addition, studies should investigate the effect of the treatment of and mechanisms behind HD-tDCS

Table 1a. Methodological quality of studies by PEDro scale.

PEDro scoring for studies on memory

Author	Criteria	1	2	3	4	5	6	7	8	9	10	Total	Classification
Nikolin al. 2015	yes	1	0	1	1	0	0	1	1	1	1	7	Good
Gözenman et al. 2016	No	1	0	1	0	0	0	1	1	1	1	6	Good
Chua et al. 2017	Yes	1	0	1	0	0	0	1	1	0	1	5	Fair
Nikolin et al. 2019	Yes	1	0	1	1	0	0	1	1	1	1	7	Good
PEDro scoring for studies on speech													
Richardson et al. 2015	Yes	1	0	1	0	0	0	1	1	1	1	6	Good
Perceval et al. 2017	Yes	0	0	1	1	1	0	1	1	1	1	7	Good
PEDro scoring for studies on cognition													
Gbadeyan et al. 2016	yes	1	0	1	1	1	0	1	0	1	1	7	Good
Maldonado et al. 2019	No	1	0	1	1	0	0	1	0	1	1	6	Good
PEDro scoring for studies on execution													
Lu et al. 2021	Yes	1	0	1	1	0	0	1	0	1	1	6	Good

Table 1b. Methodological quality assessment of studies by quality assessment tool for before-after (pre-post studies with no control group.

Author & year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Quality rating
Quality assessment tool for studies on consciousness													
Guo et al. 2019	Y	Y	Y	Y	N	Y	Y	N	NA	Y	Y	NA	66.66% Fair
Wang et al. 2020	Y	Y	Y	Y	N	Y	Y	Y	NA	Y	Y	NA	75% Good
Quality assessment tool for study on memory													
Hill et al. 2018	Y	Y	Y	Y	N	Y	Y	N	Y	Y	N	NA	66.66% Fair

in disordered consciousness through neuroimaging technology with fMRI.

Effects of HD-tDCS on memory

Study design: of the five studies, four (Nikolin et al. 2015; Gözenman and Berryhill 2016; Chua et al. 2017; Hill et al. 2018) were cross-over trials. One study was based on a randomized parallel-group design (Nikolin et al. 2015). Single blinding was performed in only two of the studies (Nikolin et al. 2015; Nikolin et al. 2019). All five studies included healthy participants from the university, except two studies (Gözenman and Berryhill 2016; Hill et al. 2018) did not mention the details of the recruitment of the participants. Participants dropped out of only one of the studies (Chua et al. 2017).

Sham HD-tDCS was used as a control intervention in all the studies. The montage type used in all the studies was anodal HD-tDCS, in which the anode is an active electrode, and the cathodes are reference electrodes. All the studies used anodal HD-tDCS in different regions, such as the dorsolateral prefrontal cortex, planum temporale, left medial temporal lobe, right and left parietal cortex, intraparietal sulcus, and dorsolateral prefrontal cortex + parietal cortex in different sessions. The intensity of the stimulation current was 2 mA, and it was applied for 20 min in three studies (Nikolin et al. 2015; Chua et al. 2017) (Nikolin et al. 2019); one study (Gözenman and Berryhill 2016) used an intensity of 1.5 mA for 20 min, and another study (Hill et al. 2018) used the current stimulation for 1.5 mA for 15 min. During the active stimulation, in all the studies, the authors ramped up the current for 30 s and ramped it down for the beginning of stimulation 30 s from the end. However, in one study (Hill et al. 2018), the current was ramped down only 10 s from the end of the stimulation.

Effects of HD-tDCS on speech

There were two studies on the effect of HD-tDCS on speech. Among them, one was on healthy participants (Perceval et al. 2017), and one was on stroke subjects (Richardson et al. 2015). One study was a randomized cross-over trial, in which the controlled intervention was conventional sponge-based tDCS (CS-tDCS) (Richardson et al. 2015), and another was a sham-controlled double-blinded between-subject design. The authors used sham HD-tDCS as a controlled intervention (Perceval et al. 2017). The current stimulation delivered in the HD-tDCS was 1 mA in each electrode for 20 min. However, in Perceval et al. (2017), the intensity was ramped up and down for 10 s during active stimulation.

Effects of HD-tDCS on cognition

Two studies focused on finding the effect of HD-tDCS on cognition. Both featured crossed-trail designs. One was single-blind (Maldonado et al. 2019) and the other double-blind (Gbadeyan et al. 2016). Both studies included young, healthy participants. Sham HD-tDCS was used as a controlled intervention in both studies. By contrast, the studies' treatment interventions were different; one study incorporated anodal HD-tDCS (Gbadeyan et al. 2016) in different brain regions such as right and left dorso lateral prefrontal cortex, right and left primary motor cortex represented in Table 2, and the other used cathodal stimulation. The stimulation parameters in one study were 1 mA for 20 min with 10 s of ramp-up and ramp-down (Gbadeyan et al. 2016); in the other study (Maldonado et al. 2019), a total current intensity of 2 mA was used with 30 s of ramp-up before the actual treatment and ramp-down after the treatment.

Effects of HD-tDCS on execution

Only one single-blinded randomized controlled trial has shown the effect of HD-tDCS on execution in healthy undergraduate students. The authors used anodal HD-tDCS as a treatment intervention and sham HD-tDCS as a controlled intervention. The treatment parameters were as follows: current intensity of 1.5 mA

Table 2. Characteristics of the studies included in the review.

Authors & year	Study design	Number of participants and characteristics	HD tDCS electrode placement and location of stimulation	Parameters and duration of treatment	Outcomes	Conclusion
Function-consciousness						
Guo et al. 2019	Pilot study	11 patients with disorder of consciousness due to trauma and hemorrhage (5 vegetative states, 6 minimally conscious states). The duration of the disorder of consciousness ranged from 3–8 months underwent Hd-tDCS stimulation	4×1 Ag/AgCl ring electrodes were placed over the scalp in especially plastic casings embedded in 32 channels EEG recording cap. Anodal electrode over precuneus area and surrounded by 4 cathodal electrodes. Anodal electrode over Pz according to international EEG system, cathodal electrodes 3.5 cm radially from Pz, roughly over Cz, P3, P4, and POz	2 mA direct current for 20 min, 2 sessions/day for 14 consecutive days.	1. Electro enchephalo gram (EEG)-coherence in the delta bands between parietal and central regions calculated 2. Coma Recovery Scale-Revised (CRS-R) taken as baseline, after a single session, after 7 days, and after 14 days of treatment	CRS-R scores increased after 7 and14 days significantly with Hd-tDCS stimulation. EEG changes in the delta band were observed significantly after 7 and 14 days of stimulation in the frontal-central and parietal cortex. This shows the evidence of the HD-tDCS in treating the disorder of consciousness due to the long-lasting effects of HD-tDCS.
Wang et al. 2020	Pilot study (Within-group repeated measures design)	11 patients with disorder of consciousness due to trauma, stroke, and hemorrhage (9 minimally conscious states, 2 vegetative states) The duration of disorder of consciousness ranging from 45 days to320 days months underwent Hd-tDCS stimulation.	4 × 1 Ag/AgCl ring electrodes were placed over the scalp in especially plastic casings embedded in 32 channels EEG recording cap. Anodal electrode over precuneus area and surrounded by 4 cathodal electrodes. Anodal electrode over Pz according to international EEG system, cathodal electrodes 3.5 cm radially from Pz, roughly over Cz, P3, P4, and POz	2 mA direct current for 20 min, 2 sessions/day for 14 consecutive days.	1. Electrophysio-logical assessment with mismatch negativity (MMN). 2. Behavioral with (CRS-R) taken as baseline, after a single session, after 7 days, and after 14 days of treatment.	There was a significant improvement in CRS-R scale after 7 days and after 14 days. MMN amplitudes improved significantly after a single session, after 7 days and 14 days. This shows that long-term HD-tDCS has a statistically significant effect on the recovery of consciousness in patients with minimally conscious state and vegetative state.

(Continued)

Table 2. Continued.

Author year	Study design	Number of participants and characteristics	Groups: Control session	Groups: Experimental session	Stimulation parameters	Outcomes	Conclusion
Function-memory							
Nikolin et al. 2015	Single-blind intraindividual, cross-over, sham-controlled experimental design Latin square experimental design	16 healthy participants from the university (21.8 ± 2.4)	Sham montage: Anode: F4, cathodes: Cp4, Cp6	First session with HD-tDCS montage left dorsolateral prefrontal cortex, (anode F3 according to 10–20 system, cathode AF3, F5, FC, FC3) 2nd session-HD-tDCS montage with planum temporale (PT) (anode Cp5: cathodes: c5, Tp7, Cp3,P5) 3rd session-HD-tDS montage over left medial temporal lobe (anode: P9, cathodes: Fp1, Fp2, Fc4	During active sessions current delivered, 2 mA for the duration of 20 min. The current increased manually ramp-like manner over the course of 30–60 s. During the sham session, the current was delivered to 1 mA, ramped back down, and then switch off.	Verbal learning and memory assessed by modified Rey Auditory verbal learning test. Working memory-3 back task Sustained attention-auditory continuous performance task	There was no significant effect of stimulation on verbal learning and memory, and there was no statistically significant effect on working memory performance, but significantly faster response times for correct response demonstrated for LDLPFC condition, but there was no significant effect of LMTL and PT stimulation on faster response times for correct responses.
			With an interval of one week, each participant completed all four sessions				
Gözenman 2016	Within-subject design	Total 24 healthy participants (not mentioned age, from where)	Sham: current delivered by tDCS or HD-tDCS	The anode was placed on the right(p4) in first experiment and the left (P3) parietal cortex in 2nd experiment while the cathode placed as a reference electrode over the contralateral cheek HD-tDCS: First experiment: four cathodal electrodes Pz, C4, P8, O2placed at equal distances from the anode on P4 Second experiment:four cathodal electrodes Pz, C3, P7, O1 placed at equal distances from the anode on P4	Active stimulation delivered with current of 1.5 m A for 20 min During sham current was given as 20 s ramp up and down at the beginning and end of stimulation	Working memory capacity by retro-cue paradigm test	There was a significant improvement in the retro-cueing paradigm in low working memory capacity
			Experimental sessions conducted 24 h apart				

(Continued)

Table 2. Continued.

Author year	Study design	Number of participants and characteristics	Groups: Control session	Groups: Experimental session	Stimulation parameters	Outcomes	Conclusion
Chua et al. 2017	Cross-over trial	Total 39 healthy college-going, students (21.42 ± 0.32) but from 36 participants data analyzed due to 2 participants could not follow third visit and one withdrawn from the study	Sham HD-tDCS over dorsolateral prefrontal cortex (DLPFC), electrode placement same as anodal HD-tDCS	HD tDCS over dorsolateral prefrontal cortex (DLPFC) Anodal placement over the F3 position, using a 10–20 system. Rest of four cathodal electrodes over the AF3, F1, F5, and FC3. HD-tDCS over the anterior temporal lobe (ATL), anode over the T7, and return four cathodal electrodes placed over the FT7, FT9, C5, and TP7	Anode delivered 2 mA current and return electrode delivered 0.5 ma each for 20 min. Plus 30 s ramp-up time at the start of stimulation and 30 s ramp downtime at the end of stimulation. Sham HD-tDCS-current ramped up to 2 mA and then back down during first 30 s and remained for 0.1 mA for 20 min ramped up to 2 mA and then back down at the end of 30 s of 20 min stimulation.	1. General knowledge recall and recognition test 2. Feeling of Knowing and metamemory task 3. Side effects such as headache, sleepiness, neck pain, scalp pain, concentration, and mood	HD-tDCS on ATL shown better recall for medium difficulty general knowledge questions than the HD-tDCS over DLPFC and sham HD-tDCS. HD-tDCS on DLPFC demonstrated significant results in non-recalled recognized tasks for easy, medium, and difficulty questions. HD-tDCS over DLPFC showed significant results for the feeling of knowing accuracy than ATL and sham HD-tDCS stimulation. There were no significant differences in stimulation conditions and the side effects.
			Participants completed three sessions with an interval of one week				
Hill et al., 2018	With-in subject design	18 healthy participants (Average 32 ± +10)	Sham HD-DCS-montage either DLPFC or DLPFC+PC	One session-HD-tDCS montage over DLPFC, the anode was placed over F3, with cathodes at Fp1, Fz, C3 and F7. Second session-HD-tDCS montage over DLPFC+PC, anode F3 and P3, cathode electrodes at Fp1, Fz, C3, F7, P7 and Pz.	Stimulation was delivered at 1.5 mA for 15 min (30 s ramp-up and 10 s ramp-down period at beginning and end of stimulation sham condition stimulation was held constant for 30 s following the ramp-up period before being ramped down to 0 mA.	Cortical reactivity by TMS-evoked potentials and electroen-cephalography (TMS_EEG) Working Memory-Digit span and Corsi block tapping tasks	Regardless of the montage, cortical reactivity is modulated as shown by the effective P60TMS-evoked potentials and dual site stimulation (DLPFC+PC) demonstrated significant changes. Significant increase in the theta and gamma power were also observed with DLPFC+PC montage Working memory performance did not show any significance regardless of the montage.
			Each participant completed three sessions separated by at least a period of two days				

(Continued)

Table 2. Continued.

Author year	Study design	Number of participants and characteristics	Groups: Control session	Groups: Experimental session	Stimulation parameters	Outcomes	Conclusion
Nikolin et al. 2019	Randomized, single-blind, parallel-group design	78 young healthy subjects from university (22.2 ± 4.0)	Sham HD-tDCS-randomized either DLPFC (or) IPC, and montages were the same as active groups.	One group-HD-tDCS on left dorsolateral prefrontal cortex LDPFC, using 10–20 EEG system, anodal electrode over F3, whereas cathodal electrodes over F5, AF3, F1, FC3 Second group-HD-tDCS on the intraparietal sulcus (IPS), 4X1 electrode configuration, anode over the P3, and cathodes over the P7, Pz, C3, O1.	Current with the intensity of 2 mA and duration of 20mins. In Both DLPFC and IPS groups, the current was ramped up over 30 s and gradually ramped down for 30 s at the cessation of stimulation	Verbal working memory task by following tests. a. Three back task 3 back d-prime 3 back reaction Time (RT) b. Divided attention task 3 dual d-prime updating task by updating RT c. Maintenance Task 2. Side effects-tingling, itching, mild burning	1. There was no significant effect of HD-tDCS stimulation on verbal memory, divided attention, updating, and maintenance task 2. There was no difference in side effect frequency and the groups. But the HDtDCs on LDLPFC reported more pain than the IPS and sham group.
Function-speech							
Richardson et al. 2015	Randomized Cross-over trail	Eight stroke subjects (60.63 ± 8.88)	CS-tDCS(anode placement overP1 to P8, cathode placed on the supraorbital region	HD-tDCS 2 anodes, 2 cathodes and periauricular points electrodes were preloaded in the EEG cap. The location of electrode placement differed in different subjects due to different anatomical lesions.	CS-tDCS:1 mA current was delivered for 20-min per session HD-tDCS: 1 mA per electrode (2 anodes, 2 cathodes) was delivered for 20-min per session Both stimulations were given for five consecutive days for one week during each treatment with rest of one week after each treatment with total period for 5 weeks Both brain stimulation was coupled with computerized anomia treatment	Naming accuracy, response timing of naming	There is an improvement in Naming accuracy and response time in both stimulation conditions. HD-tDCS stimulation improved the change in accuracy of trained items when compared to CS-tDCS which is statistically not significant
			Four patients first phase (CS-tDCS) crossed over to HD-tDCS second phase one week period of rest Four patients received the treatment order in the opposite manner.				
Perceval et al. 2017	Sham-controlled, a double-blind, between-subjects design	50 healthy adults	Sham HD-tDCS: similar to the montage of anodal HD-tDCS.	HD-tDCS: 2 concentric electrodes. One is an anode placed over the CP5 of the 10–20 EEG system i.e. on left tempero parietal cortex and the with one reference electrode.	The current was ramped up immediately prior to the first training block over 10 s to 1 mA during both stimulation conditions. Afterward, it remained constant for 20 min in anodal tDCS or 40 s during sham tDCS before ramping down (over 10 s). Both the stimulations were administered for a single session during training blocks and recognition blocks	Verbal fluency, Boston Naming Test, Stroop test, National adult Reading Test, Mood by Hospital Anxiety and depression scale, adverse effects	There is no significant difference between the stimulation groups for adverse effects. HD-tDCS resulted in faster retrieval of correct word-picture associations during the recognition phases in terms of accuracy and faster responses that were statistically significant.

(Continued)

Table 2. Continued.

Author year	Study design	Number of participants and characteristics	Groups		Stimulation parameters	Outcomes	Conclusion
			Control session	Experimental session			
Function-cognition							
Gbadeyean et al. 2016	Cross-over double-blind design	120 healthy participants	Sham HD-tDCS	First group: anodal HD-tDCS over right DLPFC: electrode placement: active electrode over F4, cathodes were placed around the center electrode. Second group: anodal HD-tDCS over left DLPFC: electrode placement: active electrode over F4, cathodes were placed around the center electrode Third group: left M1 HD-tDCS: electrode placement: active electrode over C3 cathodes were placed around the center electrode Fourth group: right M1 HD-tDCS: electrode placement: active electrode over C4, cathodes were placed around the center electrode	1 mA of current ramped up 10 s before the treatment and applied for 20 min before ramping down. Sham stimulation 1 mA current ramped up for 10 s before the commencement of the experiment and ramped after 10 s.	Conflict adaptation by Visual flanker task Congruent and incongruent trail Adverse effects	Response time of visual flanker test regardless of the trail significantly improved in DLPFC stimulation group than primary motor cortex groups Minor adverse effects only observed, and all the participants tolerated the stimulation well.
			All four groups received sham HD-tDCS after 3 days of actual stimulation				
Maldonado et al. 2019 (20)	Single-blind, cross-over trail	34 undergraduate students, finally only 24 students' data analyzed.	Sham HD-tDCS	Cathodal HD-tDCS Over posterior cerebellum with nine electrodes, whereby three negative electrodes delivered negative current, six electrodes delivered positive current, with one electrode as a reference electrode	During Active stimulation, the negative current is applied −1.48, −0.15 and −0.36, mA, positive current ranged from 0.11, 0.19, 0.22, 0.27, 0.4 and 0.78 mA for 20 min with a total current of 2 mA. During stimulation current gradually ramped up for 30 s and ramped down for 30 s after 20 min stimulation During sha stimulation at the commence of treatment current gradually increased 30 s once currents were reached gradually ramped down for 30 s. Again after 20 min, the session current gradually increased for 30 s and immediately ramped down for 30 s once the current reached. Both the treatment was given in a single session.	Cognitive paradigms By Stroop task, Stenberg task (Reaction time, accuracy, Stroop effect)	There was no significant effect of stimulation on reaction time, accuracy, and the Stroop effect. There was no main effect of stimulation type nor there was an interaction between stimulation type and load in reaction time and accuracy of the Steinberg task.

(Continued)

Table 2. Continued.

Author year	Study design	Number of participants and characteristics	Groups: Control session	Groups: Experimental session	Stimulation parameters	Outcomes	Conclusion
			With one week interval, all participants underwent either active or sham stimulation				
Function-execution							
Lu et al. 2021 (9)	Randomized, single-blinded and sham-controlled	43 health undergraduates (20.91 ± 1.95)	Sham HDtDCS	Anodal HDtDCS Anodal electrode was placed on the scalp location F3, and four cathodal electrodes were placed over AF3, F1, F5, and FC3; at the cortex (left DLPFC)	1.5 mA for 20 min 9 sessions over 3 weeks 1.5 mA just for 1 min, including 30 s at the beginning for ramped up to 1.5 mA, and 30 s at the end for ramped down	Inhibitory control-(color-word Stroop test) Cognitive flexibility by (Shifting attention test) Working memory-two backtest -functional near infra-red spectroscopy (fNIRS) during the tests	Cognitive flexibility is significantly better in anodal HDtDCS than sham group. There was no significant improvement in working memory in the anodal HDtDCs group compared to the sham group Stroop effect-related hemodynamic changes in fNIRS demonstrated low oxygen hemoglobin concentration in anodal HDtDCS group compared to sham group

HD-tDCS: High-Definition transcranial direct current stimulation, Ag/Agcl: silver/silver chloride, ATL: Anterior temporal lobe, CRS-R: Coma recovery scale-revised, CS-tDCS: Conventional sponge based transcranial direct current stimulation, DLPFC: Dorsolateral prefrontal cortex, EEG: Electro encephalography,:fNRI: Functional near infrared spectroscopy, IPS: Intra parietal sulcus, MMN: Mismatch negativity, LMTL: Left medial temporal lobe, PT: Planum temporale, PC: parietal cortex, CZ: central top, P3:left parietal, P4: right parietal, Poz: center parieto-occipital, AF3: left anterior frontal, F5: left frontal, FC: fronto-central, FC3: left frontocentral, Cp5:left parieto-central, C5: left central, Tp7: left temper-parietal, Cp3: left parieto-central, P5: left parietal, P9, left parietal, Fp1: left front-parietal, Fp2: right fronto-parietal, Fc4: right fronto-central, P2: right parietal, C4: right central, P8: right parietal, O2: right occipital for 20 min, with 30 s of ramp-up before and ramp-down after the treatment (Lu et al. 2021).

The details of included studies in terms of their authors, year of the studies, design of the studies, number of participants, characteristics of the participants, electrode placements, location of stimulation, stimulation parameters, outcomes and conclusion of each study represented in Table 2 for disorder of consciousness, memory, speech, cognition, and execution.

Discussion

The literature offers evidence supporting the use of non-invasive brain-stimulation approaches to rehabilitate physical and cognitive impairments caused by neurological disorders. Conventional tDCS is a non-invasive brain stimulation that enhances cognitive function, which is diffuse in nature. Therefore, HD-tDCS stimulation evolved to be focal in nature, involving the application of ring electrodes. We performed this review due to the ambiguity of the evidence on the effect of HD-tDCS in improving cognitive functions.

In this review, among the studies that were focused on the consciousness, there was a significant improvement in the results of the revised coma-recovery scale and the electrophysiological measures assessed by mismatch negativity after 28 sessions of HD-tDCS stimulation over the precuneus area over 14 consecutive days. The findings of this review are inconsistent with the systematic review conducted by Aloi et al. (2021) in which tDCS was used to rehabilitate prolonged disorders of consciousness. The brain regions stimulated with the use of tDCS in different studies were the left dorsolateral prefrontal cortex, cerebellum, right dorsolateral prefrontal cortex, posterior parietal cortex, orbitofrontal cortex, and bilateral frontal–parietal areas. However, the most common is the left dorsolateral prefrontal cortex. By contrast, HD-tDCS stimulates the precuneus area of the brain, which plays an essential function in consciousness. According to the default network connectivity model, the precuneus area is the most active cortical region of the brain during the conscious resting state. HD-tDCS stimulation over the precuneus area altered the metabolism effectively in this region, which led to improvements in consciousness. HD-tDCS stimulation is focal and has higher spatial accuracy, contributing to improvements in consciousness (Aloi et al. 2021).

In our review, five studies focused on the effect of HD-tDCS on improving memory. All five studies used anodal HD-tDCS on different brain regions, such as the left dorsolateral prefrontal cortex, anterior temporal lobe, intraparietal sulcus, and anterior temporal lobe. Four studies (Nikolin et al. 2015; Gözenman and Berryhill 2016; Chua et al. 2017; Hill et al. 2018) demonstrated the significant effect of anodal HD-tDCS on improvements in working memory, cortical reactivity, and response times for correct responses. All these outcomes were improved in the group focused on HD-tDCS stimulation over left dorsolateral prefrontal cortex. The review conducted by Siegert et al. (2021) also demonstrated significant improvements in working memory with tDCS stimulation over the left dorsolateral prefrontal cortex and the slowing of the progress of cognitive deterioration in older people. Since the left dorsolateral prefrontal cortex plays a leading role in cognitive functions such, as working memory, the focalized stimulation of the left dorsolateral prefrontal cortex with HD-tDCS could have upregulated the activity of this region.

Two studies have shown the effect of HD-tDCS on speech function. In (Richardson et al. 2015) this study, Richardson J applied HD-tDCS stimulation as a treatment intervention and conventional tDCS as a controlled intervention on different anatomical lesions. Both treatments were coupled with computerized anomia treatment in eight stroke subjects for five weeks and demonstrated improvements in naming accuracy and response time in both stimulations. In addition, HD-tDCS stimulation improved the change in the accuracy of trained items compared to conventional tDCS, which is statistically non-significant. This could have been due to the heterogeneity of the participants' anatomical lesions and the smaller sample size.

Another study that also focused on speech conducted by Perceval et al. (2017) on 50 healthy adults by applying HD-tDCS stimulation with an active electrode over the left tempero-parietal cortex for a single session and demonstrated statistically significant improvements in the speed and accuracy of the participants' retrieval of the correct word–picture association during the recognition phase. However, due to the presence of a smaller number of studies in this area and two heterogeneity studies, we could not compare it with the review of the effects of tDCS on primary progressive aphasia.

In this review, two studies have shown the effect of HD-tDCS on cognitive performance in healthy participants with a single session. Gbadyean et al. applied anodal HD-tDCS over the four groups' bilateral dorsolateral prefrontal cortices and primary motor cortices. They demonstrated statistically significant improvements in the response times on the visual flanker test, which evaluates the cognitive adaptation in the stimulation with the dorsolateral prefrontal cortex group (Gbadeyan et al. 2016). This could be attributed that primary motor cortex is source for motor commands and DLPFC is involved in cognitive control processing. The above explanation is the reason for significant improvements in the outcomes in the DLPFC stimulation group. Maldonado et al. applied cathodal HD-tDCS over the posterior cerebellum and stated that there was no significant improvement in the reaction time, accuracy, or Stroop effect on cognitive-paradigm tests (Maldonado et al. 2019). This could be due to that bilateral posterior cerebellum involved in cognition processing. The authors applied stimulation over right lateral posterior cerebellum, if they could have applied stimulation over posterior cerebellum bilaterally with cathodal HD-tDCS, there would have been the significant improvement in the outcome of cognitive-paradigm test.

In our review, one study conducted by Lu H et al. applied repeated anodal HD-tDCS over the dorsolateral prefrontal cortex and stated that there was a significant improvement in the cognitive flexibility component. Additionally, the Stroop effect caused hemodynamic changes, according to functional near-infrared spectroscopy. Cognitive flexibility is the core component of executive function, which is enhanced by the altered activation of the dorsolateral prefrontal cortex and the neuroplastic modulations that occur due to repeated HD-tDCS stimulation (Lu et al. 2021).

In the studies of the effects of HD-tDCS on disordered consciousness, only pilot trials were conducted. These trails featured small sample sizes and included participants with mixed types of disordered consciousness. Recommendations for future studies include larger sample sizes, randomized controlled trials, and homogeneity in the distribution of participants with disordered consciousness. All the studies of the effects of HD-tDCS effect on memory recruited healthy participants, and most were cross-over trials. Recommendations for future studies include the use of randomized controlled trials that consider a patient population with dementia to develop effective stimulation protocols and determine the effective method of stimulation of anatomical sites through which to improve memory in this patient population. The studies of the effects of HD-tDCS effect on speech are fewer in number. These studies recruited stroke subjects with smaller sample sizes, with different stimulation sites due to the presence of various lesions. In the future, more studies need to be conducted with larger sample sizes. In addition, there is a lack of studies on the effect of HD-tDCS on cognition and execution in the patient population. Recommendations for future studies include the performance of studies on patients with cognitive impairments to determine effective stimulation protocols. Finally, there is a lack of studies using neurophysiological outcomes such as functional MRI = and PET scans to determine the neural plastic changes in stimulated brain regions.

A limitation of this review is that we combined randomized studies with within-subject designs and between-subject study designs. This review focused on many cognitive functions; it is better to focus on single cognitive function. Furthermore, we combined studies with single sessions of treatment with studies applying multiple sessions of treatment, as well as studies with different treatment parameters.

Conclusion

We conclude that there is moderate level of evidence for improving higher cognitive functions such as consciousness, memory, speech, cognition, and executive functions, can be achieved with anodal HD-tDCS stimulation.

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